Recent Advances in Adult Congenital Heart Disease

Laurianne Le Gloan, MD; Lise-Andrée Mercier, MD; Annie Dore, MD; François Marcotte, MD; Réda Ibrahim, MD; François-Pierre Mongeon, MD; Anita Asgar, MD; Joaquim Miro, MD; Nancy Poirier, MD; Paul Khairy, MD, PhD

As a result of major achievements in pediatric cardiac care, a growing number of patients with congenital heart disease (CHD) are flourishing well into adulthood. This heterogeneous and aging population of patients, many of whom represent the first generation of middle-age survivors, faces unique issues and challenges. As a field, adult CHD has evolved markedly during the past decade on several fronts, including imaging, arrhythmia management, percutaneous interventions, surgical techniques, research, and multidisciplinary care that extends beyond the cardiac realm. This review highlights recent advances across the wide spectrum of key issues encountered by adults with CHD. (Circ J 2011; 75: 2287–2295)

Key Words: Adults; Arrhythmias; Congenital heart disease; Imaging; Surgery

Congenital heart disease (CHD) encompasses a spectrum of cardiac defects, ranging from trivial to incompatible with life, with survival that has markedly improved over the past 2 decades. As a field, adult CHD is inexorably coupled to advances in pediatric cardiac care and arose from its accomplishments. The first medical facility dedicated to the young was established in Paris in 1802. However, pessimism surrounding CHD pervaded until the 20th century, which witnessed extraordinary advances in diagnosis and surgical management. To highlight but a few seminal achievements, Maude Abbott provided an orderly classification of anomalies in an “Atlas of congenital heart disease” in Montreal in 1936, Robert Gross successfully ligated a patent ductus arteriosus in Boston in 1939, and Alfred Blalock and Helen Taussig described systemic-to-pulmonary artery shunting in Baltimore in 1944, rousing new hope for cyanotic babies.

It was not, however, until the mid-1960s, with growing use of cardiopulmonary bypass and supportive perioperative care, that adult CHD became more than an elusive theoretical consideration. In October 1990, and later in 2000, the 22nd and 32nd Bethesda Conferences provided the impetus for a new subspecialty, stating that the expanding population should be dealt with as a special area of interest in a formalized context, rather than the ad hoc approach that prevailed. Training recommendations appeared in 1995 and the first international management guidelines in 1996. Much progress has since been achieved on numerous fronts. The objective of this review is to synthesize recent advances in the multidisciplinary facets of care concerning adults with CHD so as to provide the reader with an up-to-date appreciation of this challenging and evolving field.

Epidemiological Patterns

A review of 62 studies suggested that heart defects concern 75 of 1,000 live births, 25% of which are at least moderate in severity. Less than one-third of infants with congenital defects 50 years ago survived to adulthood. With current care, projected estimates in developed countries indicate that 95% are expected to reach their adult years. As life expectancy improves, the population of adults with CHD continues to expand. Indeed, the number of adults now surpasses children with CHD, with a case mix pattern increasing in severity.

This remarkable achievement is mitigated by the recognition that early surgical interventions were “reparative” and not “curative”. Adult CHD survivors increasingly utilize healthcare resources. Complications may arise from hemodynamic or hypoxic stress, postoperative sequelae, residual defects, and acquired comorbidities, which are increasing in prevalence. As such, healthcare systems have been challenged to meet the demands of a complex and largely underserved population, with a need for dedicated centers and coordinated efforts for transitioning care from pediatric to adult life. It has also been increasingly recognized that true excellence in care cannot be achieved without excellence in research to provide a solid evidence-based foundation to shape the specialty.

Noninvasive Imaging

Echocardiography remains the primary and most commonly used modality for imaging and functional analysis in adults with CHD. Quality and accuracy is well established, and it is widely available, easily accessible, quick, and without contraindication. Three-dimensional echocardiography may help...
visualize precise anatomies such as atrioventricular septal defects, subaortic stenosis, Ebstein’s anomaly, and atrial septal defects before percutaneous closure, and assist in quantifying right ventricular volumes and function. Functional assessment is improved by tissue Doppler and speckle tracking techniques, although normative values for adults with CHD remain to be defined. In tetralogy of Fallot, 2-dimensional longitudinal strain appears to be a sensitive marker for right and left ventricular impairment. Transesophageal echocardiography may help guide percutaneous interventions. Three-dimensional transesophageal echocardiography shows promise in visualizing such defects as mitral valve anomalies.

Well-recognized limitations of echocardiography include operator-dependency and limited acoustic windows, often encountered in patients with multiple surgeries. Magnetic resonance imaging offers a large field of view, high spatial resolution, unlimited choice of imaging planes, and less operator-dependency. It may accurately assess intracardiac structures (Figure 1) and great vessels, and has become the gold standard for quantifying right ventricular volumes and the degree of pulmonary regurgitation in tetralogy of Fallot. Gradient-echo imaging, with steady-state free precession sequences, is useful for dynamic imaging (eg, dynamic vascular anatomy, ventricular volumes), and valvular dysfunction. Phase-contrast velocity mapping enables blood flow quantification (eg, cardiac output, pulmonary-to-systemic flow ratios, gradients). Gadolinium-enhanced angiography helps define vascular anatomy (Figure 2). T1-mapping quantitative techniques help identify myocardial fibrosis, associated with ventricular dysfunction and arrhythmias.

Computed tomography may be used when magnetic resonance imaging is contraindicated (eg, cardiac rhythm devices) or when superior images of metallic prostheses are required. Multidetector imaging allows rapid data acquisition but no functional information. Concerns regarding ionizing radiation persist despite recent dramatic dose reductions.

**Cardiac Catheterization**

Progress in cardiac catheterization for adults with CHD has been swift. From a diagnostic perspective, it may characterize left and right ventricular diastolic function, pressure gradients, pulmonary vascular resistance, shunts, coronary anatomy, and extracardiac vessels, including collaterals. In shunt lesions with echocardiographically-documented pulmonary hypertension, catheterization remains essential in guiding and monitoring response to therapy.

In recent years, advances in percutaneous interventions for adults with CHD have paralleled technological improvements. Indications for percutaneous closure of persistent or residual shunt lesions have expanded with the widening range of device shapes and sizes. Closure of ventricular septal defects (VSD) has emerged as an alternative to surgery, especially in higher-risk patients. For membranous VSDs, asymmetrical devices were engineered to reduce the risk of damaging the aortic valve, but atrioventricular block remains problematic, particularly with self-expanding devices. Patent ductus arteriosus and coronary fistulas are successfully closed with coils, occluders, and low-profile delivery sheaths. Percutaneous pulmonary valves were introduced in 2000. Patients with pre-existing ventriculo-arterial conduits or bioprostheses may benefit from the Melody valve (Medtronic, MN, USA), a bovine internal jugular venous valve sutured inside an expandable stent. Despite encouraging short- and long-term results, stent fracture occurs in up to 20%, but may be reduced by pre-stenting conduits. Recently, an alternative balloon-expanding bovine pulmonary valve was introduced by Edwards (Irvine, CA, USA). First implanted in the aortic position, it has been approved for patients with native aortic stenosis and high surgical risk. Successful implantation has also been reported in patients with bicuspid aortic valves. Patients with native aortic coarctation are increasingly treated with stent grafts to reduce risks of acute rupture and delayed aneurysm.
Advances in Adult CHD

Electrophysiology

Arrhythmias have emerged as a leading complication in adults with CHD. They may accompany the congenital defect (e.g., accessory pathways in Ebstein’s anomaly, atrioventricular block in congenitally corrected transposition of the great arteries) and/or reflect acquired predisposing factors such as volume or pressure overload, hypoxic stress, cardiopulmonary bypass, direct surgical trauma, and fibrosis. The clinical spectrum ranges from the inconsequential to sudden cardiac death (SCD), and encompasses all subtypes of brady- and tachyarrhythmias. Arrhythmias are the leading contributor to morbidity and healthcare resource utilization and the main cause of mortality. In recent years, arrhythmias have been increasingly characterized, risk stratification for SCD has improved, and technological advances have had a major impact on catheter ablation and devices. Although macroreentrant atrial circuits remain the commonest form of atrial tachyarrhythmias, atrial fibrillation is steadily increasing in prevalence with the aging population. Pharmacological therapy, including β-blockers, sotalol, and amiodarone, remains commonly utilized despite the paucity of outcome data. There is much interest, yet few data, regarding newer class III antiarrhythmic agents such as dofetilide and dronedarone.

Pacemaker Therapy

Pacemakers are the mainstay for treating highly prevalent symptomatic bradyarrhythmias. Recent years have witnessed an increased appreciation for the associated challenges, complications, and creative solutions. Recanalization of obstructed baffles to permit transvenous lead implantation using various techniques such as percutaneous angioplasty, radiofrequency perforation, and balloon-expandable stenting, has been described (Figure 4). A high incidence of lead dysfunction formation (Figure 3). Future developments are likely to facilitate access to the left-sided heart and include biodegradable material to minimize complications from metal alloys.

![Figure 2](image-url)  
**Figure 2.** Aortic coarctation shown in a maximal intensity projection of gadolinium-enhanced aortic angiography in a sagittal view. Severe isthmic coarctation can be seen, with major collateral vessels.

![Figure 3](image-url)  
**Figure 3.** Dilation of an aortic coarctation with simultaneous patent ductus arteriosus closure using a covered stent. (A) Lateral view of aortic angiography demonstrating native aortic coarctation. (B) Repeat angiography after implanting a covered stent.
has been characterized, together with the high success and low but non-negligible rate of major complications with laser extraction procedures. The association between intracardiac shunts and systemic thromboemboli has been quantified, raising awareness about potentially beneficial shunt closure prior to transvenous lead implantation.

Risk Stratification for SCD and Implantable Cardioverter-Defibrillators (ICD)

Risk stratification is a complex but highly pressing issue, considering that SCD of presumed arrhythmic etiology is the leading cause of mortality. Although inroads have been made with risk scores derived from observational data, no comprehensive standardized strategy has been prospectively validated. In patients with tetralogy of Fallot, programmed ventricular stimulation appears helpful in further stratifying patients deemed at moderate risk of SCD based on clinical, hemodynamic, and electrocardiographic factors, but is not routinely justified. Novel potential risk factors have emerged, including left ventricular diastolic dysfunction and the extent of myocardial fibrosis by magnetic resonance imaging.

In contrast, efforts at stratifying patients with transposition of the great arteries and Mustard or Senning baffles have been disappointing, with suggestive but inconsistent signals largely limited to systemic ventricular systolic dysfunction, atrial tachyarrhythmias, and lack of β-blocker therapy. Notably, programmed ventricular stimulation appears poorly predictive of clinical events. Risk stratification efforts may be complicated, in part, because supraventricular arrhythmias are a common trigger for fatal ventricular arrhythmias. Although the indications for ICD for secondary prevention are rarely disputed, evolving indications for primary prevention must balance anticipated benefits against high rates of inappropriate shocks and complications. Importantly, it may be hypothesized that a substantial proportion of inappropriate or unnecessary shocks may be prevented by tailored programming.

Catheter Ablation

Catheter ablation is considered the treatment of choice for re-
current or potentially life-threatening supraventricular arrhythmias and a therapy for reducing or preventing appropriate shocks in patients with ICDs. Critical isthmuses implicated in tachyarrhythmia circuits have been better defined. Major advances in 3-dimensional mapping systems, cardiac imaging, and ablation technologies (eg, irrigated and large-tip radiofrequency catheters; cryoablation) now allow most arrhythmias to be safely and effectively targeted (Figure 5). Nevertheless, the onset of new arrhythmias and/or recurrences remain problematic in certain forms of CHD, such as atriopulmonary Fontans.

Resynchronization Therapy
Cardiac resynchronization therapy in adults with CHD is at an early stage of development. Case reports and case series have noted dramatic improvements in some, but clinical experience in others has been disappointing, perhaps in part, because of inappropriate case selection and/or technical issues. Multicenter prospective studies are required.

Surgery
The need to classify and track congenital surgeries led to the creation of multicenter databases in the 1990s by the Society of Thoracic Surgeons and European Association for Cardio-Thoracic Surgery. By 2000, a common nomenclature was adopted and an International Paediatric and Congenital Cardiac Code system was created in 2005. Three risk stratification scores were validated for pediatric congenital heart surgery (ie, RACHS-1, Basic and Comprehensive Aristotle Scores, STS-EACTS Congenital Heart Surgery Mortality Score). Though less adapted to adults, these scores may be improved by integrating age as a risk marker. In most adults with CHD, surgery may be undertaken with acceptable risk. More accurate perioperative imaging, better management of comorbidities, and highly-trained intensive care teams have contributed to improving outcomes.

Surgical indications and techniques continue to evolve in response to lessons learned from prior cohorts. For example, total cavopulmonary connections were developed to improve hemodynamics, reduce thrombosis, and decrease arrhythmias in patients with univentricular hearts. Transatrial transpulmonary approaches to tetralogy of Fallot have largely replaced ventriculotomies, and arterial switches have supplanted intratrial baffles in patients with complete transposition of the great arteries. In patients with Marfan syndrome and aortic root dilation, valve-sparing procedures have become the preferred surgical approach when feasible, with root replacement and reimplantation of coronary arteries.

Pulmonary Valve Replacement in Tetralogy of Fallot
The preferred contemporary surgical approach to tetralogy of Fallot...
Fallot is to accept a non-severe degree of pulmonary stenosis in order to avoid free pulmonary regurgitation. Nevertheless, many adults with tetralogy of Fallot have had transannular pulmonary patches with progressive right ventricular dilatation, such that timing of pulmonary valve replacement is frequently debated.41 Because bioprosthetic valves are used, the potential beneficial effects must be weighed against associated risks, including multiple reinterventions. In general, pulmonary valve replacement is reasonable when severe pulmonary regurgitation is associated with moderate to severe right ventricular dysfunction or enlargement (eg, right ventricular end-diastolic volume >150–160 ml/m²),42,43 moderate to severe tricuspid regurgitation, and/or symptomatic or sustained atrial or ventricular arrhythmias.44 Benefits include a reduction in right ventricular volume, together with a transient decrease in QRS duration.65 However, in patients at risk for ventricular arrhythmias, pulmonary valve replacement alone does not appear to provide sufficient protection against SCD.66,67 It remains uncertain whether directed or empirical concomitant surgical ablation affords sufficient protection.68,69

**Transplantation**

Orthotopic heart transplantation is increasingly indicated in adults with CHD and failing systemic ventricles.71 Currently, adults with CHD account for 3% of heart and nearly 40% of heart–lung transplant recipients.72,73 Cardiac transplantation remains characterized by excess early mortality (≤18%),74 with long-term survival rates comparable to non-congenital patients.75 Numerous prior surgeries, anatomic considerations and intraoperative reconstructions contribute to procedural complexity. Prior sensitization to HLA antibodies is of concern. Accurate pre-listing evaluation of pulmonary vascular resistance is essential but not without difficulty (eg, non-pulsatile pulmonary blood flow in Fontan patients).76 Patients with complex malformations should be referred early for transplant assessment, because the risk is lower in ambulatory patients. Recent advances in pulmonary vasodilators and implantable devices (eg, axial flow blood pumps for failing Fontans)77 may have a major effect on future transplantation indications.

**Pulmonary Arterial Hypertension**

PAH, defined as an elevated mean pulmonary arterial pressure ≥25 mmHg at rest,73 is prevalent in 1.6–12.5 adults per million and 5–10% of adults with CHD.78 An estimated 25–50% of patients with PAH and CHD have Eisenmenger syndrome.79,80 Numerous cardiac defects predispose to PAH, with the size and location of shunts influencing its likelihood and severity. Once present, PAH is associated with high morbidity, mortality, and impaired quality of life.81 However, the prognosis with Eisenmenger syndrome is superior to idiopathic PAH, with survival rates of 80% at 5 years and 40% at 25 years.82 Beyond early shunt repair,83 the only “curative” option is heart–lung transplantation, which carries high morbidity and mortality.

Targeted therapies aimed at addressing pathophysiological mechanisms are spawning new hope.83 Three classes of pulmonary vasodilators have emerged: prostanoids, phosphodiesterase-5 inhibitors, and endothelin receptor antagonists. Though data are limited, prostanoids (epoprostenol, treprostinil, iloprost) are associated with improvements in functional capacity, oxygen saturation, and hemodynamics in CHD.84 Concerns with chronic intravenous delivery include systemic thromboemboli and systemic infections.85 With regards to the phosphodiesterase-5 inhibitors (sildenafil, tadalafil), sildenafil in the context of Eisenmenger syndrome led to a significant reduction in pulmonary artery pressures and pulmonary vascular resistance, and improved functional capacity.86 Tadalafil was also well tolerated and associated with improvements in exercise capacity and quality of life in a 16-week, double-blind, placebo-controlled study that included few congenital patients.87

Among the 2 endothelin receptor antagonists currently available (bosentan, ambrisentan), the most solid supporting data in CHD are with bosentan. The Bosentan Randomised Trial of Endothelin Antagonist Therapy-5 (BREATHE-5) was a 16-week, double-blind, placebo-controlled trial in patients with Eisenmenger syndrome and New York Heart Association (NYHA) functional class III symptoms.88 Bosentan significantly and safely reduced pulmonary vascular resistance and mean pulmonary arterial pressure, and increased the 6-min walk distance. International guidelines now recommend bosentan for patients with Eisenmenger syndrome and NYHA class III symptoms as a class I indication.89 A multicenter, double-blind, placebo-controlled trial (EARLY trial) suggested that bosentan may benefit patients with NYHA class II symptoms.90 Observational studies have reported a survival advantage91 and some data suggest that these therapies may delay the need for heart–lung transplantation. Others have hypothesized that intracardiac shunts considered inoperable because of severe pulmonary vascular disease may become amenable to surgery with pharmacological therapy.92 Targeted therapies are being tested in other conditions, such as failing Fontan circulations.93 Liver aminotransferases should be monitored, as liver toxicity, though rare and typically reversible, can be potentially fatal.94

**Pregnancy**

Major cardiovascular changes occur during pregnancy, including increased blood volume and cardiac output, and decreased systemic and pulmonary vascular resistance.95 Labor and delivery carry acute pressure and volume changes, potentially poorly tolerated by the mother and/or fetus. Pre-pregnancy counseling and risk assessment is, therefore, essential.96 Four factors predictive of maternal primary cardiac events were identified in a prospective study of pregnant women with congenital and acquired forms of heart disease: prior cardiovascular event (heart failure, transient ischemic attack or stroke, arrhythmia); NYHA class III or IV symptoms or cyanosis; left heart obstruction (mitral valve area <2 cm², aortic valve area <1.5 cm², or peak left ventricular outflow tract gradient >30 mmHg); and systemic ventricular ejection fraction <40%.97 With 1 point assigned for each factor, primary cardiac events occurred in 4%, 27%, and 62% of women with 0, 1, and 2 points, respectively.98 Independently validated, this risk score demonstrated a high sensitivity and negative predictive value.99 Decreased subpulmonary ventricular systolic function and/or severe pulmonary regurgitation was later proposed as an additional predictive factor independent of this risk score in a cohort of pregnant women exclusively with CHD.100 Fetal and neonatal complications, including prematurity, small weight for gestational age, and mortality, should likewise be discussed with patients. Predictive factors include NYHA class III or IV symptoms, cyanosis, left heart obstruction, smoking history, and anticoagulation therapy during pregnancy.100 The risk of CHD recurrence may be as high as 2–8%,97 depending on the type of CHD. Fetal echocardiography is recommended between 18 and 22 weeks of gestation. An individualized multidisciplinary approach should be pro-
vided, offering cardiologic, obstetric, and genetic care. Contraceptive options should also be addressed when pregnancy is considered.

Conclusion

This review highlights recent advances in various aspects of care for adults with CHD, including changing epidemiological patterns, noninvasive imaging, cardiac catheterization, electrophysiology, surgery, PAH, and pregnancy. Major developments over the past decade have increased our understanding of repaired cardiovascular anatomy and physiology, deepened our appreciation for potential late complications, and offered the potential to tailor therapy in order to substantially improve quality of life and survival. To better serve the needs of this growing diverse population, the human resource infrastructure should be adapted to meet the demands of adults with CHD through dedicated centers, clinics, research, and training programs.

Disclosure

Funding: Dr. Khairy is supported by a Canada Research Chair in Adult Congenital Heart Disease and Electrophysiology.

References

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