Munetaka Masuda
Koichiro Niwa *Editors*

Adult Congenital Heart Disease

Focusing on Intervention

Springer

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Preface

This book describes the most popular topics concerning adult congenital heart disease (ACHD), especially focusing on indications and re-intervention procedures for some major ACHDs.

Thanks to advances in medical and surgical therapy for congenital heart disease over the last half century, many patients who underwent surgical correction reached adulthood. However, as can be seen from the explosive increase in the number of ACHD patients, it became apparent that postoperative residua and sequelae could result in so-called late complications such as cardiac failure, arrhythmias, thromboembolic events, aortopathy, and so on that need medication, catheter intervention, and/or reoperation in adulthood.

The purpose of this book is to highlight complicated problems in connection with ACHD, including its present status in Japan, as well as methods for its management including medical and surgical treatment to the world. The content primarily focuses on two areas—general information for cardiologists and information on re-intervention for interventionists and cardiac surgeons—setting it apart from the majority of books on congenital heart disease.

This book is an accumulation of leading cardiac surgeons, cardiologists, and anesthesiologist in Japan and includes in-depth information on sequelae following surgical procedures. We believe that this book provides new insights to promote comprehensive understanding of ACHD management for cardiologists, pediatric cardiologists, cardiac surgeon, medical engineers, nurses, and other related people.

We wish to express our great appreciation to the authors of this book for their contribution. We also greatly acknowledge Mrs. Mariko Yamauchi, Department of Surgery, Yokohama City University, and Mrs. Machi Sugimoto and Mr. Kiyohiko Takayama, Springer Japan, for their support of assistance in preparing the book.

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Abstract

Abbott M published *Atlas of Congenital Heart Disease* in 1936, which was based on 1000 pathology specimens personally studied. This is a formal big sized text on anatomy of congenital heart disease (CHD). Forssmann W performed the first cardiac catheterization on a living human being (himself) under the influence of former experiment using a horse by Bernard C (1844). The successful surgery on CHD was witnessed by Gross R in 1938 and independently by Frey in 1939. Lillehei WC in 1954 repaired tetralogy of Fallot at a first time using cross circulation.

Improvements in quality and level of care in CHD have resulted in increased life expectancy of CHD patients to adulthood. However, CHD in adults was not even a theoretical consideration until Perloff JK and Somerville J appeared in the 1960s. Thanks to these giant contributions, CHD is no longer considered simply in terms of age at onset but also in terms of the age range that survival now permits—continuum from fetal life to the neonate, the child, the adolescent, the young adult, and on to advanced age. Surgical treatment in CHD is seldom curative. Postoperative residua, sequelae, and long-term surgical complications vary in severity and require regular medical attention. Unoperated and postoperative patients with moderate to complex lesions require lifelong surveillance. Because of this, a number of specialized centers, consisted of multidisciplinary team, have been evolved in the 1970s–1980s and continue on to lasting in recent two to three decades.

Keywords

Imaging • Intervention • Surgery • Society • Care facility

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1.1 Introduction

Improvements of care in the fields of congenital heart disease (CHD) have resulted in the survival and increased life expectancy of CHD patients to adulthood. Today, 90% of those born with CHD grow up to become adults.

Even though, surgical treatment made survival to adulthood possible for CHD patients, it is seldom curative. In postoperative patients with CHD, even if the procedure is performed at the proper timing and without acute complication, disease-specific and/or operative procedure-specific anatomical and functional abnormalities can happen and progress after surgery. These abnormalities are classified as residua, sequelae, and early/late complication [1] (Table 1.1).

Residua are observed before surgery and continue postoperatively, such as right ventricular outflow tract stenosis (RVOTS) in repaired tetralogy of Fallot (TOF). Sequelae occur after surgery, such as pulmonary regurgitation (PR) in repaired TOF. An example of an acute complication is unexpected nerve palsy secondary to a surgical procedure. In moderate and severe CHD, there are residua and sequelae specific to the type of CHD. With few exceptions, reparative surgery is not curative and requires long-term surveillance. Residua and sequelae may progress in severity with age and induce late complications, such as arrhythmias, heart failure especially right ventricular (RV) failure, thromboembolism, sudden death, and sometimes reoperation; cardiac intervention and catheter ablation could be necessary long after repair. There are many other obstacles that further complicate ACHD (Table 1.2), including pregnancy and delivery, non-cardiac surgery, hepatitis, psychosocial problems such as depression, cognitive abnormalities, health insurance coverage problems, and extra-cardiac complications inherent in the comprehensive care of these patients, making close follow-up and proper management mandatory. The most common cause of death is postoperative arrhythmia [2]. Therefore, unoperated and postoperative patients with moderate to complex lesions require lifelong surveillance. Postoperative residua, sequelae, and long-term surgical complications vary in severity and require regular medical attention by experienced cardiologists (Tables 1.1 and 1.2). Because of this, a number of specialized centers have been established in the last three to four decades in Europe and North America, and then in Asia and South America, to respond to this need. This evolving field of adult congenital heart disease (ACHD) will now include board certified specialists as one of the internal medicine specialists in North America, and, possibly, the trend will spread into other international regions.

Table 1.1 Residua, sequelae, and late complications

1. *Residua*: lesion which existed before surgery and left over after surgery or getting worse with age (i.e., left axis deviation, mitral regurgitation)
2. *Sequelae*: lesion which inevitably happens as a result of surgery (pulmonary regurgitation after tetralogy of Fallot repair, surgical scar)
3. *Complications*: lesions that happen unexpectedly due to surgery (nerve palsy)
4. *Late complications*: lesion, unexpected or expected, non-op or post-op, occurred with age (heart failure, sudden death, arrhythmias, thrombosis, cyanotic organ damage)

Table 1.2 Clinical problems in adults with congenital heart disease

Cardiac-related issues
1. Mortality, morbidity, QOL, occupation
2. Residua, sequelae, complication after initial repair, cardiac surgery, redo surgery
3. Catheter intervention and ablation
4. Arrhythmia, heart failure, sudden cardiac death
5. Pulmonary hypertension
6. Infective endocarditis
7. A multi-system systemic disorders in cyanotic CHD
8. Aortopathy, aortic dilatation, high elasticity of aorta, aortic dissection
9. Acquired cardiovascular disease (obesity, diabetes mellitus, ischemic disorders, etc.)
Non-cardiac issues
1. Reproductive issues, inheritance
2. Non-cardiac surgery
3. Influence of aging and metabolic syndrome, smoking, alcohol drinking habit
4. Exercise, recreational sports
5. Travel by aircraft, driving license
6. Transition issues
7. Psychosocial considerations
8. Social security (health and life insurance, physically handicapped, pension)
9. Liver disease (hepatitis, liver cirrhosis, hepatic cancer)
10. Renal failure

1.2 History of CHD

In the fifteenth century, Leonardo da Vinci recognized a patent foramen ovale, TOF, bicuspid aortic valve, while these anomalies were actually described by Danish anatomist Steno in 1673 [3], but was not diagnosed in vivo until 1888, by the reports of Fallot [4]. After his report, this complex abnormality was called tetralogy of Fallot. In 1879, Roger described the morphology and clinical features of small ventricular septal defect, then this anomaly consequently referred to as Roger's disease [5].

Diagnosis and anatomy of CHD was not recognized even in concept until Abbott appeared in the late nineteenth century. In the 1990s, when she came to the McGill Museum, she found the specimen of Holmes heart at the first time. Also, she wrote on the bicuspid aortic valve as follows: "the presence of a bicuspid aortic valve appears to indicate, at least in a portion of the cases in which it occurs, a tendency for spontaneous rupture." She already knew that bicuspid aortic valve has a tendency to dilate and rapture. Osler advised her to culminate her remarkable anatomical textbook, *Atlas of Congenital Heart Disease* (1936), which was based on 1000 pathology specimens personally studied [6].

The twentieth century witnessed a remarkable development of diagnostic methods and a tremendous success of cardiac surgery. Until the early twentieth century, it was difficult to establish the diagnosis of CHD during a patient's lifetime. As a result, CHD drew mostly the attention of pathologists.

1.3 Diagnosis of CHD

Several imaging modalities are applied for CHD to diagnose when it is suggested by the symptoms and physical examination.

In the past decades, the number of diagnostic catheterization procedures has steadily replaced by interventional procedures, and imaging methods have shifted toward less invasive or noninvasive techniques. Even so, intracardiac pressure and pulmonary vascular resistance can be measured only by catheterization, and even in these days, cardiac catheterization is necessary in some type of CHD such as candidates for Fontan (single ventricular physiology) or pulmonary hypertension (PH). Echocardiography, MRI, and CT imaging have gradually gained a well-established role in the morphological and functional assessment of the heart and great vessels [7].

1.3.1 Cardiac Catheterization

Diagnosis and treatment of CHD has often depended on cardiac catheterization. In 1844, Bernard, born in Rhone, born from the parents of wine merchant, is famous as an author of the textbook, "Introduction a L' etude De la Medicine Experimentale" (1865), catheterized the ventricles of a horse [3]. A few years later, intracardiac pressure was measured by Cheveau and Marey [3]. Forssmann, Berlin, performed the first cardiac catheterization using ureter catheter on a living man—he himself—under the influence of former experiment of Bernard [8] in 1929. Cardiac catheter was soon employed for the tool for the diagnosis of CHD. Then, further major step forward is current use of the catheter for therapeutic interventions.

1.3.2 Echocardiography

Echocardiography started in the 1970s–1980s, initially M-mode then B-mode image (2DE). Then, balloon atrioseptostomy in transposition of the great arteries (d-TGA) was performed in NICU under two-dimensional echocardiographic control [9] without using ionizing radiation.

In 1982, Namekawa performed real-time two-dimensional Doppler echocardiography (so-called color Doppler echo), and then it was widely used for evaluation of acquired heart (especially valvular disease) and CHDs [10, 11].

In the 1990s, 80% of children were referred for surgery on the basis of noninvasive diagnosis. As ACHD are much more difficult to examine by echo than children, however, transesophageal echo (TEE) affords accurate diagnosis of CHD in adults. Three-dimensional reconstruction, intravascular echo, and tissue velocity imaging may yield new insights into the anatomy and function of ACHD.

1.3.3 MRI

MRI, which was widely available in the 1980s, is extremely useful for delineation of the anatomy of the heart and great vessels, as well as for quantifiable assessment

of blood flow characteristics. MRI provides excellent spatial resolution without limitations in the orientation of views. The development of specific techniques (fast gradient echo, velocity mapping, echo planner imaging, myocardial tagging, and spectroscopy) allows us for quantification of physiological and pathological hemodynamic conditions. The late gadolinium enhancement technique provides assessment of the fibrosis and scarring of the myocardium of ventricles. The clinical indications for MRI in ACHD are well established for the evaluation of anatomy and/or function especially in complex CHD. It is considered a gold standard for the anatomical and functional evaluation of the RV [7]. However, MRI cannot directly measure the pressure and resistance of the vessels that is important to assess hemodynamics of Fontan circulation or PH. Also, in patients with arrhythmias such as atrial fibrillation, or with pacemaker, MRI could not apply until recently.

MRI angiography also used for the detection of coronary artery lesions and ventricular performance in patients with Kawasaki disease and coronary artery aneurysm [12].

1.3.4 CT

Several newer CT technologies (e.g., spiral and multislice CT, dual-source CT) are in use as minimally invasive procedure: the high resolution of the image provides excellent spatial separation. A CT angiography is an inevitable examination before operation especially reoperation. Coronary arteries are well visualized especially in patients with Kawasaki disease (KD) with coronary artery aneurysm or stenosis [13]. However, common finding of calcification of the coronary artery aneurysm with stenotic lesion in KD is an obstacle for evaluation. Ionizing radiation of CT was also demerit for use especially in children and young adults with CHD.

Unfortunately, neither MRI nor CT can accurately define intraluminal pressures and pulmonary vascular resistance. Therefore, catheterization is currently the only way to measure systemic or pulmonary pressure and resistance accurately.

1.4 Management of CHD

1.4.1 Catheter Intervention (Table 1.3)

Nowadays, catheter technique is no longer used only for diagnostic purpose, and catheter intervention may replace certain cardiac surgical procedures in CHD. Balloon atrioseptostomy in the critically ill newborns with d-transposition of the great arteries (d-TGA) was reported in 1966 [14]. Balloon percutaneous valvuloplasty of pulmonary valve stenosis was performed in 1982 [15] and that of aortic valve stenosis in 1984 [16].

Balloon angioplasty, possibly combined with stenting, can be used to manage aortic coarctation, even in native aortic coarctation [17]. Especially, in patients with re-coarctation, catheter dilatation with stenting is the procedure of choice recently.

Closing a patent ductus arteriosus performed by Porstmann, Geyersdorf, in 1967 [18] was the first catheter-based closing technique in CHD. After the advance of

Table 1.3 Milestones in the history of catheter intervention for CHD

Procedure	First performed (years)	Reporter
Balloon atrioseptostomy	1966	Rashkind WJ, Miller WW [14]
Balloon valvuloplasty of pulmonary stenosis	1982	Kan JS, White RI, Mitchell SE et al. [15]
Balloon valvuloplasty of aortic stenosis	1984	Lababidi Z, Wu RJ, Walls TJ [16]
Balloon dilatation of coarctation of the aorta	1983	Lock JE, Bass JL, Amplatz K et al. [17]
Transcatheter closure of patent ductus arteriosus	1966	Porstmann W, Wierny L, Warnke H [18]
Transcatheter closure of atrial septal defect	1974	King TD, Mills NL [19]
Transcatheter closure of atrial septal defect	1997	Masura J, Gavora P, Formanek A, Hijaji ZM [20]
Transcatheter closure of ventricular septal defect	1987	Lock JE, Block PC, McKay RG, Baim DS, Keane JE [21]

more sophisticated devices, interventional closure of patent ductus arteriosus (PDA) has been getting broader acceptance. Many ACHD patients are benefitted from the development of interventional closure of atrial septal defect (ASD) or a patent foramen ovale (PFO). Catheter-based closure of ASD was initially reported in 1974 [19], and the method has found a wide acceptance since the 2000s, when Amplatzer septal occluder became available [20]. The transcatheter closure of ventricular septal defect (VSD) is used for muscular defects and then for perimembranous VSD [21]. However, device closure of perimembranous VSD develops complete atrioventricular block that results in pacemaker implantation in some cases.

1.4.2 **Cardiac Surgery** (Table 1.4)

The successful history of PDA ligation dates from 1938 when Gross, Boston Children's Hospital, ligated the PDA of a 7-year-old girl in the hope of preventing subsequent infective endocarditis and reducing volume overload of the heart [22] and was performed independently by Frey, Dusseldorf, in the same year [23].

Crafoord, Stockholm, performed the first surgical repair of coarctation of the aorta (COA) in 1944 [24].

Blalock first created palliative subclavian and pulmonary anastomosis in TOF as suggested by the pediatric cardiologist Taussig, in 1944 [25, 26]. Thomas V, surgical technician and assistant of Blalock, developed this technique using animals with Blalock, before Blalock performed the so-called Blalock-Taussig (BT) shunting [3]. Late after that episode, the Vivien Thomas Young Investigator Award, given by the Council on Cardiovascular Surgery and Anesthesiology, was beginning in 1996.

Table 1.4 Milestones in the history of cardiovascular surgery for CHD

Congenital heart disease	First surgery (year)	Report (surgeon)
Patent ductus arteriosus	1938	Gross R, Boston [22]
		Frey EK, Dusseldorf [23]
Coarctation of the aorta	1944	Crafoord C, Nylin G, Stockholm [24]
Blalock-Taussig shunt	1944	Blalock A, Baltimore [25, 26]
Tetralogy of Fallot	1954	Lillihei WC, Minneapolis [27]
Transposition of the great arteries (atrial switch)	1958	Senning A, Stockholm [28]
Transposition of the great arteries (atrial switch)	1963	Mustard WT, Toronto [29]
Transposition of the great arteries (arterial switch)	1975	Jatene AD, Brazil [30]
Transposition of the great arteries (arterial switch)	1976	Jacoub MH, London [31]
Tricuspid atresia	1968	Fontan F, Bordeaux [32]
Hypoplastic left heart syndrome (HLHS)	1980	Norwood W, Boston [33]
Cavo-pulmonary connection (CPC)	1988	Leval M de, London [34]

Gross in 1952 closed ASD in the open heart using direct suture. Closure of a VSD and correction of TOF in the open heart employing controlled cross-circulation were pioneered by Lillehei in 1954 [27]. Techniques of managing d-TGA by redirecting venous return at atrial level were proposed by Senning from Stockholm [28] and by Mustard from Toronto [29]. Anatomical correction of TGA (arterial switch) was devised by Jatene in Sao Paulo in 1975 [30].

In 1968, the concept of total right heart bypass becomes reality, when Fontan performed his first atriopulmonary connection in order to place the pulmonary and systemic circulation in a patient with tricuspid atresia (TA). Since the initial report published in 1971 by Fontan and Baudet [32], the original technique of Fontan has undergone several modifications. Total cavo-pulmonary connection (TCPC) was introduced in 1988 by M de Leval. Fontan operation has been extensively applied for palliation of wide variety of complex cyanotic CHD with one available ventricle [34].

An aortic atresia is complicated by severe hypoplasia of the ascending aorta and left ventricle, and it is a universally fatal lesion in early infancy without palliative surgery. Norwood, Boston, reported a new palliative procedure for hypoplastic left heart syndrome that results in early survival of two infants with aortic atresia in 1981 [33]. On the basis of experience with a third patient, an operation for future physiologic correction is proposed.

These historical surgical events heralded one of the most successful rehabilitation programs that medicine has witnessed. Formidable technical resources permit remarkably accurate anatomic and physiologic cardiac diagnoses and astonishing feats of reparative surgery [35].

Survival patterns have dramatically improved, and thus CHD is no longer considered simply in terms of age at onset but also in terms of the age range that survival now permits—continuum from fetal life to the child, the adult, and on to advanced age [36, 37].

1.5 Natural History

The term natural history is not a proper term. The natural history of any disease is a definition of what happens to people with the disease who do not receive any treatment for it. Natural history is therefore not synonymous with unoperated or without catheter intervention. Nonsurgical therapeutic interventions hardly are considered natural [3]. Unoperated adults enjoy the benefits of advances in medical treatment. Proper care of patients after operation requires knowledge of the postoperative CHD, the type and effects of surgical or catheter intervention, and postoperative residua, sequelae, and late complications. Accordingly, a wide range of residua and sequelae remain and require prolonged, if not indefinite, medical attention.

Eisenmenger V in Vienna reported a patient with large VSD, and cyanosis at the age of 32 years old died of intrapulmonary hemorrhage in 1897 [38]. Later in 1958, Paul Wood in the UK introduced the term Eisenmenger syndrome [39], which is a CHD with irreversible pulmonary vascular obstructive disease, contraindication of surgical repair. Eisenmenger syndrome reveals multi-organ disorders, and the incidence of sudden death is very high. So this syndrome is following natural history and has a poor prognosis. However, prevention of late complications and recently developed pulmonary vasodilation therapy makes them surviving longer than before. In recent trend of early operation of CHD in childhood, the number of Eisenmenger syndrome is decreasing, but there are still many patients with this syndrome are surviving in adult.

1.6 Incidence of CHD

Worldwide prevalence of CHD has been a topic of interest [37, 40, 41], but certain qualifications and definitions are necessary to interrupt epidemiologic information.

CHD is generally taken to connote the presence at birth of a structural abnormality of the heart, great arteries, or great veins that is actually or potentially functional significance [40, 41]. Included in this definition, however, congenital complete heart block is not a gross structural abnormality, and small VSD that closes spontaneously within 6 months of life is not functionally significant. An isolated PDA in an infant with a gestational age younger than 38 weeks, without heart failure, and with ductal closure by several weeks should be excluded from CHD [40].

Incidence of CHD varies significantly if sibling or patient is affected. Moderate malformations occur in approximately 3 per 1000 live births and complex malformation in approximately 2.5–3% per 1000 live births with significant lesion-specific

variation [42]. Collective incidence is estimated at 0.6% of live births [36], excluding the BAV, which occurs in approximately 2.0% of live births [37, 43, 44].

1.7 Increasing Number of Adults with Congenital Heart Disease

Data from the large referral centers in Europe and North America revealed that a number of ACHD patients continue to increase due to the success of medical and surgical care of pediatric [37, 45]. As a consequence, the proportion of ACHD patients outnumbers children with CHD in many countries of the Western world. In the Asia-Pacific region, however, available data are limited to only a few countries, and the proportion of adults with CHD varies from country to country: from 75% in Singapore, 51% in Japan, 32% in Thailand, and 22–26% in Korea to 20% in Taiwan [46, 47]. In Japan, there are currently a larger number of adults with CHD than children with CHD, and nearly 9500 operations are performed annually in this patient population [48].

Approximately 90% of infants born with CHD can be expected to reach adulthood [46, 49]. The number of patients is increasing at a rate about 5% per year, with an ACHD population in Japan approaching 0.5 million. There are about 10,000 new cases per year in Japan and about 1.5 million new cases worldwide [47].

Long-term care necessarily concerned with unoperated patients who reach adulthood but is increasingly concerned with the growing number of patients who reach adulthood because of operation or catheter intervention and who need for continuous medical surveillance [50, 51].

1.8 History of Societies and Great Contributors in the Field of ACHD

CHD in adults has emerged as a major area of cardiovascular medicine—a recognized subspecialty [51]. Board certificated specialists in ACHD have emerged in the USA in 2015.

The importance of ACHD worldwide is reflected in the International Society for ACHD (ISACHD), and it spreads out to other regions, European Society of Cardiology (ESC), Grown-Up Congenital Heart (GUCH) Society, Asia-Pacific Society for ACHD (APSACHD), and Japanese Society for ACHD (JSACHD). ACHD was formally recognized as a new cardiovascular specialty in 1990 at the 22nd Bethesda Conference, Congenital Heart Disease after Childhood: An Expanding Patient Population [52]. The 22nd Bethesda Conference [53] entitled "Care of the Adults with Congenital Heart Disease," following the first two Bethesda Conferences, has been devoted to the same topic. Webb GD from the Toronto General Hospital was invited to participate in the 32nd Bethesda Conference, at which ISACCD had its inception that focused on patient care, training, education, research, and collaboration among international countries [51–57].

In Europe, ESC GUCH group has been working. The European meeting in ACHD organized by ESC aims to provide an independent educational forum for healthcare professionals across Europe. This annual meeting was first held in London and has since been located in several major cities in Europe, including Paris, Amsterdam, and Germany. The meeting is aimed at cardiologists and allied medical professionals with an interest in ACHD as well as specialists in the field.

On the other hand, in Asian countries, Japanese Gathering for ACHD was established in 1999, and Korean GUCH Society was established in 2002. The JSACHD was formally established in 2010 [57]. APSACHD was organized in 2008 at Jeju Island in Korea, and nearly 16 countries joined; official meeting has been held every 2 years at the same time of Asia-Pacific Pediatric Cardiac Society (APPCS) meeting, that is, Korea, Japan, Taiwan, and India [47, 58].

1.9 Caring Systems in ACHD: Treatment Facilities and Human Resources

Because of the complexities inherent in the comprehensive care of ACHD patients, specialized tertiary care facilities emerged in the late 1970s in North America and Europe [59, 60]. The comprehensive care by multidisciplinary teams, including adult and pediatric cardiologists, cardiac surgeons, specialized nurses, and other cardiac and non-cardiac consultants, has made the care of ACHD patients with moderate to severe CHD. Centers have emerged within teaching hospitals having pre-existing pediatric cardiology unit with capabilities in multi-imaging modalities and surgical treatment to care for ACHD. Availability of other cardiovascular specialists (vascular medicine, electrophysiology, and imaging), obstetrician-gynecologists, psychiatrists, infectious disease specialists, hematologists, nephrologists, rheumatologists, clinical geneticists, pulmonologists, and specialized nurses is also important to address other issues associated with CHD. However, there appears to be a significant shortfall in tertiary care provision for ACHD, which will require further planning and resource allocation [61].

Regarding cardiac providers for ACHD, proper transition from pediatric cardiologists and cardiovascular surgeons to ACHD specialists and/or cardiologists that are well trained in the field of ACHD is necessary [62]. In Europe and North America, medical and surgical management has been developed from middle of the twentieth century, and the importance of ACHD has been recognized earlier than other international region. Other than some areas in North America and Europe, this system has not been sufficiently developed. In many parts of the world, such as Asia-Pacific area, pediatric cardiologists are still principal caregivers for ACHD [47].

In 1978, Perloff JK established Ahmanson/UCLA Adult Congenital Heart Disease Center, care center for ACHD. Also in the UK, Somerville J established Grown-Up Congenital Heart Disease (GUCH) Center in Royal Brompton Hospital in 1975. She

was originally working as a cardiovascular surgeon, changed her mind to move to cardiology, and established ACHD unit independent from pediatric cardiology.

Following these two centers, special institutions for caring ACHD have been established during the 1980–1990s in North America, Europe, and followed by Asian countries. These centers evolved and organized by the physicians who were trained mainly in these two centers.

1.10 History of Textbook on CHD and ACHD (Table 1.5)

There are several textbooks on CHD (sometimes only mentioned only several CHDs) from year 1749. Abbott collected a lot of specimens of various CHD and published the *Atlas* in 1936. But there may be a limited clinical interest, because many of them cannot be compatible with life, and there was nothing to relieve symptoms (Table 1.5). Regarding ACHD, Roberts, then followed by Perloff, published the textbook on that subject. Then, several other textbooks have been published from the USA, Europe, and Japan.

Table 1.5 Historical textbook on CHD and ACHD

Author(s)	Title	Published year
1. Congenital heart disease		
Jean-Baptiste de Senac	*Disease of the Heart*	1749
Thomas B Peacock	*On Malformations of the Human Heart*	1858
Emmet Holt	*The Diseases of Infancy and Childhood*	1897
William Osler	*The Principles and Practice of Medicine*	1892
Maude Abbott	*Atlas of Congenital Cardiac Disease*	1936
Helen Taussig	*Congenital Malformations of the Heart*	1947
James W Brown	*Congenital Heart Disease*	1939
Paul Wood	*Diseases of the Heart and Circulation*	1950
Joseph K Perloff	*Clinical Recognition of Congenital Heart Disease*	1972
2. Adult congenital heart disease		
William C. Roberts	*Adult Congenital Heart Disease*	1987
Joseph K Perloff et al.	*Congenital Heart Disease in Adults*	1991
Gary D Webb	*Adult Congenital Heart Disease* (CD-ROM)	1998
Michael A Gatzoulis et al.	*Diagnosis and Management of Adult Congenital Heart Disease*	2003
Koichiro Niwa et al.	*Adult Congenital Heart Disease*	2005
Jana Popelova et al.	*Congenital Heart Disease in Adults*	2008
Carole A Warnes	*Adult Congenital Heart Disease* (*American Heart Association Clinical Series*)	2009

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Facilities for Patient Care

2

Ryota Ochiai and Atsushi Yao

Abstract

The central role in a care delivery system for adult congenital heart disease (ACHD) should be performed by specialized ACHD centers. They should be well-staffed and equipped high volume centers, both for outpatient and inpatient care. The population that each specialized ACHD center should cover is assumed to be from 2 to 10 million. They will also provide education and training for the ACHD specialist and promote research and innovation. Methods for linking the roles of specialized ACHD centers and related facilities differ depending on the regional medical care system and medical resources, and appropriate methods should be found to suit each region. It is essential to clarify the preferences of the patients themselves in terms of treatment systems, giving due consideration to geographical access to medical institutions; it is also important for medical personnel to support such actions, with the expectation of political action by patient associations. Patients with ACHD may be examined in parallel by both distant specialized ACHD centers and a local nonspecialized facility, which complicates the monitoring of patient behavior. Therefore, it is essential to build a comprehensive database that incorporates specialized ACHD centers and nonspecialized facilities, as well as pediatric medical institutions such as children's hospitals, to ascertain the behavior adopted by patients with ACHD, the medical services these patients are using, and the outcomes achieved by each facility. Even if appropriate medical facilities are established, they are meaningless unless the

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facilities are utilized by patients. Therefore, transition programs must be further developed in the future. At the same time as transition programs are developed for individuals and groups, research is needed to evaluate the effectiveness of these programs.

Keywords
Adult congenital heart disease • Specialized adult congenital heart disease center • Care delivery system • Transition of care

2.1 The Need for Specialized Adult Congenital Heart Disease Centers

The central role in a care delivery system for adult congenital heart disease (ACHD) should be performed by specialized ACHD centers. These are large, multidisciplinary centers of excellence that are able to meet all potential needs of ACHD patients over the course of their lives, with strong affiliations and referral pathways to related facilities. They will also provide education and training for the ACHD specialist and promote research and innovation. A need for these centers has been proposed in the United States, Canada, Europe, and Asia. Although the number varies across guidelines and previous studies, the population that each specialized ACHD center should cover is assumed to be from 2 to 10 million [1–4]. A Canadian study showed that a significant increase in referrals to specialized ACHD centers followed the introduction of the guidelines, and referral to a specialized ACHD care was independently associated with significant mortality reduction [5].

2.2 Criteria for Specialized ACHD Centers

Specialized ACHD centers should be well-staffed and equipped high volume centers, both for outpatient and inpatient care. Moons et al. [6] listed the following three criteria as the minimal requirement for specialized ACHD centers: (1) They must offer pediatric cardiology or congenital cardiac surgery, (2) must have on staff at least one cardiologist dedicated to ACHD, and (3) must have more than 200 ACHD patients under regular follow-up care. They also showed the criteria in Table 2.1 as an optimal care structure. The European Society of Cardiology (ESC) proposed more detailed and rigorous definitions (Table 2.2) in their position paper published in 2014 [7].

Previous research has reported that of the above conditions, there is a low fill rate for items relating to number of surgeries [6, 8, 9]. Successful outcomes of surgery are associated with the number of surgeries, particularly for those with high risk [10]. Furthermore, there are also reports that in-hospital death rates in adult patients with congenital heart disease are reduced when these surgeries are performed by surgeons who are specialists in congenital heart disease, compared to when these

Table 2.1 Cited/amended from optimal care structure for specialized ACHD centers [7]

1. Specialized ACHD centers must employ at least one, and preferably two, cardiologist(s) specifically trained and educated in the care of adults with CHD
2. Specialized ACHD centers should provide care in connection with pediatric cardiology and/or congenital cardiac surgery
3. Specialized ACHD centers must treat a sufficient number of patients and perform a sufficient number of procedures to be effective and to develop and maintain high levels of performance
4. Specialized ACHD centers must conduct a minimum of 50 ACHD operations per year
5. A fully equipped electrophysiology laboratory staffed by properly trained electrophysiologists with experience in detecting arrhythmias inherent to CHD and with experience in pacemaker technology, ablation technology, and defibrillator implantation must be available
6. Specialized ACHD centers must employ at least one nurse specialist trained and educated in the care of ACHD patients

Table 2.2 Cited/amended from requirement for specialized ACHD centers [8]

Staff requirements	
Adult/pediatric cardiologist with ACHD certification	At least 2
ACHD imaging specialist (echo, CMR, CT)	At least 2
Congenital invasive cardiologist	At least 2
CHD surgeon	At least 2
Anesthesiologist with CHD experience and expertise	At least 2
Invasive electrophysiologist with ACHD experience	At least 1
Psychologist	At least 1
Social worker	At least 1
Cardiovascular pathologist	At least 1
Equipment requirements	
ECG	
Holter monitoring	
Stress ECG	
Ambulatory blood pressure monitoring	
Event recorder	
Cardiopulmonary exercise testing	
Echocardiography (including transesophageal echo, 3D echo)	
CMR imaging	
Cardiac computed tomography	
Catheterization laboratory	
Electrophysiology laboratory	
Pacemaker/ICD implantation	
Pacemaker/ICD aftercare equipment	
Cardiac surgery operating room	

surgeries are performed by surgeons who are specialists in adult acquired heart disease [11]. Thus, it is vital for specialized ACHD centers to employ surgeons with a wealth of experience and who are specialists in congenital heart disease.

2.3 Patients Who Should Be Followed Up at Specialized ACHD Centers

According to the 2003 ESC guidelines, patients should be assigned a name for their diagnosis and classified into three groups (simple, moderate, severe), with appropriate care levels advocated for each group: (a) patients who require care exclusively in specialized ACHD centers, (b) patients in whom shared care can be established with appropriate general adult cardiac services, and (c) patients who can be managed in nonspecialized facilities (with access to specialized care if required) [3]. However, in the new 2010 version, classifications based on diagnosis were abandoned, and the guidelines emphasized that all patients should be examined once at a specialized ACHD center, where they would undergo initial evaluation and receive recommendations for long-term care [12]. To ensure that all patients are examined at specialized ACHD centers, it is important that both the patient and their attending physician (this could be a pediatric cardiologist, cardiovascular surgeon, general pediatrician, etc.) understand the importance of being examined at a specialized ACHD center and to ascertain where they are located. Therefore, it is essential that academic bodies and other such parties in each country acknowledge specialized ACHD centers and publish a list of these centers. Patient education is also vital, given that there are those who do not adequately understand the necessity of undergoing examinations starting in childhood onward and are subsequently lost to follow-up.

2.4 The Role of Specialized ACHD Centers in Training and Research

Specialized ACHD centers not only provide treatment but also function as an education hub. In 2012, the American Board of Internal Medicine classified ACHD as a subspecialty for basic internal medicine specialists, and the board created a formal training program [13]. The conditions for becoming a specialist include 24 months of ACHD fellowship training. It is essential that specialized ACHD centers, which treat many of the patients, also fulfill the role of a training program provider.

Specialized centers with many patients have a role in promoting research related to the treatment of ACHD. A number of guidelines have been published to date, but much of the research contained in those guidelines lacks evidence. Causes include the wide range of diseases associated with ACHD and the small number of patients in each facility. It is important that specialized ACHD centers with many patients not only promote research in their own center, but these centers should also take a leadership role in promoting research in this field, through multicenter joint research projects that include other specialized centers.

2.5 Strategies for the Development of Specialized ACHD Centers

The necessity and role of specialized centers have been mentioned in many guidelines, but at present, the number of specialized centers is less than ideal [6, 8]. The number of specialized centers is inadequate because the number of patients followed up in each center is small; moreover, there is a lack of human and financial resources invested in ACHD. These factors are interrelated; if there are insufficient numbers of patients, it is not possible to adequately invest in medical resources, and if there is inadequate investment in medical resources, then it is impossible to treat many patients. We would like to introduce Japan's example as a strategy to break out of this vicious cycle. Historically in Japan, patients with congenital heart disease were continued to be followed up by pediatricians even after they reached adulthood, and there were only a few cardiologists who were interested in treating ACHD. However, with establishment of the Japanese Society for Adult Congenital Heart Disease, the number of cardiologists interested in ACHD has slowly increased. Subsequently, cardiologists established the Japanese Network for Cardiovascular Department for ACHD, a cardiovascular medicine organization, and specialized ACHD outpatient centers were established by cardiologists throughout Japan; thus, multidisciplinary specialized ACHD centers were established in various regions around Japan [14]. This is a case in which development of human resources preceded demand.

Actions taken by patient groups are also important. Increasing the number of patients in specific centers in principle reduces the number of patients at other centers, which forces some patients to transfer between hospitals or to attend multiple medical institutions. It is essential to clarify the preferences of the patients themselves in terms of treatment systems, giving due consideration to geographical access to medical institutions; it is also important for medical personnel to support such actions, with the expectation of political action by patient associations.

2.6 Role Division Between Specialized ACHD Centers and Related Facilities

It is essential that all patients with ACHD be examined once at a specialized ACHD center; however, depending on the patient's circumstances, and access to transportation to the center, subsequent routine follow-up consultations may be conducted in related nonspecialized facilities. Depending on the country and the region, there are doctors who specialize in ACHD within related nonspecialized facilities, and there may be centers with more than 200 ACHD patients receiving regular follow-up care. However, specialized ACHD centers must be facilities that are able to consistently handle all the potential needs of ACHD patients over their lifetime, and if a center is not equipped to handle inpatient medical care functions, then that center is a nonspecialized facility. The important point is the development of a referral relationship to ensure that when patients who are receiving follow-up in nonspecialized

facilities require inpatient care for surgical treatment or prenatal and postnatal care, etc., it should be possible to smoothly transfer them to specialized ACHD centers.

The importance of the referral relationship is the same in emergency medical care. If a patient presents with arrhythmia, it may be more beneficial for the patient to be seen first at a local nonspecialized facility rather than traveling to a distant specialized ACHD center. Thus, it is important to establish a system whereby the patient can be transported to a specialized ACHD center from a nonspecialized facility if needed.

In this way, patients with ACHD may be examined in parallel by multiple medical institutions, which complicate the monitoring of patient behavior. Therefore, it is essential to build a comprehensive database that incorporates specialized ACHD centers and nonspecialized facilities, as well as pediatric medical institutions such as children's hospitals, to ascertain the behavior adopted by patients with ACHD, the medical services these patients are using, and the outcomes achieved by each facility. Construction of a database is crucial for promoting research with a high level of evidence in the field of ACHD.

2.7 Transfer and Transitional Care

One of the special features in the care delivery system for ACHD patients is the transition of care. "Transition" is defined as the process of moving from a pediatric medical system to an adult system, where "transfer" refers to the actual point in time at which responsibility for patient care is "handed off" to the adult provider. For the implementation of successful transfer, a well-planned transition is necessary. Transition should aim at more than just successful transfer. The American Academy of Pediatrics states, "The goal of transition in health care for young adults with special health care needs is to maximize lifelong functioning and potential through the provision of high-quality, developmentally appropriate health care services that continue uninterrupted as the individual moves from adolescence to adulthood" [15]. Table 2.3 shows critical requirements for transitional care.

Even if an adequate number of specialized ACHD centers are provisionally established, if the patients do not receive appropriate medical care, then the system is meaningless. In Canada, 15 specialized ACHD centers were established by the 1990s, but reports indicate that only 47% of patients were receiving appropriate medical care in those centers [16]. Furthermore, successful transfer was shown to be significantly related to documented recommendations and patient beliefs that ACHD care should be provided at a specialized ACHD center. Comorbid conditions, refraining from substance use, using dental antibiotic prophylaxis, and attending cardiac appointments without parents or siblings were also shown to be correlated with successful transfer. Based on these results, it is essential not only to explain the necessity of care in specialized ACHD centers to support appropriate patient transfer and prevent patients being lost to follow-up but to provide support for personal care in daily life.

Table 2.3 Cited/amended from "Critical first steps to ensuring successful transitioning to adult-oriented health care [14]"

1. Ensure that all young people with special health-care needs have an identified health-care professional who attends to the unique challenges of transition and assumes responsibility for current health care, care coordination, and future health-care planning
2. Identify the core knowledge and skills required to provide developmentally appropriate health-care transition services to young people with special health-care needs and make them part of training and certification requirements for primary care residents and physicians in practice
3. Prepare and maintain an up-to-date medical summary that is portable and accessible
4. Create a written health-care transition plan by age 14 together with the young person and family
5. Apply the same guidelines for primary and preventive care for all adolescents and young adults, including those with special health-care needs, recognizing that young people with special health-care needs may require more resources and services than other young people to optimize their health
6. Ensure affordable, continuous health insurance coverage for all young people with special health-care needs throughout adolescence and adulthood

2.8 The Timing of Transitional Care

The central role in transitional care should be performed by pediatric health-care providers. The recent ACC/AHA Guidelines on the Management of Adults with Congenital Heart Disease recommended that the transition process start at 12 years of age to prepare the patient for transfer to adult care [17]. The American Heart Association emphasizes that the timing of transition should be guided by emotional maturity and developmental level of the patients [18]. As there is virtually no evidence specifying the age at which progression to transitional care is beneficial, the age for starting transitional care differs depending on the existing literature and guidelines. However, it is essential that pediatric health-care providers proceed with planned transition prior to transfer.

People engaged in medical care for adults are required to provide transitional care. Patients are prone to being lost to follow-up outside of transfer periods, particularly when they change residences because they start university, start working, get married, or for other such reasons. During periods when the patient's living situation is stable, such as while they are students or when they come home during long holiday breaks, they are able to receive medical care at the institution where they were seen during their childhood, but once the patient enters the workforce or gets married, returning to the original medical institution becomes more difficult. Medical personnel engaged in care of these patients during adulthood must reiterate the necessity of ongoing care to the patient and the patient's guardian, if necessary, and must refer these patients to appropriate medical institutions. Furthermore, there may also be patients in their 30s, 40s, or older who were told that the surgery they underwent as children was a "curative operation," so they may not be aware of the

necessity of ongoing medical care. These types of patients cannot be seen in pediatric departments due to their age, and must first be seen at a clinical department that treats adults, starting with the department of cardiology. There are also female patients who visit the hospital after a long period without follow-up because they have become pregnant. It is essential to educate these types of patients, and the education should be primarily conducted by the medical personnel who are engaged in the care of such patients during adulthood.

2.9 Transitional Care Program

Transitional care is normally conducted during outpatient and inpatient treatments. Inpatient treatment is a stressful event for the patient, but it is also an opportunity to seriously confront the disease, and sometimes this can be an opportunity to make significant headway in the patient's understanding. There are virtually no intervention studies using transitional care programs, but it is said that intervention using binders and pamphlets called "health passports" is effective [18]. "Health passports" contain information including the patient's emergency contact details, the medication they are taking, imaging of their heart, the treatment and tests they have received to date, and whether the patient has any allergies. Thus, the "health passport" can be used to enable a shared understanding of the disease with other people and can also deepen the patient's own understanding of the disease [19].

Transitional care may come in a variety of forms, in addition to the aforementioned individualized care; this care can also provide patient classrooms for numerous patients and offer peer counseling between patients, etc. Problems relating to transfer such as deciding which medical institution will take over patient care are strongly dependent upon the individual and are influenced by many factors including the patient's medical condition, place of residence, etc. However, group education can be effective for issues and concerns that are common to many people, such as work, pregnancy, and childbirth. In these instances, if these sessions are held at a specialized ACHD center where there are many patients, it may be possible to separate the patients into a number of groups based on the severity of their condition or on their gender, etc., which will lead to more effective and in-depth discussion.

2.10 Summary and Key Points

Building an affiliated system of specialized ACHD centers and related facilities can be expected to improve patient outcomes and promote education and research.

The establishment of specialized ACHD centers requires not only the action of medical personnel but also political action, including that of patient groups.

Methods for linking the roles of specialized ACHD centers and related facilities differ depending on the regional medical care system and medical resources, and appropriate methods should be found to suit each region.

Even if appropriate medical facilities are established, they are meaningless unless the facilities are utilized by patients. Therefore, transition programs must be further developed in the future. At the same time as transition programs are developed for individuals and groups, research is needed to evaluate the effectiveness of these programs.

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Part II

Medical Consideration

Postoperative Residua and Sequelae

3

Kei Inai

Abstract

Current advances in surgical treatment and catheter intervention enabled a large number of patients survive well into adulthood. In proportion as the adult survivors increase, increasing number of late complications occurred. In particular, postoperative residua and sequelae severely affect patients' health-related quality of life especially in adults. In this chapter, the author focused on postoperative complications in adult patients with congenital heart disease and took up the problems after surgery for tetralogy of Fallot, D-transposition of the great arteries, congenitally corrected transposition of great arteries, and Fontan operation, because these diseases are popular in the clinical setting. Especially, right ventricular failure of tetralogy of Fallot and systemic right ventricular failure of transposition of the great arteries are important concerns. Moreover, post-Fontan complications are known as "Fontan disease" and various organ failures, i.e., liver cirrhosis and protein loosing enteropathy, as well as cardiac dysfunction. Nowadays, ACHD specialists are constantly facing the difficulties how to treat these complications. The author also mentioned necessary interventions regarding both catheter use and surgery in these patients.

Keywords

Postoperative complications • Tetralogy of Fallot • d-TGA • Congenitally corrected TGA • Fontan operation

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3.1 Introduction

Due to improvements in heart surgery, many young patients have been able to grow into adulthood. However, several postoperative complications have been observed even in the late postsurgery period [1]. In this chapter, the author describes postoperative residua and sequelae in adult patients with congenital heart disease that are often encountered in the clinical setting and also describes necessary interventions regarding both catheter use and surgery.

3.2 Tetralogy of Fallot

Several postoperative problems have been observed in adult patients with tetralogy of Fallot (TOF) [2, 3]. When cardiomegaly is revealed on chest x-ray, tests for a residual hemodynamic lesion and/or sequellae, such as the residual leak of a ventricular septal defect (VSD), significant pulmonary regurgitation (PR), and severe tricuspid regurgitation (TR), should be conducted (Fig. 3.1).

Moreover, a high index of suspicion must be maintained for pulmonary artery stenosis and right ventricular outflow tract (RVOT) stenosis in these patients.

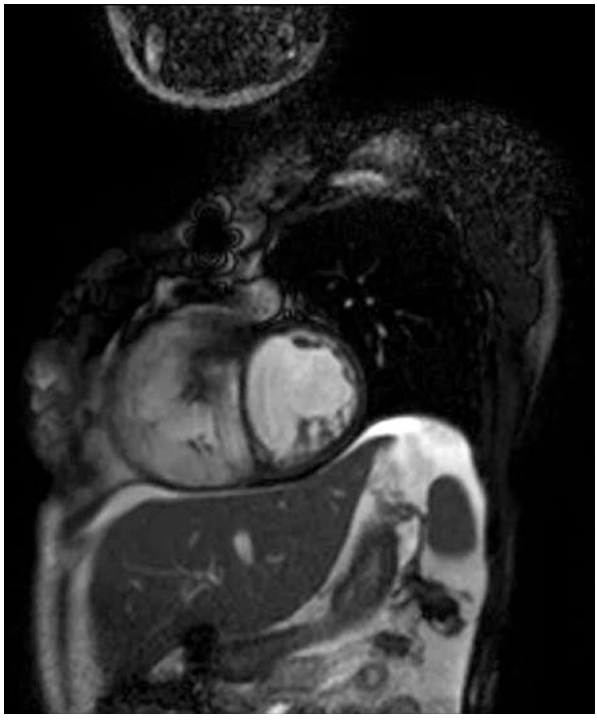

Fig. 3.1 RV enlargement after TOF repair. MRI imaging of a 29-year-old woman after the intracardiac repair of a TOF. Note the markedly enlarged RV. RV end-diastolic volume is 168 mL/m^2 and RVEF is 35%

The development of arrhythmias (atrial or ventricular) also indicates an underlying hemodynamic abnormality. In particular, right atrial and/or right ventricular enlargement eventually causes both atrial and ventricular arrhythmias. Basically, the common arrhythmogenic mechanisms include operative scars and natural conduction obstacles that create narrow corridors capable of supporting macro-reentry; however, the hemodynamic abnormalities may also affect arrhythmogenicity. It is reported that atrial reentrant tachycardia is observed during extended follow-up in more than 30% of patients. In addition, malignant ventricular arrhythmias have also been noted in about 10% of patients [4, 5]. Notably, the overall incidence of sudden cardiac death is estimated at 0.2% per year of follow-up [6, 7].

3.2.1 Catheter Intervention

Adult patients with TOF often have residual lesions amenable to catheter intervention. Patients with residual pulmonary artery stenosis are often treated using catheter balloon dilation and/or stent implantation [8, 9]. A peak instantaneous echocardiography gradient greater than 50 mmHg or an RV/LV pressure ratio greater than 0.7 should be an indication for catheter intervention. Pulmonary artery branch stenosis with a disproportional lung perfusion greater than 7:3 is also an indication for balloon dilatation.

Residual RV outflow tract obstruction may be relieved by RV outflow tract stenting. It is especially important that the RV outflow tract stenting is not allowed to cause coronary compression.

Currently, percutaneous pulmonary valve replacement (PVR) is performed worldwide. The original criteria for percutaneous Melody valve implantation (Medtronic, Inc., Minneapolis, Minnesota) for PR included RV-to-pulmonary artery conduits of 16 mm, balloon sizing of the narrowest area to 14 and 20 mm, and greater than moderate PR or severe conduit stenosis (gradient 35 mmHg) [10]. Some complications following Melody valve implantation such as stent fracture and endocarditis have been reported [10, 11]. Although there is a paucity of evidence concerning antibiotic prophylaxis for endocarditis in this situation, the current guidelines recommend prophylaxis for prosthetic valves [12].

Despite its rarity, hypoxemia in postoperative patients should be searched for the cause of that, in those possibly having a PFO or ASD with a right-to-left shunt that could be treated with percutaneous device closure.

As mentioned above, arrhythmias are important factor for the prognosis and outcome in adult TOF patients. Thus, appropriate antiarrhythmic therapy including catheter ablation and intracardiac device (ICD) implantation should be performed (see Chap. 5).

Lastly, when catheter intervention is considered for adult patients with congenital heart disease, collaboration between ACHD interventional cardiologists, electrophysiologists, and ACHD surgeons is mandatory to determine the most feasible treatment.

3.2.2 Surgical Intervention

PR is the most common indication for late reoperation. PVR is indicated for moderate to severe PR and decreased exercise tolerance. A successful PVR results in significant improvement in LV ejection fraction (EF), which correlates with the pre-PVR RV end-diastolic volume. It is reported that an increase in RV greater than 170 mL/m^2 will not return to normal even after PVR. Furthermore, Therrien et al. reported that in order to maintain adequate RV contractility, PVR should be considered before RV function deteriorates (at least >EF 40%). Recently, the benefits of earlier reoperation (in adolescence or young adulthood) have been highlighted [13].

TR may be secondary to RV dilation due to significant PR or structural valve deformities possibly related to a VSD patch or chordal disruption at initial repair. TR can also be affected by permanent pacing or ICD leads. Tricuspid repair can be accomplished using an eccentric, purse-string, or ringed annuloplasty [14]. Tricuspid replacement may be required if prior repairs have failed or if there are major leaflet abnormalities, however, it is reported that the risk of surgery is greater with tricuspid replacement than tricuspid valve plasty [14].

VSD reclosure is indicated for significant L-R shunt that causes significant LV volume overload. In the acute phase after initial repair, LV volume overload due to a VSD leak may cause severe LV failure, because the LV in a TOF patient is relatively small before repair and is susceptible to acute volume overload. Also in the late period, when LVEF deteriorates with the progression of RV enlargement, a residual VSD leak may also affect LV function.

A dilated ascending aorta is also a major problem in adult patients with TOF, and because its natural history and treatment outcomes are not well-known, the timing of aortic intervention remains controversial. Dissection and aortic rupture in this patient group are rare [15]. Aortic valve regurgitation does not necessarily accompany aortic dilation. In general, replacing the ascending aorta is indicated if it is greater than 55 mm in diameter [15].

Rarely, the surgical relief of a subaortic stenosis is needed in TOF patients. Diagnostic uncertainty may occur concerning a double outlet right ventricle in which the aorta overrides more than 50% of the right ventricle. In such cases, a VSD patch is more extensive and predisposes to postoperative subaortic obstruction, which should be carefully excluded.

Surgery for arrhythmias may be performed mainly for atrial tachyarrhythmias such as atrial reentry tachycardia, atrial fibrillation, and flutter, concomitant with reoperation [16]. Atrial flutter should be treated with cryoablation or radiofrequency ablation of the right atrial isthmus. Paroxysmal atrial fibrillation should be treated with right atrial maze, and chronic atrial fibrillation should be treated with biatrial maze procedure [17]. The most common arrhythmia following maze surgery is a junctional rhythm or sick sinus syndrome, which may require a permanent pacemaker implant.

Some postoperative patients may experience LV dysfunction. This may be related to a prolonged cardiopulmonary bypass, poor myocardial protection from an early surgical intervention, or trauma to a coronary artery at the time of repair, or it

may be secondary to severe RV enlargement and/or dysfunction (ventricular-ventricular interaction). Although medications for heart failure may be necessary in RV and LV dysfunction, evidence for β-blockers and angiotensin receptor inhibitors in these patients have been scarce to date. Therefore, cardiac resynchronization therapy or heart transplantation may be applied when refractory heart failure inevitably progresses [17].

3.3 Dextro-Transposition of the Great Arteries

Dextro-transposition of the great arteries (d-TGA) is defined as combination of AV concordance and ventriculoarterial discordance. Consequently, in d-TGA, the aorta arises right and anterior to the pulmonary artery and arises from the right ventricle. Additional congenital cardiac lesions include VSD, which occurs in up to 45% of cases; left ventricular outflow tract (LVOT) obstruction, which occurs in approximately 25% of cases; and coarctation of the aorta occurring in approximately 5% of cases [18].

The infant with d-TGA will generally present with cyanosis, and some form of admixture of blood is required for survival. For the past two decades, arterial switch operation in the neonatal period has been the primary surgical repair of choice for uncomplicated d-TGA. In patients who present late (after 6–8 weeks of age), pulmonary artery banding to prepare the left ventricle is often necessary. Patients with d-TGA and associated VSD may undergo an initial pulmonary artery banding or shunt procedure, depending on the presence or absence of subpulmonary artery obstruction. If there is an associated large VSD, a right ventricle outflow reconstruction (Rastelli-type procedure) may be performed as a primary procedure. In the 1960s–1970s, atrial switch operations, such as the Senning or Mustard procedure were often performed on these patients [19]. The long-term outcomes differed depending on which procedure was selected.

The frequency of late complications may be determined by the degree of residual hemodynamic abnormalities, and these are becoming more common. All adult patients with d-TGA should be seen at least once annually by an ACHD specialist, with attention given to rhythm disorders, as well as ventricular and valvular function. Selected patients should undergo exercise testing, including stress radionuclide scintigraphy and cardiopulmonary exercise test. If significant abnormalities are found during these examinations, or if the patient is symptomatic, more frequent follow-up visits are indicated.

3.3.1 Residua and Sequelae After the Atrial Switch Procedure

These procedures involve an atrial baffle that redirects the systemic venous blood to the left ventricle through the mitral valve, which remains committed to the pulmonary artery. The pulmonary venous blood is redirected to the tricuspid valve and right ventricle, which remains committed to the aorta. The atrial switch

(Mustard or Senning procedure) operation for d-TGA has characteristic long-term problems [19].

The most important long-term complication of this procedure is the failure of the systemic right ventricle and TR, which indicates systemic AV valve regurgitation. These complications have a major impact on morbidity and mortality in patients with d-TGA. Other complications include conduction and arrhythmia disturbances, such as sick sinus syndrome, supraventricular tachyarrhythmia, and complete AV block, which may lead to sudden death or the implantation of permanent pacemakers for prevention of that [20]. In addition, common early structural complications such as baffle obstruction, which commonly affects the superior limb rather than the inferior vena cava, may be encountered. Facial suffusion and edema, that is the "superior vena cava syndrome," occasionally occur. Inferior vena cava obstruction may cause hepatic congestion or even cirrhosis. Baffle leaks are known to occur in up to 25% of patients. Most are small but cause cyanosis to some extent and predispose to paradoxical embolism, particularly in the presence of atrial arrhythmias and an endocardial pacemaker. Pulmonary venous obstruction may be rarely seen. Moreover, pulmonary stenosis (subpulmonary and/or valvular) may occur, in part related to the abnormal geometry of the left ventricle, which becomes distorted and compressed by the enlarged systemic right ventricle. Finally, rare but important complications including pulmonary arterial hypertension (PAH) and residual VSD may also arise.

Cardiac echocardiography is the first-line and also the main tool for anatomic and hemodynamic assessment in most d-TGA patients after an atrial switch operation. Evaluation for intraatrial baffle anatomy and shunting or obstruction may warrant echocardiography with contrast medium injection. However, the assessment of systemic RV function is challenging using echocardiography. In addition to the routine evaluation of ventricular size and function, measurement of the dP/dt of the AV regurgitant jet, tricuspid annular plane systolic excursion (TAPSE), and the Tei index may provide further information [21–23]. Tissue Doppler evaluation of myocardial acceleration during isovolumic contraction has been validated as a sensitive, noninvasive method of assessing RV contractility [24]. One advantage of the Tei index is its ability to represent the indices of both systolic and diastolic function without geometric constraints. In addition, a relationship between the Tei index and brain natriuretic peptide (BNP) has been shown and may provide valuable information if assessing RV function in the adult patient using echocardiography becomes difficult [22]. Transesophageal echocardiography (TEE) is an informative tool that may be used to visualize the atrial anatomy, presence of a baffle leak or obstruction, and intracardiac thrombus. MRI or CT is used to further assess atrial baffle patency, systemic ventricular function, and coronary anatomy [25]. Cardiac MRI is usually superior to TEE for evaluating the configuration of the extracardiac great arteries and veins. MRI has also been shown to be closely correlated with the equilibrium radionuclide ventriculography assessment of RVEF [26].

Cardiac catheterization is the definitive tool for assessing hemodynamics, baffle leak, superior vena cava or inferior vena cava pathway obstruction, pulmonary

venous pathway obstruction, myocardial ischemia, unexplained systemic RV dysfunction, subpulmonary stenosis, LVOT obstruction, or PAH, with a possibility for vasodilator testing. Cardiac catheterization in patients after the atrial switch operation also provides the opportunity for intervention.

Concerning arrhythmic complications, regular ECG follow-up is mandatory to detect sick sinus syndrome (SSS) which represent a slow junctional rhythm or complete AV block. Other rhythm abnormalities such as tachyarrhythmia may be further elucidated by ambulatory rhythm monitoring (Holter or event recorder). Exercise testing to determine functional capacity and the potential for arrhythmias may be helpful.

3.3.2 Residua and Sequelae After the Arterial Switch Procedure

The health-related quality of life of patients after the arterial switch operation is known to be better than those undergone the atrial switch operation [27, 28]. Long-term concerns after the arterial switch procedure include coronary perfusion abnormality, myocardial ischemia, ventricular dysfunction and arrhythmias, and pulmonary stenosis (branch stenosis and/or stenosis at anastomotic sites), as well as the development of aortic or pulmonary regurgitation (Figs. 3.2 and 3.3). Significant neoaortic root dilatation and valve regurgitation may develop with time, in part related to older age at the time of the operation or to an associated VSD with previous pulmonary artery banding [28, 29].

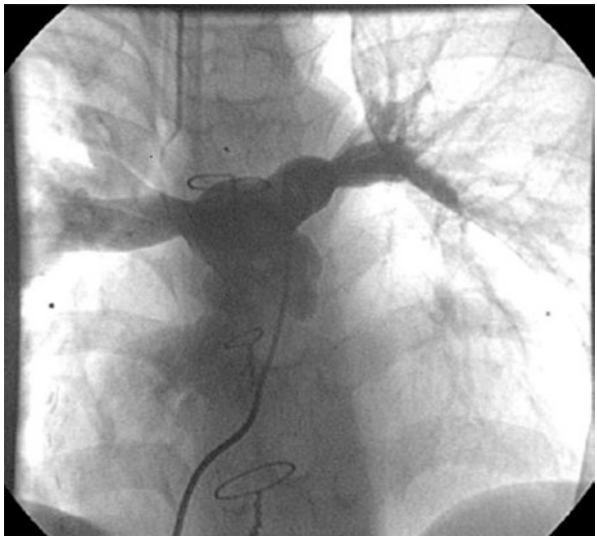

Fig. 3.2 Pulmonary branch stenosis after an arterial switch operation for d-TGA. Bilateral pulmonary branch stenotic lesions are shown

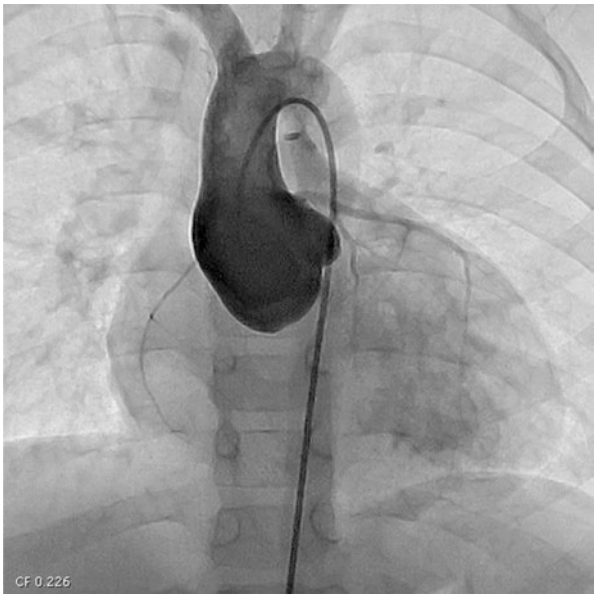

Fig. 3.3 Aortography after an arterial switch operation for d-TGA. Aortic root dilatation is shown, as well as sinus of Valsalva dilatation

In the clinical setting, many patients may be asymptomatic. However, it should be noted that systolic murmurs related to pulmonary and/or aortic obstruction, and diastolic murmurs of aortic regurgitation should not be overlooked.

ECG can be helpful in detecting ischemic changes, occasionally noted at rest, which suggests the presence of coronary stenosis. This should be evaluated further by stress ECG testing. Moreover, RV and LV hypertrophy suggest the presence of ventricular outflow obstruction or arterial regurgitation; this should also be noted.

Echocardiography after the arterial switch procedure may mostly reveal anatomical complications, including pulmonary stenosis [30, 31], aortic root dilatation, and neoaortic valve regurgitation [32]. Although coronary complications cannot be assessed properly using echocardiography, stress echocardiography may help to detect myocardial ischemia. MRI and CT angiography have been particularly useful for diagnosing aortic dilatation and coronary stenosis. Patients with intramural or single coronary arteries are at risk of coronary complications [33, 34]. Evaluating coronary ischemia using noninvasive methods may not be sufficiently sensitive. Notably, typical symptoms of coronary ischemia may be absent even when significant ostial coronary stenosis exists in these patients. In such cases, coronary arteriography using a cardiac catheter is recommended. Apart from ordinary coronary arteriography, aortic root angiography, especially the “cusp shot,” is highly recommended for detecting ostial stenosis (Fig. 3.4).

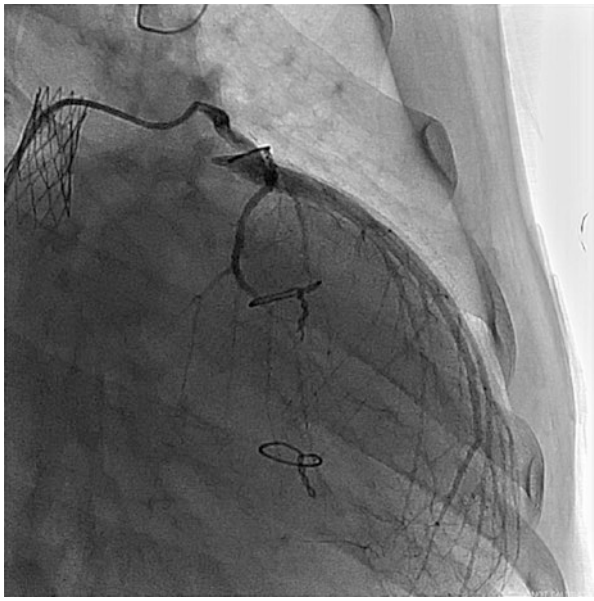

Fig. 3.4 Coronary stenotic lesion after an arterial switch operation for d-TGA. Coronary arteriography revealed stenotic lesion of left main trunk, segment 5

3.3.3 Residua and Sequelae After the Rastelli-Type Operation

The Rastelli-type operation for d-TGA with pulmonary stenosis (PS) and VSD (the so-called d-TGA type 3) has recognized complications, which include RVOT or pulmonary conduit obstruction, suprasystemic RV pressure leading to RV dysfunction, and significant TR [18]. Subaortic stenosis may also occur due to the insufficient size of the intraventricular rerouting pathway. Tachyarrhythmias may arise from atriotomy and/or ventriculotomy incisions, residual VSD, RV enlargement due to PR, aortic root dilatation, and aortic valve regurgitation. These concerns are similar to those of TOF.

Echocardiography is the primary imaging modality in patients with prior Rastelli-type operations. Recurrent RV or LV outflow obstruction can be usually and properly detected by Doppler echocardiography. Assessing RV pressure and the occurrence of conduit obstruction can be facilitated by measuring TR velocity. Additional important features should include the assessment of PR, residual or baffle-margin VSD, and the development of PAH.

3.3.4 Management and Intervention

With regard to medication, the positive role of ACE inhibitors and beta blockers remains unclear. Moreover, it should be noted that beta blockers may precipitate

complete AV block in patients with preexisting sinus node dysfunction. Therefore, it should be used cautiously, particularly after an atrial switch operation.

Interventional catheterization plays a crucial role in the management of adult patients after an atrial switch, arterial switch, or Rastelli-type operation. Successful stent implantation for the relief of a symptomatic atrial baffle obstruction, as well as percutaneous placement of transcatheter implants for baffle leak elimination, has been reported in adult survivors of the atrial switch operation. Transcatheter dilation and stenting of central pulmonary artery stenosis are possible therapeutic choices. When branch pulmonary artery stenosis is found in adults after a Rastelli-type operation, hybrid management, which includes preoperative stenting, intraoperative stenting, or intraoperative patch with or without conduit replacement, is recommended. Dilation with or without stent implantation of conduit obstruction may be indicated when RV pressure is greater than 70% of systemic levels or the peak-to-peak gradient is greater than 50 mmHg.

Reoperation for patients with d-TGA is occasionally inevitable and is important for preserving good health. Although conversion to an arterial switch in adulthood has previously been attempted, it has not been generally considered a reasonable option for the management of RV failure in patients after an atrial switch [35]. Patients with severe symptomatic superior or inferior vena cava obstruction or pulmonary venous pathway obstruction should be referred for reoperation when catheter intervention is not effective. It has been noted that when attempting endocardial pacemaker implantation in these patients, a detailed assessment of the atrial baffle for obstruction and leakage must be undertaken, because an endocardial pacing device may exacerbate any obstruction in the atrial baffle. Patients with a baffle leak that demonstrates a Qp/Qs greater than 1.5 or a right-to-left shunt with arterial desaturation at rest or with exercise should be considered for surgery when device placement is impossible. Severe TR may need a surgical intervention such as tricuspid valve replacement (TVR,) but a major part of TR after an atrial switch operation is the consequent on severe RV dysfunction. Therefore, TVR is not common in these patients comparing with adults with congenital corrected transposition of the great arteries. In cases of severe RV dysfunction with severe TR, heart transplantation should be the last option.

Patients needing reoperation after an arterial switch operation are uncommon. The most common reoperation is a repeat RVOT reconstruction because of a severe RVOT obstruction with a peak-to-peak gradient greater than 50 mmHg or RV/LV pressure ratio greater than 0.7, which is not amenable or responsive to catheter intervention. PVR should be considered when severe PR is present, and there is significant RV dilatation or RV dysfunction; however, reoperation of this reason is uncommon. Coronary ostial stenosis may be repaired using coronary bypass grafting or ostial arterioplasty techniques. Significant AR presenting with LV enlargement should be considered as an AVR. Patients who have developed aortic root dilation (greater than 55 mm) may be treated with root replacement.

Reoperation after a Rastelli-type operation should be considered for symptomatic conduit and/or pulmonary artery stenosis with a peak gradient greater than or equal to 50 mmHg and/or RV/LV pressure ratio greater than 0.7. Reoperation for

severe conduit regurgitation should be performed when decreased exercise tolerance; severe RV dysfunction; severe RV enlargement, development, and/or progression of atrial or ventricular arrhythmias; and greater than moderate TR are present. Relief of severe symptomatic subaortic stenosis with a mean gradient greater than 50 mmHg should be considered.

3.4 Congenitally Corrected Transposition of the Great Arteries

Congenitally corrected transposition of the great arteries (CCTGA) is defined as an abnormality consisting of atrioventricular discordance and ventriculoarterial discordance. Therefore, the left ventricle pumps blood to the pulmonary artery, and the right ventricle has the heavier workload of pumping blood to the aorta. In other words, the morphological right ventricle functions as the systemic ventricle, whereas the morphological left ventricle functions as the pulmonary ventricle (Fig. 3.5). These features definitely influence both the natural history and postoperative sequela and determine the patient's lifelong outcome.

The clinical course of CCTGA varies depending on the presence and severity of associated lesions [36, 37]. Predominant are the following: VSD (70%), PS (40%), and some abnormalities of the tricuspid valve (90%). Tricuspid abnormality, most commonly, is an Ebstein-like deformity in which the valve is displaced inferiorly toward the cardiac apex [38]. Conduction abnormalities are also common, with spontaneous complete heart block occurring at a rate of approximately 2% per year

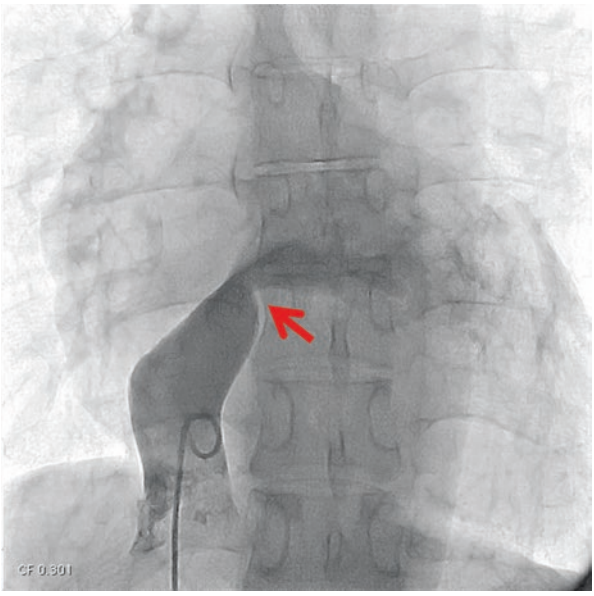

Fig. 3.5 Senning route of the patients with CCTGA after the double switch operation. Baffle obstruction (*red arrow*) is shown (contrast imaging from inferior vena cava)

[39, 40]. If the patients do not have any associated lesions, they may be asymptomatic but more often they present with congestive heart failure and usually with moderate to severe TR.

3.4.1 Physiologic Repair for CCTGA

Traditionally, physiologic repair is performed for patients with CCTGA, such as VSD closure, PS release, and (TVR). The indication for surgery in adult patients is not reasonable but often the onset of symptoms due to associated TR or RV dysfunction. Surgical intervention in the adult often consists of TVR alone. Ideally, it should be performed before the RVEF is less than 45% [41, 42]. However, in physiologic repair, the problem remains in which the RV as the systemic ventricle. Graham et al. reported that 25% of adult patients have advanced systemic RV dysfunction in their 40s, even without any associated lesions [43]. This rate is thought to increase as time progresses. Furthermore, complete AV blocks are common after surgical repair of a VSD or following a TVR. Thus, there are several severe postoperative problems following physiologic repair.

3.4.2 RV Failure of CCTGA

Most patients eventually have severe TR and an RVEF less than 45% [41, 42]. With progressing RV dysfunction, the RV and the annulus dilate causing the failure of leaflet coaptation and progressive regurgitation. Moreover, the tricuspid valve is often morphologically abnormal, and with time, there is worsening of regurgitation. Progression of TR may also occur as a result of pacemaker implantation, related to septal shift and further distortion of the tricuspid valve (TV) annulus. VSD closure may also exacerbate TR, probably by the same mechanism. It has been proposed that the TV should always be replaced if the regurgitation is moderate or severe at the time of intracardiac repair of other lesions [44]. Because the morphological RV may not be intrinsically suited to function long term as the systemic ventricle, such patients live for relatively shorter periods, and survival to the seventh decade is very rare. The precise mechanisms of RV failure are not clear but are probably related to microscopic structural features of the RV myocardium and coronary perfusion mismatch [45]. Certainly, RV failure is a major cause of morbidity and mortality in adult patients with CCTGA [46]. Atrial tachyarrhythmias are also common and occur more commonly in those with RV dysfunction and TR [47].

3.4.3 Anatomic Repair of CCTGA

To solve these problems, the double switch operation was developed in the 1990s. This surgical repair in infants and children is often aimed at restoring the left ventricle as the systemic ventricle [48–51]. The double switch operation is an anatomic

repair consisting of the atrial switch and arterial switch operations. This procedure can correct blood stream physiologically and LV switch to the systemic ventricle. However, in adulthood, adequate left ventricular function must be ascertained, because at this time the LV may not function optimally as the systemic ventricle. Double switch operation in adults is known to have a high mortality, even after LV training using pulmonary arterial banding. Therefore, pulmonary arterial banding is not a procedure of choice in adults at this point of time. If significant PS is present and arterial switch is not indicated, an anatomic repair consisting of atrial switch, interventricular rerouting from LV to aorta, and RV outflow tract reconstruction is a possible choice. Some researchers have documented the medium to long-term outcomes of the anatomic repair in patients with CCTGA [47–52]. Atrial switch of venous return must be performed using the Mustard or Senning procedure as previously mentioned. The potential for late complications is already recognized in patients with d-TGA who have undergone these procedures. Aortic dilation and AR progression are of primary concern with regard to the arterial switch. If RV outflow tract reconstruction is performed, the possibility for conduit stenosis and pulmonary regurgitation should be noted. Intraventricular rerouting may subsequently result in subaortic stenosis, even in the late period, and reoperation for subaortic stenosis is occasionally required. This sequela is due to insufficient VSD size and/or fibrotic tissue growth in the rerouting course or just below the aortic valve. Although VSD enlargement is occasionally needed in the first anatomic repair, extensive incision of the ventricular septum may induce some degree of ventricular dysfunction. After anatomic repair in some patients, even when a VSD enlargement is not performed, systemic ventricle dysfunction may progress. In this case, as with physiologic repair, heart transplantation should be considered if systemic ventricular dysfunction progresses [53–56].

Consequently, optimal postoperative care is needed in these patients. Yearly evaluation using echocardiography and/or MRI is highly recommended.

For these patients, the minimum of an annual follow-up is mandatory, with special attention paid to the following:

RV function, TR or evaluation of TV prosthesis function, pulmonary conduit stenosis or regurgitation, residual VSDs, and development or progression of AR. AV block and/or atrial tachyarrhythmia should be monitored for regularly using Holter electrocardiography.

3.5 Fontan Operation for Single Ventricular Physiology

The Fontan procedure has been used to treat tricuspid atresia since 1971 and is now applied for various congenital heart diseases with single ventricular physiology. An increasing number of survivors of this procedure are reaching adulthood and are facing various late complications as a result of Fontan physiology [57]. They encounter noncardiac health problems as well as cardiovascular problems. Understanding the long-term outcomes of the Fontan operation is becoming increasingly important, and the optimal intervention for these sequelae must be addressed.

The 10-year survival after a Fontan operation is 90%, depending on the number of risk factors present at the time of the initial Fontan operation [58]. After the operation, various systemic organ failure progress and cause poor health-related QOL in the patients. For example, recently the survival rate of protein loosing enteropathy (PLE) has improved with advances in treatment, while the 5-year survival of patients with PLE was approximately 50% in the 1990s, although PLE still remains difficult to treat-no definite treatment [59].

3.5.1 Catheter Intervention After the Fontan Operation

After the Fontan operation, cardiac catheterization is pivotal for assessing and/or treating various late complications of the procedure. Routine assessment using catheterization is recommended for investigating ventricular dysfunction, systemic AV valve regurgitation, cardiac output and systemic vascular resistance/pulmonary vascular resistance, obstruction of Fontan route to pulmonary artery, and presence of a venovenous and/or arteriopulmonary shunt. Moreover, it is important to monitor for systemic ventricle outflow obstruction at the bulboventricular foramen, VSD, or subaortic conus hypertrophy. When the right atrium is severely enlarged, especially in a Fontan operation with an atriopulmonary connection, the pulmonary vein may become compressed and lead to pulmonary venous stenosis which is responsible for increased pulmonary pressure.

Any degree of obstruction, even if the pressure gradient is very small, in the Fontan route is clinically important. If morphological stenosis is present in the Fontan route and pulmonary tree, catheter balloon dilatation is indicated for avoiding failing Fontan circuit (Fig. 3.6). Patients with cyanosis (oxygen desaturation at rest and decreasing of oxygen saturation with exercise) should be carefully investigated to ascertain the cause and existence of the right-to-left shunt. It is important to note that persistent Fontan fenestration, venovenous collaterals, and pulmonary arteriovenous malformations may lead to worsening cyanosis and systemic thromboembolism, particularly when there is an elevation in central venous pressure and/or worsening fluid retention. An angiographic search for atrial level of right-to-left shunts and shunts from the inferior cava, superior cava, hepatic vein, and innominate vein to the left atrium and/or pulmonary vein are mandatory, as well as a search for pulmonary arteriovenous malformations (Fig. 3.7). Catheter interventional closure of these residual shunts using coils or ASD devices is usually possible, except for multiple pulmonary AV malformations [60].

For patients with PLE, an angiographic evaluation should be performed for AV valve stenosis or regurgitation, as well as Fontan route obstruction. In addition, aortography should be conducted to determine whether prominent aortic-pulmonary collaterals are present, which may cause increasing resistance to effective pulmonary flow. Creation or enlargement of a fenestration may be necessary for decreasing central venous pressure to relieve PLE symptoms, and this is unfortunately but often temporarily effective [61].

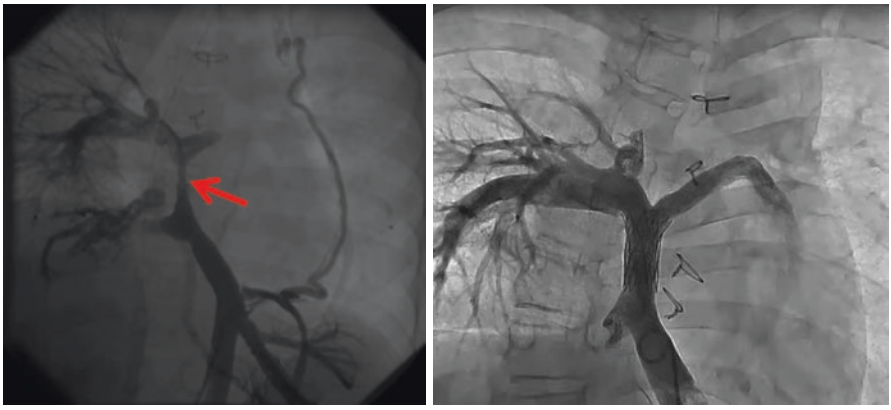

Fig. 3.6 Fontan route stenosis late after Fontan operation. *Left panel*: Fontan route arteriography revealed severe stenosis (*red arrow*). *Right panel*: Pulmonary arteriography after the stenting for the stenotic lesion

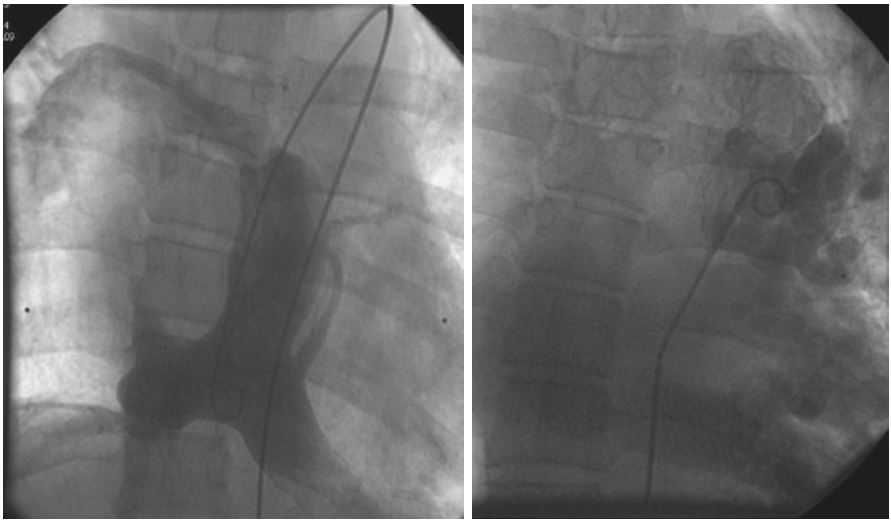

Fig. 3.7 Pulmonary arteriovenous malformation after Fontan operation. *Left panel*: Most of hepatic flow directly go into right pulmonary artery. *Right panel*: In the left lung, large and tortuous arteriovenous malformation is shown

Because catheter intervention for patients late after a Fontan operation has become increasingly important, properly evaluating the anatomical and physiological features prior to a Fontan procedure and the appropriate prediction of possible severe complications has become indispensable. For example, the development of venovenous and arteriopulmonary collaterals and pulmonary AV malformation are occasionally predictable prior to the progression of the symptoms.

3.5.2 Arrhythmia Management

The most frequent complication after a Fontan operation is arrhythmias, particularly atrial tachyarrhythmias [62]. Although, cardiac ablation has been tried to cure various atrial tachyarrhythmias and ventricular tachycardia, the intervention is often technically difficult in these patients due to special hemodynamics and anatomy. Prior to an intervention for arrhythmias, atrial tachyarrhythmia should prompt a comprehensive noninvasive imaging evaluation to identify associated atrial/baffle thrombus, anatomic abnormalities of the Fontan pathway, or ventricular dysfunction [63]. In addition, cooperation between pediatric cardiologists specialized in the anatomy of congenital heart disease and electrophysiologists is required. If cardiac ablation is unsuccessful, implantation of an atrial antitachycardia pacemaker or antiarrhythmic drugs should be considered. Furthermore, anticoagulants should be given to all patients with atrial arrhythmias.

3.5.3 Surgical Intervention After a Fontan Operation

Reoperation after a Fontan procedure is indicated for some cases. Firstly, a residual baffle leak that results in right-to-left shunt with cyanosis, if not amenable to transcatheter closure, may be an indication for baffle leakage repair. Secondly, it is also indicated for moderate to severe systemic AV valve regurgitation that leads to significant volume overload and/or ventricular dysfunction [64]. Thirdly, as previously mentioned, significant subaortic stenosis (peak-to-peak pressure gradient is greater than 30 mmHg) is occasionally an indication for reoperation. Fourthly, the creation or closure of a fenestration should also be considered when catheter intervention fails. Reoperation for any Fontan route obstruction, pulmonary venous obstruction, and development of venous collaterals or pulmonary AV malformation not amenable to catheter intervention may be occasionally considered, although this is uncommon.

When patients suffer from a complete AV block or sick sinus syndrome, a pacemaker insertion, epicardial in most cases, is required [65]. In Fontan circuit, the pacemaker lead cannot reach the ventricle transvenously. Moreover, after total cavopulmonary connection (TCPC) procedure, since vena cavae directly connect pulmonary artery, the pacemaker lead cannot insert in right atrium.

Another issue concerning reoperation for Fontan patients is TCPC conversion, which is the revision of an atriopulmonary connection to an intracardiac lateral tunnel or extracardiac conduit and can be useful for prevention of refractory atrial tachyarrhythmias. An accompanying Maze procedure should also be performed [66–68].

There are some indications for TCPC conversion, including a giant atrium with or without thrombus, refractory arrhythmias, pulmonary venous obstruction by the enlarged right atrium, and ventricular dysfunction. However, optimal timing for this procedure remains controversial.

Finally, heart transplantation and/or a mechanical support device may be considered for severe ventricular dysfunction or PLE [69–71].

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Heart Failure in Adults with Congenital Heart Disease

4

Hideo Ohuchi

Abstract

The number of adults with congenital heart disease (ACHD), especially those with complex CHD, is increasing substantially. The major clinical characteristics include (1) a high prevalence of right-sided heart failure (HF) due to systolic and/or diastolic dysfunction of the right ventricle (RV), which is frequently seen in repaired patients with tetralogy of Fallot (TF); (2) pressure and/or volume overload to the ventricles due to intra- and/or extracardiac shunting, atrioventricular or semilunar valve stenosis, and/or regurgitation; and (3) a morphologic RV as a systemic ventricle seen in those with congenitally corrected transposition of the great arteries or in those after an atrial switch operation. In addition, some CHD-specific conditions are also included in these pathophysiologic conditions, such as cyanosis (hypoxia) in unrepaired patients with complex CHD, Eisenmenger syndrome, and single ventricular physiology, i.e., Fontan circulation. The impaired function of the noncardiac organs may also be involved in some ACHD patients. Furthermore, surgery-related issues, including perioperative myocardial damage and electrical pathophysiology, can modify and make the ACHD HF pathophysiology more complex. The application of an established anti-HF strategy used in non-ACHD patients with left-sided HF to ACHD patients is questionable and possibly limited efficacy. Although most of the ACHD HF pathophysiology appears progressive, and determining the optimal timing for surgical interventions, such as pulmonary valve replacement, is often difficult because some of those procedures are prophylactic. Thus, a comprehensive understanding of ACHD HF, including noncardiac issues, is required to manage

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ACHD CHF and anticipate a better long-term outcome in these patients. In this review, the common ACHD HF pathophysiology and major specific ACHD conditions are discussed.

Keywords
ACHD • Heart failure • Restrictive physiology • Denervation • Exercise capacity

4.1 Introduction

The basic concepts and classifications of heart failure (HF) pathophysiology are well established in adults with acquired heart disease in which the main cause of HF stems from systolic and/or diastolic dysfunction of the left ventricle (LV), i.e., left-sided HF. These classifications include the New York Heart Association (NYHA) functional class [1], Framingham criteria for chronic HF and Forester classification based on hemodynamics [2], Nohria-Stevenson classification based on physical findings [3], and the more recent clinical scenario based on systolic blood pressure for acute HF [4]. However, none of these classifications are suitable to stratify HF severity in adult congenital heart disease (ACHD) in which right-sided HF is much more common. Nonetheless, the NYHA classification has been arbitrarily applied for the stratification of HF in ACHD patients because of the lack of an alternative standard classification. Furthermore, a management strategy for ACHD with HF has not yet been established because the diversity of HF etiology and scarcity of each ACHD category with HF make it difficult to conduct randomized controlled trials (RCT) to evaluate the benefits of potential therapies. Accordingly, current clinical practice for ACHD patients largely depends on guidelines mainly based on retrospective and/or prospective observational studies [5, 6].

ACHD patients often exhibit impaired ventricular function and hemodynamic abnormalities, including irregularities of the pulmonary circulation, structural and/or residual lesions, intra- and/or extracardiac shunting, conduit stenosis, and impaired function of the atrioventricular (AV) valves. The myriad combinations of these abnormalities make the HF pathophysiology more complex in ACHD patients than in adults with acquired heart disease, especially in postoperative complex ACHD patients because of the additional surgery-associated issues (Fig. 4.1). Common subgroups of ACHD patients are (1) those with morphological right ventricle (RV) as a systemic ventricle, (2) those with single ventricular physiology, and (3) unrepaired patients with cyanosis.

The first part of this review systematically describes HF pathophysiology of ACHD patients. The second part describes three major postoperative pathophysiologies, namely, those resulting from the repair of tetralogy of Fallot (TF), morphological RV as a systemic ventricle, and Fontan circulation. Finally, current knowledge on the management of ACHD patients with HF is summarized.

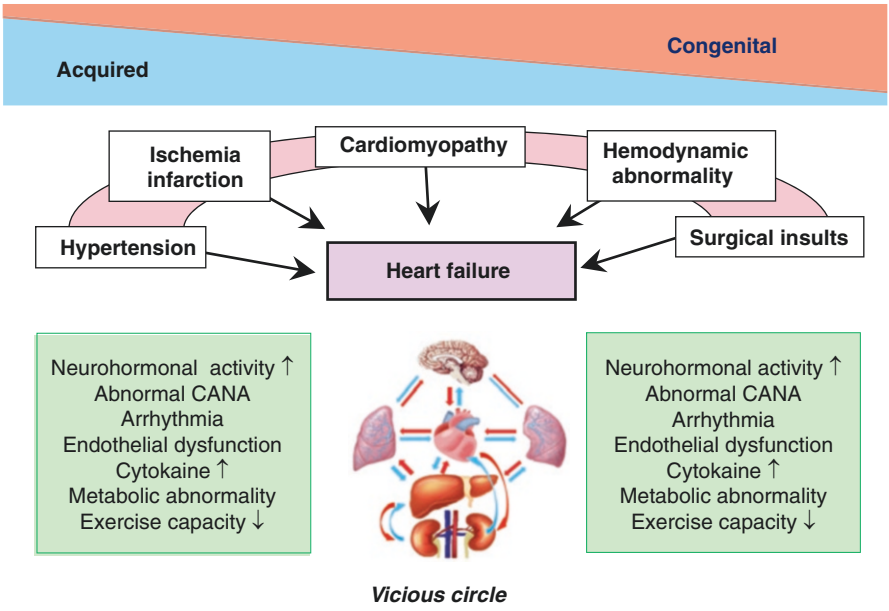

Fig. 4.1 Etiologies of heart failure (HF) differ between adults with acquired heart disease and those with congenital heart disease. In HF due to any cause, plasma levels of neurohumoral factors and inflammatory cytokine are increased, cardiac autonomic nervous activity is abnormal, the endothelium is dysfunctional, and both metabolic abnormalities and arrhythmias are frequently observed. These deficits reduce exercise capacity, further exacerbating cardiovascular pathology

4.2 Heart Failure Pathophysiology in ACHD

Heart failure is a complex pathophysiology that generally involves many noncardiac organs and organ−organ interactions (Fig. 4.2). Furthermore, postoperative ACHD patients have unique complexities that may involve pulmonary, autonomic, myocardial, conduction, arterial, and renal dysfunction as described below.

4.2.1 Pulmonary Dysfunction

The primary function of the cardiopulmonary system is to deliver oxygen to all organs efficiently, and the oxygen uptake capacity of the respiratory system imposes a critical limit on oxygenation. In patients with left-side HF, the lungs become edematous and poorly compliant due to a rise in left atrial pressure, leading to a smaller vital capacity (VC). As a result, the breathing pattern during physical activity is characterized by "rapid-and-shallow" respiration where the ventilatory efficiency progressively worsens [7]. Cardiac operations can result in multiple deleterious effects on the VC of ACHD patients [8], of which restrictive ventilatory

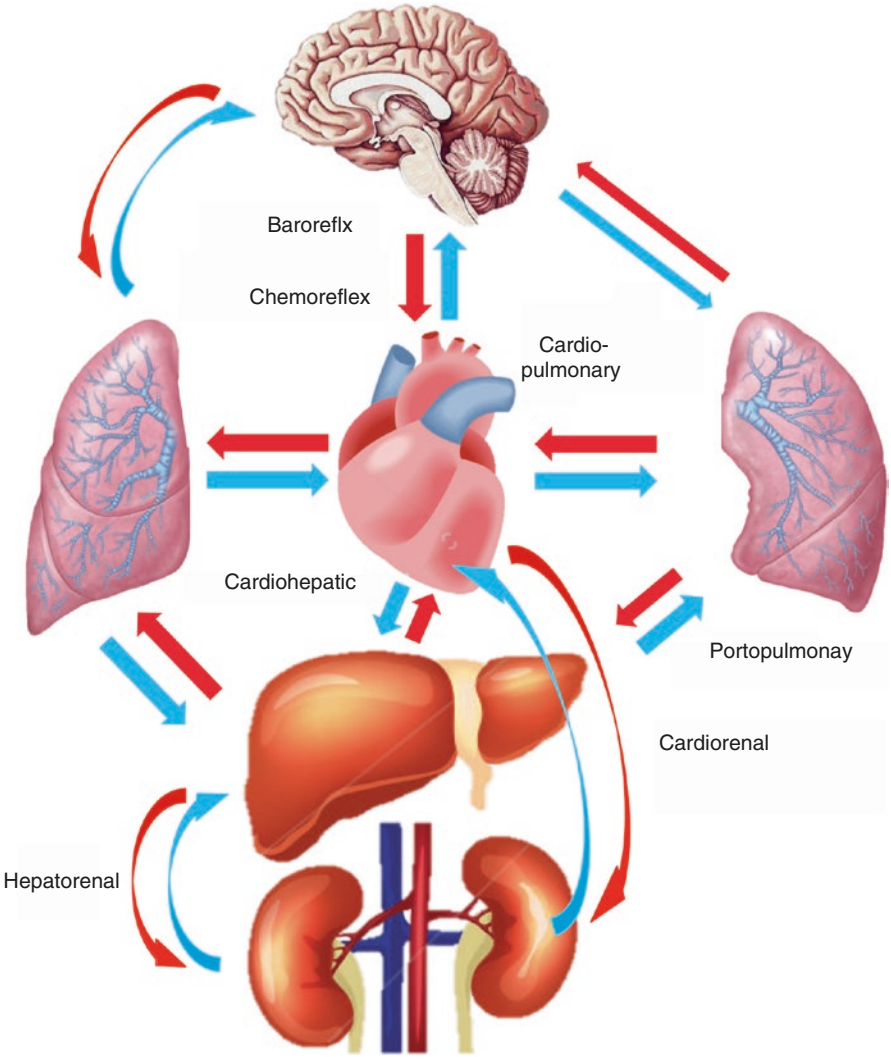

Fig. 4.2 In patients with heart failure, both cardiac and noncardiac organs are impaired. These impairments often interact, leading to additional clinical entities, such as cardiorenal syndrome

impairment is the most common. A high prevalence of scoliosis is also seen in these patients, which has a negative impact on VC [8]. In addition, surgery-related phrenic nerve palsy reduces pulmonary gas exchange. All of these complications must be checked in routine practice because low VC has an adverse impact on ACHD prognosis [8], although the underlying mechanisms are unclear. At the same time, vagal nerve input to control cardiac sympathetic tone may decrease because of small tidal volume, which can be detected by the reduced power of the high-frequency component of heart rate (HR) variability, i.e., diminished respiratory sinus arrhythmia [9].

Restrictive ventilatory impairment and the loss of respiratory sinus arrhythmia may have adverse effects on pulmonary circulation as well as pulmonary gas exchange and may lead to hypoxia, especially in ACHD patients with right-side HF and abnormal pulmonary circulation. Furthermore, small lung capacity is a risk factor for reoperation and heart transplantation.

Recently, sleep apnea due to obesity has been recognized as an important factor contributing to HF. Obesity is one of the strongest and most common risk factors for future cardiovascular disease, and there is a growing evidence of high obesity prevalence in ACHD patients [10]. Thus, the growing obesity epidemic may further increase HF incidence/severity in ACHD by promoting sleep apnea. Such patients may benefit from respiratory assist devices.

4.3 Dysfunctional Cardiac Autonomic Nervous Activity (CANA)

The central nervous system controls the cardiovascular system through projecting sympathetic and parasympathetic nerves. In healthy adults, sympathetic and parasympathetic activities are well balanced. In non-ACHD HF patients, sympathetic dominance occurs because of diminished parasympathetic (vagus) nerve activity [11, 12]. This imbalance is usually proportional to HF severity and thus predicts prognosis. In healthy adults, low systemic blood pressure is sensed by the arterial baroreflex center, and HR increases through the suppression of vagal inputs (reduced vagal tone). Sympathetic dominance in HF can be detected by the high washout ratio of the norepinephrine analogue metaiodobenzylguanidine (MIBG) as measured by scintigraphy, which reflects the accelerated turnover of norepinephrine at sympathetic nerve terminals. These physical phenotypes of HF, low systemic blood pressure, high HR, loss of HR variability, and high washout ratio of MIBG usually parallel HF severity and predict poor prognosis [13]. Thus, assessing CANA status provides useful information on HF pathophysiology in typical non-ACHD patients.

However, the associations between CANA and HF severity differ in postoperative ACHD because of the inevitable damage to sympathetic nerves during cardiac surgery, which interrupts central nervous system signals to great vessels, conduction systems, and atrial and ventricular myocardia ([14], Fig. 4.3). The type and number of cardiac surgeries determine the degree of CANA abnormality. These abnormalities are mainly due to surgical denervation, and severe CANA abnormality can resemble that after cardiac transplantation. The effects of sinus node and ventricular myocardium denervation and damage are detailed below.

4.3.1 Sinus Node Injury

Surgical maneuvers around the superior vena cava or right atrium may injure the sinus nodal artery, leading to sinus node dysfunction and slower HR. In addition, postsynaptic hypersensitivity to vagal acetylcholine may be involved in this

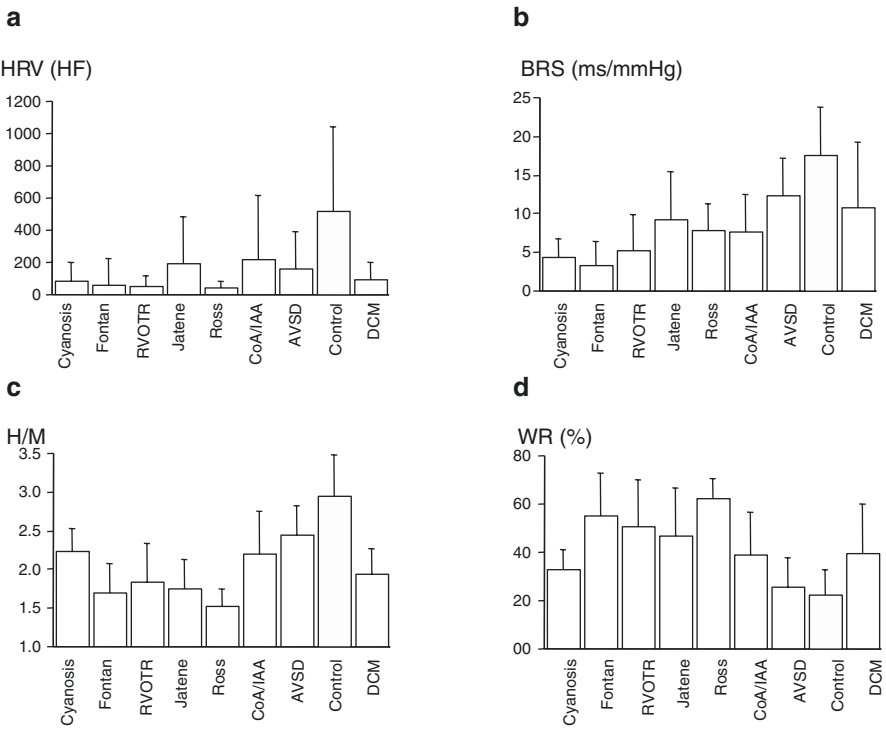

Fig. 4.3 Most repaired patients with congenital heart disease (CHD) as well as those with simple lesions show impaired cardiac autonomic nervous activity. *HRV* heart rate variability (**a**), *AVSD* atrial/ventricular septal defect, *BRS* arterial baroreflex sensitivity (**b**), *CoA/IAA* coarctation/interruption of the aorta, *DCM* dilated cardiomyopathy, *HF* high frequency, *H/M* ratio of heart to mediastinal metaiodobenzylguanidine (MIBG) activity (**c**), *RVOTR* right ventricular outflow tract reconstruction, *WR* washout ratio of MIBG (**d**)

pathophysiology [15]. Slower resting HR is frequently seen in athletic adults because of enhanced vagal tone. However, lower HR in postoperative ACHD patients with low aerobic capacity usually indicates an impaired function of the sinus node, in part, due to perioperative surgical insults [16]. Thus, some ACHD patients show inappropriately low HR that is insufficient to compensate for impaired hemodynamics and low systemic blood pressure. In addition, it is frequently difficult to maintain proper systemic blood pressure during rapid postural change because of a diminished vagally mediated quick HR response. Thus, β-receptor stimulation or atrial pacing, rather than atropine infusion, may be effective for increasing HR. Atropine infusion is effective only when vagally mediated HR is preserved.

4.3.2 Ventricular Myocardium Injury

Ventricular denervation is inevitable during arterial switch operation for the transposition of the great arteries (TGA) and Ross operation for aortic valvular disease because these procedures involve a complete transection of the cardiopulmonary

nerves that run along the right and left coronary arteries [17]. Therefore, MIBG scintigraphy is not an appropriate tool to estimate sympathetic nervous activity in these ACHD patients, and this may also hold true to some extent in other surgically treated ACHD patients, especially those with a history of multiple cardiac surgeries [9]. Cardiac reinnervation can occur after these procedures as it does after cardiac transplantation; however, there is currently no effective treatment for promoting reinnervation as the factors promoting natural reinnervation are unknown. Further, postoperative ACHD patients may not complain of any chest pain from cardiac origin even if they have significant myocardial ischemia from coronary artery stenosis because of sensory denervation, especially after arterial switch or Ross operation. Thus, stress electrocardiography (ECG) and/or imaging should be applied to detect the stenotic lesion(s) of coronary arteries in these ACHD patients instead of symptoms.

4.4 Ventricular Dysfunction

The etiologies of ventricular dysfunction include pressure overload due to outflow stenosis, volume overload due to valvular regurgitation and intra/extracardiac shunting, hypoxia before definitive repair, the intrinsic problem of RV myocardium as a systemic ventricle, ischemia due to coronary artery stenosis, tachycardia-induced dysfunction, and intra/interventricular dyssynchrony [5]. In addition, the restrictive changes of the ventricle due to pericardial adhesion and myocardial fibrosis have adverse influences on ventricular function and make HF pathophysiology more complex in postoperative ACHD patients [18, 19].

Pharmacological approaches have limited efficacy in the management of pressure and volume overload due to structural abnormalities; hence, surgical or catheter-based interventions may be required in some ACHD patients. Pulmonary valve replacement (PVR) is one of these interventions [20]; however, the optimal timing of this procedure is still debated. Late definitive repair may predispose cyanotic patients to a subclinical progression of myocardial fibrotic change due to long-standing hypoxia and volume overload [21]. Right ventricular and tricuspid valve (TV) functions should be carefully monitored in ACHD patients with RV as a systemic ventricle to assess suitability for anatomical tricuspid valve replacement.

The conventional anti-HF strategy using angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) and β blockers may be effective for dilated LV with systolic dysfunction in some ACHD patients with relative tachycardia. However, these strategies may be harmful in postoperative ACHD patients with sinus node dysfunction and ventricular restrictive physiology. Furthermore, the long-term efficacy of these conventional strategies is uncertain for subpulmonary ventricular systolic and diastolic dysfunctions. In these scenarios, atrial pacing with appropriate HR corresponding to HF severity may be effective, although finding the optimal HR may be challenging.

Cardiac resynchronized therapy (CRT) has been applied to postoperative ACHD HF patients with some efficacy [22]. The electrophysiological assessment of QRS duration or various imaging modalities may reveal ventricular dyssynchrony; however, a standard diagnostic method has not been established, especially for patients

with non-LV as a systemic ventricle. CRT focusing on the longitudinal direction in systemic RV or the site opposite two-chamber dyssynchrony in Fontan circulation with unbalanced ventricles may be effective for some cases [23].

Right ventricular restrictive physiology characterized by end-diastolic forward flow in the main pulmonary artery is a pathophysiology unique to postoperative ACHD patients, especially repaired TF patients; however, the clinical significance is controversial [24, 25]. The restrictive pathophysiology is one phenotype of the RV diastolic dysfunction and may differ from other types of RV diastolic dysfunction characterized by other criteria, such as HF with preserved RV ejection fraction [18, 19], a more severe subtype of RV pathophysiology. Management strategies for these diastolic dysfunctions are not yet established as the strategies have not been established in HF with preserved LV ejection fraction.

4.5 Electrophysiological Dysfunction

Electrophysiological abnormalities are often associated with atrial and/or ventricular remodeling. The QRS duration reflects RV volume in postoperative TF and systemic ventricular volume in Fontan patients [26–29]. Fragmented QRS complex in adult patients with Ebstein anomaly is associated with risk of arrhythmia and with the severity of the anomaly [30]. The electropathophysiology and its relations with clinical profiles and management strategies are further described in Chap. 5.

4.6 Aortopathy

In the general population, metabolic disorders and obesity lead to endothelial dysfunction, which increases the risk of arteriosclerosis. In turn, arteriosclerosis and hypertension are strong factors predisposing to HF. Arteriosclerosis and hypertension also contribute to HF in ACHD patients. In addition, stiffened dilated ascending aorta, histologically characterized by medial necrosis in the aortic wall, i.e., aortopathy, resembling that of Marfan syndrome, has been described in various types of ACHD, particularly TF [31]. The stiffened dilated aorta has adverse impacts on ventricular function by augmenting blood pressure reflection and decreasing diastolic pressure, i.e., greater pulse pressure, resulting in ventricular pressure overload with impaired coronary perfusion [32]. This may in turn reduce exercise capacity [33] and contribute to metabolic syndrome, obesity, hypertension, arteriosclerosis, and ultimately HF. As demonstrated in Marfan syndrome, ACEIs/ARBs may be beneficial by preventing further progression of aortopathy in some selected ACHD patients.

4.7 Renal Dysfunction

Renal dysfunction due to cardiovascular disease, termed cardiorenal syndrome, has a strong impact on cardiovascular prognosis [34]. ACHD patients are categorized as typical type II cardiorenal syndrome when chronic cardiac problems lead to renal

dysfunction [35, 36]. Elevated central venous pressure (CVP) in ACHD patients with right-sided HF causes renal congestion, whereas low systemic blood pressure results in lower perfusion pressure in the kidney. This vicious interaction may be associated with poor cardiovascular prognosis [37].

Sinus node dysfunction with blunted HR response and stiffened arterial and venous vessels are frequently combined in postoperative ACHD patients [9, 38, 39]. As a result, all organs are perfused through stiffened great vessels by a cardiovascular system with a limited ability to homeostatically regulate cardiac output, especially during stress. For instance, dehydration by any cause may lead to prerenal failure because of impaired baroreflex function, sinus node dysfunction, and less compliant vessels.

4.8 Reduced Exercise Capacity

Impaired exercise capacity is one of the cardinal features of chronic HF. The causes of this impairment are multifactorial [6]. Peak oxygen uptake (VO_2) during cardiopulmonary exercise testing (CPX) is the gold standard metric of exercise capacity. The following equations explain the major determinants of peak VO_2:

$$\begin{aligned} VO_2 &= CO \bullet AVO_2D \\ &= EDV \bullet EF \bullet HR \bullet 1.34 \bullet Hb \bullet \left(SaO_2 - SvO_2\right) \\ &= AOP / Rs\left(\text{or } PAP / Rp\right) \bullet 1.34 \bullet Hb \bullet \left(SaO_2 - SvO_2\right) \end{aligned}$$

where, CO = cardiac output, AVO_2D = arteriovenous oxygen content difference, EDV = ventricular end-diastolic volume, EF = ventricular ejection fraction, HR = heart rate, Hb = hemoglobin level, SaO_2 = arterial oxygen saturation, SvO_2 = mixed venous oxygen saturation, AOP = arterial pressure, PAP = pulmonary pressure, Rs = systemic artery resistance, and Rp = pulmonary artery resistance. The parameters EDV•EF, HR, Hb, SaO_2, and SvO_2 reflect cardiac function, sinus node function and CANA, oxygen transport capacity, pulmonary gas exchange, and peripheral factors, including skeletal muscle metabolism, respectively. The resistance terms Rs and Rp reflect the endothelial function of the systemic and pulmonary arteries, respectively. In addition, ventricular morphology, the synchronicity of ventricular contraction, and AV valve function also have significant impacts on peak VO_2. Perioperative myocardial insults, such as fibrotic change and diastolic restriction due to pericardial adhesion and/or calcification, are major causes of ventricular diastolic dysfunction, leading to limited EDV and impaired exercise capacity [18]. Thoracic surgeries, including palliative operations, inevitably cause restrictive ventilatory impairment, which is one reason for ventilation/perfusion mismatch in the lung and for small tidal volume during exercise. Small tidal volume leading to rapid-and-shallow respiration also increases dead space ventilation during exercise, which is in part responsible for low SaO_2 in some ACHD patients. Oxygen is consumed mainly by skeletal muscle during exercise; therefore, deconditioning (disuse) atrophy of skeletal muscle is a major reason for low peak VO_2 in chronic diseases, including cardiovascular disease [40]. At the same time, reduced skeletal muscle bulk impairs

muscle blood pumping, which normally plays a crucial role in preserving cardiac preload during exercise. Furthermore, a stiffened aorta adversely impacts ventricular function due to augmented reflex pressure and diminishes vascular volume reserve capacity, both of which may also reduce exercise capacity [33, 41, 42]. Reduced peak VO_2 is closely associated with poor prognosis in ACHD patients; therefore, interventions that increase exercise capacity, such as aerobic exercise training, may improve prognosis.

4.9 Biomarkers

Biomarkers are important assessment tools for HF severity in ACHD patients [43]. The clinical significance of plasma natriuretic peptide (NP) levels, especially brain NP (BNP), has been most intensively studied and validated in some cases. However, the clinical utilities of other possible markers, such as catecholamines and renin–angiotensin–aldosterone system hormones, have not been as extensively examined. Plasma NP levels are already increased in asymptomatic ACHD patients with HF irrespective of whether RV is a subpulmonary or systemic ventricle. The determinants of elevated plasma NP include RV volume overload due to intracardiac shunting, pulmonary and/or AV valve regurgitation, RV dysfunction due to pressure overload, and hypoxia due to unrepaired complex lesions or Eisenmenger syndrome (ES). Plasma NP levels are frequently lower in postoperative ACHD patients than in adults with non-ACHD HF even if NYHA class is equivalent [9, 18, 44], and the cutoff value for prognosis is usually lower in postoperative ACHD patients because of the restrictive physiology. Nevertheless, the high levels of NP and catecholamine predict poor prognosis, including mortality in ACHD patients with NYHA class $\geq$ III [unrepaired, ES, and pulmonary hypertension (PH)] [45]. In particular, a progressive increase in plasma BNP during follow-up strongly predicts mortality [46, 47]. However, evidence for the prognostic efficacy of biomarkers is mainly based on studies including a relatively small number of ACHD patients with mild HF, mostly NYHA class $\geq$ II (repaired TGA or TF patients). These limitations weaken the associations between biomarker levels and cardiac function. However, in adult Fontan patients, the high plasma levels of NP and catecholamines are associated with poor prognosis [48, 49]. In addition, BNP reflects RV volume reduction after PVR and improved PH after medical treatment [50, 51]. Therefore, measuring plasma biomarkers can provide clinically useful information for assessing HF pathophysiology, especially in complex ACHD patients. Although the clinical significance of higher plasma NP for assessing ACHD patients with stretched atrial and/or ventricular myocardium (congestive HF) is well established, abnormally low NP may be a reflection of ventricular underfilling due to low cardiac output, for instance, from dehydration, which is also a critical pathophysiology. Thus, comprehensive HF assessment by multiple modalities, including physical examination, is mandatory for the care of ACHD patients.

The unique HF pathophysiology of ACHD characterized by surgery-related CANA abnormality and restrictive ventricular function is presented schematically

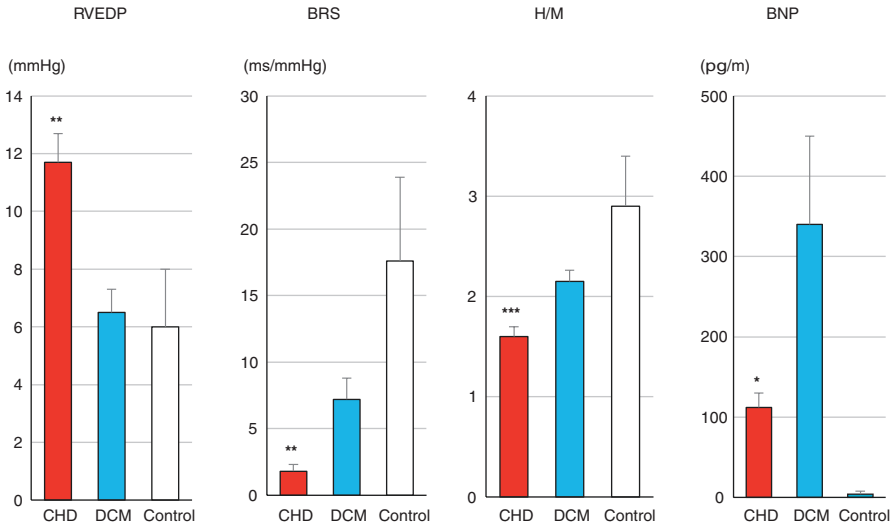

Fig. 4.4 Comparison of clinical variables among postoperative patients with congenital heart disease, dilated cardiomyopathy patients without surgery, and controls. The two patient groups are comparable in terms of systemic ventricular ejection fraction and functional capacity. *, **, and *** = $p < 0.05$, 0.01, and 0.001, vs. DCM, respectively

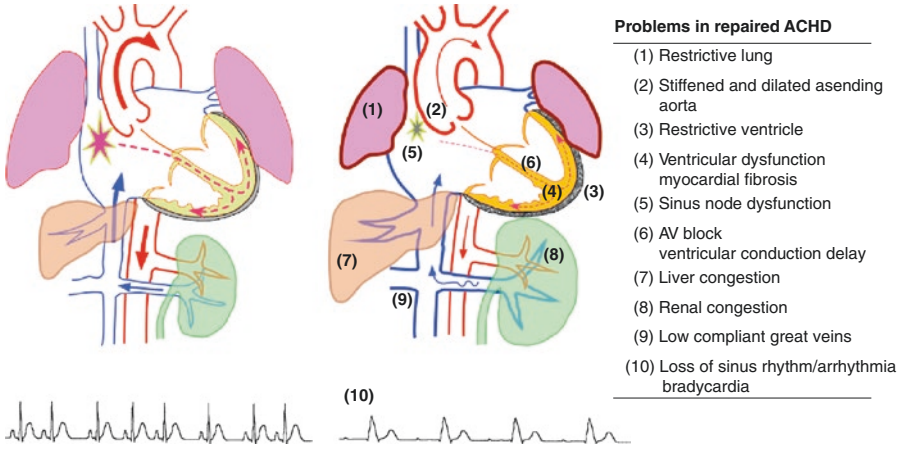

Fig. 4.5 The pathophysiology of postoperative ACHD is summarized

in Fig. 4.4, together with a comparison of clinical variables among postoperative patients with CHD, those with dilated cardiomyopathy (DCM, no surgery), and healthy controls. The two patient groups are comparable in terms of systemic ventricular EF and functional capacity. However, they show distinct hemodynamics, CANA variables, and plasma BNP levels. Finally, HF pathophysiology is summarized in Fig. 4.5. Some of these pathophysiological features are, to some extent, applicable to the following specific postoperative ACHDs.

4.10 Specific Pathophysiology

4.10.1 Tetralogy of Fallot

TF is the most common cyanotic CHD. Thirty years after definitive repair, postoperative survival rate is more than 90% [52]. However, despite this low long-term mortality, repaired adult TF patients have significant postoperative residual lesions and complications that include RV dysfunction due to RV outflow problems [pulmonary stenosis and/or pulmonary regurgitation (PR)] [53], LV dysfunction partially due to RV–LV interactions [54, 55], and clinically relevant atrial and/or ventricular arrhythmias, which may cause sudden cardiac death [56].

4.10.2 Right Ventricular Problems

TF is occasionally considered as a disease of the RV infundibulum; hence, management strategies may be focused on preserving infundibulum structure and function [57]. There is wide agreement on interventions for significant RV outflow stenosis because it is a major determinant of exercise capacity [18] and is closely associated with RV hypertrophy and clinically relevant arrhythmias. However, mild residual RV outflow stenosis may mitigate the need for PVR, probably due to lower PR and a positive RV–LV interaction [58, 59]. Significant RV volume overload due to PR is tolerable for a long time; however, PR-related RV dilatation ultimately becomes a main driver of adult TF pathophysiology, and PVR is required in some patients with severe PR [53]. Although firm criteria for PVR are not yet established, repaired TF patients with a RV volume ≥150–170 (mL/m^2) plus other clinical findings, such as QRS ≥ 180 ms, exercise intolerance, and significant ventricular arrhythmia, are considered good candidates for PVR. A meta-analysis of PVR in repaired TF revealed significant clinical benefits, including RV volume reduction, LV volume increase with improved EF due to positive RV–LV interactions, improvement of NYHA class, and shortening of QRS duration [20]. Better exercise capacity predicts better postoperative course after PVR [60]; however, the long-term prognostic impact of PVR for TF is unknown [61]. Regarding tricuspid regurgitation (TR), which is also common in late after the TF repair, significant TR has an adverse impact on prognosis in normal structural heart [62]. However, its impact on morbidity and mortality remains unclear in repaired TF. Recent study showed little beneficial impact of concomitant TV repair of TR (≥ moderate) on short to mid-term postoperative RV function and TR when compared with those without TV repair at the time of PVR although both RV function and TR improve significantly in both groups [63].

4.10.3 Restrictive Physiology (RP)

RP is a unique RV pathophysiology defined by the presence of diastolic forward flow in the main pulmonary artery [24], which can be seen in both

pathophysiologies with large and small RV volumes [64]. However, the clinical significance remains unclear [18, 64]. RP is seen in pediatric TF patients with poor postoperative course [25], whereas RP prevents PR and contributes to preserved exercise capacity in repaired adult TF patients [24, 64]. Fibrotic change and/or the extracardiac restriction of RV due to pericardial issues may be responsible for RP. Right ventricular fibrotic change is closely associated with the impaired ventricular function as well as poor prognosis in these patients. In addition, diastolic dysfunction defined by echocardiographic variables, including those from tissue Doppler imaging, is associated with a high prevalence of ventricular tachycardia [65]. Furthermore, there is an additional severe phenotype of RV pathophysiology, the RV-version of HF with preserved EF (RV-HFpEF) [18]. Similar to the LV-version of HFpEF, there is currently no standard management strategy for RV-HFpEF.

4.10.4 LV Deficits

Low LVEF (≤55%) is not uncommon in ACHD (45% of patients) [66] and is a risk factor for sudden death. The rate of appropriate shock by an implantable cardioverter-defibrillator is high in repaired TF patients with LV end-diastolic pressure ≥ 12 mmHg [67], and poor LV function is a risk factor for unsuccessful anti-arrhythmic catheter ablation [68]. Furthermore, the prognostic power of LV dysfunction may be greater than that of RV dysfunction [69].

4.10.5 Stratification of HF

Plasma BNP level and CPX-derived variables can be used to stratify HF severity in repaired adult TF patients. Plasma BNP ≥ 52 pg/mL predicts fivefold higher mortality [70]. However, plasma BNP level alone may underestimate HF severity because of possible RP, which can lower myocardial stress even if end-diastolic pressure is high ([9, 18, 44], Fig. 4.4). Low peak VO_2 (≤36% of predicted normal value) and low ventilatory efficiency (high VE/VCO_2 slope ≥ 39) predict high mortality in these patients [71].

4.10.6 Management of HFs

RCTs examining medical management of repaired TF patients have been few [72]. In one RCT, β blockers and ACEIs/ARBs were ineffective in the overall analysis [73], but subanalysis indicated that 6-month administration of ACEI (Ramipril) improved LVEF with significant volume reduction in selected repaired TF patients with RP [74]. Another study found favorable results using CRT with biventricular stimulation in a small number of patients (n = 5) [75]. Larger-scale RCTs are required before this procedure can be applied in daily practice.

4.11 Transposition of the Great Arteries with RV as a Systemic Ventricle

Dextro-TGA (d-TGA) is the most common cyanotic CHD followed by TOF. It is managed by atrial switch operation (Mustard/Senning procedure: venous switch operation [VSO]) or arterial switch operation (Jatene procedure). VSO contributed to the dramatically improved survival rate of d-TGA in the 1960s. However, long-term postoperative pathophysiology has emerged that includes RV dysfunction as well as TR and rhythm disturbance [26, 76, 77]. Congenitally corrected TGA (c-TGA) is a rare form of CHD with pathophysiology resembling that of d-TGA after VSO in which RV acts as a systemic ventricle and features RV dysfunction, TR, and arrhythmias [78]. Congenitally c-TGA patients frequently have combined lesions, such as pulmonary stenosis, ventricular septal defect, Ebstein anomaly, and AV block, all of which have significant negative impacts on prognosis.

The overall 40-year post-VSO survival rate is approximately 50%; however, the survival rate is approximately 70% if the patient survives the immediate postoperative period [76]. Although the impact of atrial switch procedure type, either Mustard or Senning, on mortality is still unclear, combined lesion(s), pulmonary stenosis, and ventricular septal defects increase mortality [76]. In adult c-TGA patients, the prevalence of clinical HF and moderate to severe RV dysfunction at 45 years of age is 25–30% for those without combined lesions and 60–70% for those with substantial combined lesions [78]. The possible etiologies of RV dysfunction include myocardial ischemia and infarction [79, 80] associated with reduced coronary flow reserve and the resulting limitation on exercise capacity as well as the single coronary physiology of RV [81, 82]. Systemic RV fibrosis is associated with ventricular dysfunction and poor prognosis [77], although the cause of RV fibrosis remains unclear. However, a causal relationship between RV dysfunction and TR has not been established.

4.11.1 Assessment of Systemic RV function

The QRS duration and QTc reflect RV volume and RVEF, respectively, whereas QT dispersion is associated with clinical arrhythmia [27]. During follow-up, these ECG parameters worsen in ACHD patients with RV pressure load [83]. The Tei index and RV longitudinal strain are useful echocardiographic variables to evaluate RV function and predict prognosis [84, 85]. Plasma BNP levels are also useful to assess RV dysfunction and TR severity [86, 87]. Plasma BNP $\geq$ 85 pg/mL may predict cardiac events in repaired d-TGA after VSO [88]. Intriguingly, moderate pulmonary outflow stenosis protects against HF in c-TGA patients, probably because of a shift of the interventricular septum, which prevents the TV orifice from dilating and promotes positive RV–LV interactions [85], leading to better prognosis [89].

4.11.2 Exercise Pathophysiology

Exercise capacity and related systemic blood pressure responses are impaired in d-TGA and c-TGA patients [90–92], and these impairments are associated with poor prognosis [92]. RVEF and Tei index predict exercise capacity [93]. Rigid (less compliant) atrium may be responsible for the blunted increase in stroke volume during exercise in adults after VSO, resulting in lower exercise capacity, whereas this mechanism may not be applicable to adult c-TGA patients [94]. Interestingly, the rate of cardiac events, including AV block, is lower in c-TGA patients with dextrocardia (situs inversus) than those with levocardia (situs solitus) [95].

4.11.3 Management of Adults with d-TGA or c-TGA

The ARB, valsartan, may prevent exercise capacity from declining during follow-up in d-TGA and c-TGA patients, although no benefits of valsartan on RV remodeling or cardiac events have been demonstrated [96]. On the other hand, exercise training is effective for improving exercise capacity [97], and CRT may be effective in selected patients [22, 23]. For severe TR, TV replacement surgery rather than TV plasty is recommended before RVEF falls below 40% [98, 99].

4.12 Single Ventricular Physiology (Fontan Circulation)

The Fontan operation is performed for complex CHD patients with functional single ventricular physiology, such as those with tricuspid atresia, to eliminate hypoxia and volume overload to the functional systemic ventricle (FSV). The procedure has developed from atriopulmonary connection to total cavopulmonary connection comprising intra-atrial rerouting and extracardiac rerouting (ECR). ECR is currently the main procedure for CHD patients with FSV [100].

4.12.1 Pathophysiology of Fontan Circulation

Because of the lack of a subpulmonary ventricle, elevated CVP and suction power of FSV (diastolic function) are critical for creating the driving pressure needed for pulmonary flow in patients with Fontan circulation. Consequently, high CVP, low cardiac output due to diminished cardiac preload and elevated Rs, and mild but significant hypoxia characterize Fontan patients. In addition to low Rp, the augmentation of cardiac preload by lower limb muscle pumping and respiratory suction also contribute to circulation. Fontan patients have limited exercise capacity, 50–60% of normal, irrespective of the type of surgical procedures [101]. There are growing concerns regarding the chronic adverse influences of venous

hypertension on multiple organs, especially on hepatorenal and intestinal function. Of these adverse influences, the most pressing problems are cardiovascular deficits, such as arrhythmias and impaired FSV function (including atrioventricular dysfunction); respiratory deficits, such as pulmonary arteriovenous fistulae and plastic bronchitis; hemostatic problems, such as pulmonary embolism, stroke, and hemoptysis [102–104]; protein-losing enteropathy (PLE); and hepatorenal dysfunction [36]. Liver problems are now recognized as a distinct entity, Fontan-associated liver diseases, which include liver cirrhosis and hepatocellular carcinoma.

The 20-year mortality-free rate after surgery for Fontan circulation patients ranges from 69 to 87% [105–107], and survival rate has dramatically improved mainly because of improved early postoperative survival rate. However, long-term morbidity and mortality are still high irrespective of the type of surgical procedure.

4.12.2 Assessment of HF

The elevated plasma levels of norepinephrine, BNP, and uric acid are associated with higher clinical event rates [108, 109]. Fontan patients show a blunted HR response and reduced peak VO_2 due to impaired CANA [110–112]. Major CPX-derived variables, especially lower peak VO_2, predict morbidity and mortality in Fontan patients [111]. Impaired FSV contractility with lower work efficiency and higher afterload may contribute to failing Fontan circulation [28]. A recent FSV volume study using MRI revealed that large FSV (end-diastolic index $\geq$ 125 mL/m^2) plus the presence of PLE predicted poor prognosis [113]. In addition, FSV morphology, LV FSV or non-LV FSV, also determines its function and pathological relevance. The QRS duration is longer in Fontan patients with non-LV FSV, and this may stem from dyssynchronized ventricular contraction in some cases [28], with negative impacts on hemodynamics during tachyarrhythmia and exercise [28, 114]. A stiffened aorta also has an adverse impact on FSV function by augmenting pressure reflection at lower coronary perfusion pressure due to lower diastolic pressure [115]. Furthermore, endothelial impairment is associated with reduced exercise capacity [116, 117]; therefore, nitric oxide-associated vascular function, including that of the pulmonary vasculature [118], is important for better Fontan physiology.

4.12.3 Management of HF

Management strategies for HF in failing Fontan patients have not been established. It is convenient to separate medical interventions into two types depending on the pathophysiology targeted: treatments for impaired pulmonary circulation and treatments for deficient systemic circulation. The latter include FSV issues.

4.12.4 Systemic Circulation

Diuretics are effective for inappropriate fluid retention, such as edema, pleural effusion, and ascites. However, diuretic use is an independent risk factor for mortality; thus, an unjustified use of diuretics should be avoided, as demonstrated in adult HF patients with non-CHD [107, 119]. No clear benefits of ACEIs/ARBs have been demonstrated in either pediatric or adult Fontan patients for the improvement of CANA and exercise capacity, at least after a relatively short administration period [120–122]. However, the long-term impacts of ACEIs/ARBs on survival are unknown. There are only a few case reports on the efficacy of β blockers [123]. Most postoperative ACHD patients, including Fontan patients, tend to have a slower resting HR, probably due to surgery-associated sinus node dysfunction [16]; therefore, an inappropriate administration of β blockers may be harmful for hemodynamics. Considering this general lack of drug efficacy, pacemaker implantation may be an option to guarantee adequate HR for the management of HF as well as refractory arrhythmias. In case of AV block, special attention should be paid to the pacing site of FSV to avoid dyssynchronous contraction. The pacing site should be in the longitudinal direction in patients with RV as FSV and at the opposite sites of both ventricles in patients with unbalanced biventricle as FSV [23].

4.12.5 Pulmonary Circulation

Better pulmonary circulation is crucial for an improved long-term outcome of Fontan physiology as high Rp easily collapses the circulation. The PDE-5 inhibitor sildenafil (20 mg three times a day) for 6 weeks improved ventilatory efficiency and exercise capacity [124], and a single daily dose of tadalafil (1 mg/kg) for 6 weeks improved exercise capacity as well as cardiac function [125]. The improved HR response and prevention of exercise-induced elevation of Rp and Rs, rather than augmented stroke volume due to higher cardiac preload, are responsible for these benefits [126]. There may be no direct beneficial cardiac effect of PDE-5 inhibitors during exercise [127]. A single dose of the pulmonary arterial hypertension medication iloprost (5.0 μg) improved exercise capacity, especially in patients with low baseline capacity [128]. The efficacy of the endothelin-1 receptor blocker bosentan was also demonstrated in RCT [129]. The administration of bosentan (62.5 mg twice a day for 2 weeks, followed by 125 mg twice a day for 12 weeks) improved exercise capacity and NYHA class compared with those in controls (2.0 vs. 0.6 mL/kg/min, $p < 0.05$). However, long-term PA remodeling (decreased medial thickness and increased intimal thickness) may influence the efficacy of pulmonary artery dilators [130].

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Rhythm Disturbance/Sudden Death

5

Aya Miyazaki

Abstract

The arrhythmogenicity in adult congenital heart disease (ACHD) is mainly related to two factors: congenital abnormalities in the conduction system and acquired unique hemodynamic abnormalities. Aging is an important factor that affects these arrhythmogenicity, mainly resulting in a deterioration of rhythm disturbance. The key to congenital abnormalities in the conduction system is the atrial morphology of both the atria and atrioventricular connection through which the conduction system passes. The acquired unique hemodynamic abnormalities in ACHD are represented by disorders of the subpulmonary right ventricle, systemic right ventricle, Fontan circulation, and unrepaired cyanotic congenital heart disease. Previously reported risk stratification tools for sudden cardiac death in adults with non-congenital heart disease are also relevant in ACHD, especially electrocardiographic findings, but their sensitivities are far from excellent. Disease-specific treatment strategies based on understanding individual arrhythmogenicities are essential for rhythm disturbance in ACHD.

Keywords

Rhythm disturbance • Sudden cardiac death • Conduction system • Hemodynamic abnormality • Aging

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5.1 Introduction

Progress in surgical techniques and medical care has significantly improved the survival rates of patients with congenital heart disease [1]. Therefore, the number of patients with adult congenital heart disease (ACHD) keeps increasing every year. Among late comorbid disorders, rhythm disturbance is a prime concern in ACHD [2]. The arrhythmogenicity in ACHD is mainly related to two factors: congenital abnormalities in the conduction system and acquired unique hemodynamic abnormalities. In addition, aging is an important factor that affects these arrhythmogenicity, mainly resulting in a deterioration of rhythm disturbance (Fig. 5.1). The changes caused by aging in congenital or acquired arrhythmogenicity are big concerns in the field of ACHD.

Furthermore, sudden death is a major cause of death, accounting for 7–26% of all deaths in ACHD. The incidence of sudden death also increases with age [3]. Most but not all sudden deaths in these patients presumably arise from rhythm disturbance [4]. Therefore, preventing sudden death in ACHD is another concern. However, we still do not have generalized risk stratification for the primary prevention of sudden death in CHD because of the marked heterogeneity of the underlying cardiac defects [5].

Subsequent to the improvement in survival rates of ACHD, the answers to these concerns will be provided by the clinical findings of the long-term survivors of

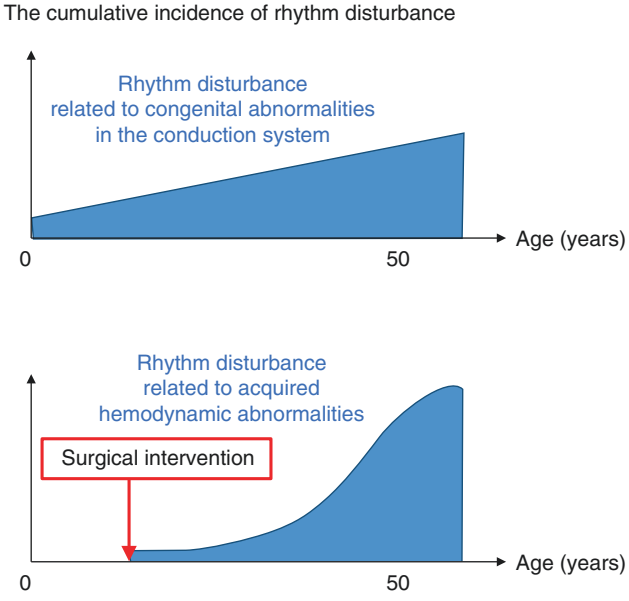

Fig. 5.1 The presumable curve of the incidence of rhythm disturbance related to congenital abnormalities in the conduction system (*upper*) and acquired hemodynamic abnormalities (*lower*)

ACHD. In this chapter, we consider the changes caused by aging in the congenital and acquired arrhythmogenicity, showing the representative cardiac abnormalities in ACHD. Then, we discuss the features of sudden death due to rhythm disturbance.

5.2 Congenital Abnormalities in the Conduction System

The key to the congenital abnormalities in the conduction system is the atrial morphology in both atria and the atrioventricular (AV) connection where the conduction system passes through. A summary of the impact of aging on rhythm disturbance related to the congenital conduction abnormalities in representative diseases is shown in Table 5.1.

5.2.1 Atrial Situs

In atrial isomerism, so-called heterotaxy syndrome, the atrial appendages are mirror images of each other, either morphologically right or left atrial appendages. A terminal crest, which works as an anatomical barrier for the reentrant circuits, is reported to exist bilaterally in 87% of the patients with right atrial isomerism but is absent bilaterally in 88% of those with left atrial isomerism [6]. The presence of bilateral terminal crest is the reason of a high incidence of intra-atrial reentrant tachycardia (IART) in right atrial isomerism [7]. Atrial fibrillation (AF) and non-reentrant supraventricular tachycardia (SVT) were frequently observed rather than macro-reentrant tachycardia in left atrial isomerism [8]. The lack of anatomical barriers and the high prevalence of sinus node dysfunction with aging may account for the higher incidence of AF and non-reentrant SVT in left atrial isomerism [8, 9].

Various conduction abnormalities are often observed in hearts with atrial isomerism. In the pathological findings of 35 hearts (10 with right atrial isomerism and 25

Table 5.1 Impact of aging on rhythm disturbance in congenital conduction abnormalities in representative diseases

	Right atrial isomerism	Left atrial isomerism	AVD
Sinus node dysfunction	–	↑↑	–
AV block	–	(↑)	↑↑
Atrial arrhythmias	↑↑	↑↑	–
Atrial fibrillation	–	↑↑	
Twin AV nodes reciprocating tachycardia	(↓)	(↓)	(↓)
Ventricular arrhythmias	–	–	–

Parenthetical arrows indicate no evidence but the expected result
AV atrioventricular, *AVD* atrioventricular discordance
↑, increase with age; ↓, decrease with age; –, no remarkable change with age

with left atrial isomerism), bilateral sinus nodes were present in 90% of the hearts with right atrial isomerism, whereas solitary and hypoplastic sinus nodes were present in 44% and not found in 56% of the hearts with left atrial isomerism [10]. Twin AV node physiology was present in all of hearts with right atrial isomerism but in only 32% of those with left atrial isomerism [10]. Conduction bundles under the AV node were also reported to be unique. Some had a common conduction bundle between two separate AV nodes (twin AV nodes), and some had separate bundles in the twin AV nodes, with or without a connecting sling [10, 11]. In the cases with twin AV nodes, SVT involving two AV nodes (twin AV node reciprocating tachycardia) is sometimes observed. Wu et al. [12] reported that twin AV nodes were more frequent in right atrial isomerism with balanced ventricles instead of a dominant ventricle and would increase the risk of SVT. SVT in such patients could be managed by ablation or medication and was not associated with mortality. They also mentioned that SVT episodes were uncommon after the age of 15 years, maybe because the reentry between twin AV nodes is less sustained in adult patients with larger hearts and slower AV conduction owing to the maturation of the AV nodal conduction. Further, another unique form of SVT, adenosine-sensitive focal junctional tachycardia, was reported [13]. There are several controversial issues in these unique SVTs, such as their incidence, prognosis, and the participation or not of connecting slings.

5.2.2 AV Connection

AV connection is related to the development of the AV conduction system. The conduction system in AV discordance (AVD) is thought to be related to septal alignment. In congenitally corrected transposition of the great arteries (ccTGA), which is a representative anomaly of AVD, malalignment of the interatrial and interventricular septa usually results in a gap that prevents a normally located AV node (posterior AV node) from communicating with the ventricular conduction bundles, forming an anterior AV node [14]. The anterior AV node is situated in the right atrium at the lateral junction of the pulmonary and mitral valves, and the bundle courses anterior to the pulmonary artery to reach the anterior part of the interventricular septum. In cases of AVD with the presence of a small or atretic pulmonary trunk, the septa were well aligned and the posterior positioned AV node, the so-called posterior AV node, connected to an AV bundle [15]. The superiority of a posterior or anterior AV node is determined by whether the septa are aligned or maligned, and some have both AV nodes (twin AV nodes) with a connecting sling [15]. AV block spontaneously develops with aging because of the abnormal AV conduction system. However, in a study of a small number of cases (n = 8), AV block was reported to rarely occur in ccTGA with situs inversus because of the predominant posterior AV node, which might be related to good septal alignment [16]. Further, twin AV node reciprocating tachycardia and adenosine-sensitive focal junctional tachycardia could occur in this setting.

5.3 Acquired Unique Hemodynamics

A summary of the impact of aging on rhythm disturbance related to acquired hemodynamic abnormalities is shown in Table 5.2.

5.3.1 Diseases of the Subpulmonary Right Ventricle

Representative diseases of the subpulmonary right ventricle (RV) are repaired tetralogy of Fallot (TOF) and double-outlet right ventricle (DORV). Atrial and ventricular arrhythmias and exertional dyspnea from progressive RV dilatation due to chronic pulmonary regurgitation or severe residual RV outflow tract obstruction occur in 10–15% of patients within 20 years after the initial repair [17]. The prevalence of these arrhythmias increases with age; in particular, atrial fibrillation and ventricular arrhythmias markedly increase after 45 years of age [18]. The arrhythmogenicities of this disease are reported in many papers.

Regarding ventricular arrhythmias, histological findings in repaired TOF with ventricular tachycardia (VT) showed degeneration, adiposis, fibrosis, and scattered myocyte islets in the area of the RVOT [19, 20]. Late gadolinium enhancement (LGE), cardiovascular magnetic resonance (CMR), and a fragmented QRS complex are useful markers to observe myocardial fibrosis in the RV of repaired TOF and are related to the arrhythmic events [21, 22]. Further, common anatomical isthmuses for VT are present in repaired TOF and DORV, and a VT isthmus ablation was reported to be possibly curative only in patients with a preserved ventricular function and isthmus-dependent reentry [23].

To the best of our knowledge, there have been no histological evaluations of atrial tachyarrhythmia, but the right atrial area index measured by CMR was a strong predictor of new-onset atrial tachyarrhythmia [24]. The arrhythmogenic substrate of atrial tachyarrhythmia is mostly related to the right atrial side, especially the right atrial free wall [25, 26].

Table 5.2 Impact of aging on rhythm disturbance in acquired hemodynamic abnormalities

	Subpulmonary RV disease	Systemic RV disease	Fontan circulation
Sinus node dysfunction	↑	↑↑ (AtSO-TGA)	↑↑
AV block	–	–	–
Atrial arrhythmias	↑↑	↑↑ (AtSO-TGA)	↑↑
Atrial fibrillation	↑	↑	↑
Ventricular arrhythmias	↑	↑	↑

AtSO-TGA transposition of the great arteries after an atrial switch operation, *AV* atrioventricular, *RV* right ventricle

↑, increase with age; ↓, decrease with age; –, no remarkable change with age

5.3.2 Diseases of Systemic RV

The representative diseases of systemic RV are transposition of the great arteries after an atrial switch operation (AtSO-TGA) and ccTGA. Both diseases carry a risk of atrial and ventricular tachyarrhythmia, which may be related to ventricular dysfunction and fibrosis deteriorating with age [27–30]. However, the arrhythmias that occur within these unique hemodynamics were mostly evaluated in patients with AtSO-TGA.

Regarding ventricular arrhythmias in AtSO-TGA, to the best of our knowledge, there have been no histological findings or evaluations of common anatomical isthmuses. The risk factors of sustained VT and/or sudden death have been reported to be age, systemic ventricular functions, and duration of the QRS complex [29, 31]. The RV ejection fraction was negatively correlated with age and LGE CMR, and QRS duration was negatively correlated with RV ejection fraction and positively correlated with LGE CMR [29, 32]. Moreover, LGE CMR was associated with clinical outcome, mainly new-onset atrial and ventricular tachyarrhythmia [33]. Given these results, the etiology of ventricular arrhythmias in AtSO-TGA was suspected to be related to RV fibrosis. Another possible etiology is that the rapid ventricular response in SVT induces ventricular arrhythmias.

Regarding atrial arrhythmias in AtSO-TGA, the common anatomical isthmuses of IART and origin of focal atrial tachycardia have been well described [34]. The recent technique of catheter ablation promised a good success rate [35]. However, SVT often becomes life-threatening, and its mechanism is still controversial [36]. There are several hypotheses: atrial tachycardia rates tend to be slower than with atrial flutter, leading to 1:1 conduction, which in turn may result in hemodynamic instability; SVT itself may induce VT or ventricular fibrillation with a rapid ventricular response [37, 38, 34]. Further, the incidence of sinus node dysfunction increases with age as well as atrial tachyarrhythmia [39].

5.3.3 Fontan Circulation

With the modification of the Fontan procedure and progress in surgical techniques, the mortality rate and incidence of arrhythmias have decreased in patients with Fontan circulation [40]. In the original Fontan procedure, the pulmonary artery is directly connected to the atrium, the so-called atriopulmonary connection (APC). In this type of procedure, the atria are exposed to both pressure and volume overload. In a total cavopulmonary connection (TCPC), both the supra vena cava and the infra vena cava connect to the pulmonary artery. Several types of TCPC exist: intra-atrial rerouting or intra-atrial lateral tunnel, intra-atrial graft, and extracardiac rerouting (ECR). In the modern era, the ECR type of TCPC is performed most frequently because ECR has several benefits to avoid atrial suture lines and preserve low atrial pressure compared with other types of TCPC [41].

In patients with Fontan circulation, the incidence of atrial tachyarrhythmia and sinus node dysfunction increases with age [42–44]. The most frequent atrial

tachyarrhythmia is IART followed by AF, focal atrial tachycardia, and reentrant SVT [43, 44]. In a report of long-term outcomes of 1052 patients at the Mayo Clinic, the proportion of IART, AF, focal atrial tachycardia, and reentrant SVT among 412 patients who were diagnosed new arrhythmias after the Fontan operation were 74%, 39%, 26%, and 9%, respectively [44]. There is no doubt that the APC-type Fontan procedure has the highest risk of atrial tachyarrhythmia among the different types of Fontan procedure. In the report of catheter ablation for IART in APC Fontan, both age and time since Fontan surgery were correlated to the extent of low-voltage areas [45]. The incidence of atrial arrhythmias in TCPC is lower than that in APC; however, it still occurs over time. Whether ECR is of greater benefit in avoiding atrial tachyarrhythmia and sinus node dysfunction than intra-atrial lateral tunnel is a controversial issue [41, 43, 46, 47]. We also need to know that the atrial tachyarrhythmia deteriorates the hemodynamics of the Fontan circulation, and the presence of atrial tachyarrhythmia was associated with higher morbidity and mortality [48, 49].

Ventricular tachyarrhythmia has also been reported as a late comorbidity of the Fontan procedure, but the incidence is lower than that of atrial tachyarrhythmia (3.5–10%) [42, 44]. The ventricular myocardial fibrosis measured by LGE CMR was reported to be related to the incidence of ventricular tachyarrhythmia [50].

5.3.4 Unrepaired Cyanotic Congenital Heart Disease

Atrial and ventricular arrhythmias also increase in patients with unrepaired cyanotic congenital heart disease, although there are no reports that discuss this in detail thus far. However, this population accounted for approximately 10% of sudden cardiac deaths in a cohort of patients with ACHD [4, 51]. And we found that unrepaired cyanotic congenital heart disease accounted for 13 (43%) of the 30 ACHD patients given oral amiodarone and eight (15%) of the 54 ACHD patients with AF (unpublished data). Arrhythmia events are supposed to be related to the myocardial damage due to the long-term hypoxemia and the atrial and ventricular overload due to the high pulmonary blood flow.

5.4 Sudden Death

The proportion of sudden cardiac death among the modes of death in ACHD has gradually decreased in recent decades, possibly because of the progress in medical care, accounting for 23% of 176 deaths from 1958 to 1996 [52], 19% of 1189 deaths from 1970 to 2011 [51], and 7% of 524 deaths from 1991 to 2013 [3]. An article about the trend of mortality in ACHD from 1979 to 2005 also showed that the incidence of arrhythmic deaths gradually decreased [53]. Currently, sudden cardiac death is the second largest cause of mortality in ACHD patients following heart failure, and it also increases with age [3]. However, no randomized clinical trials have been performed to delineate risk factors for sudden cardiac death in ACHD thus far [54].

In adults with myocardial infarction or left ventricular dysfunction (non-CHD), there are several risk stratification tools for sudden cardiac death: cardiac imaging, electrocardiography (ECG) depolarization abnormalities, autonomic measures, ECG repolarization measures, and provocative testing/screening for nonsustained arrhythmias [55]. The value of these tools applying to ACHD is shown in Table 5.3. Systemic ventricular dysfunction was reported as a significant predictor according to multivariate analyses in two representative papers of sudden cardiac death in ACHD [51, 56]. The QRS duration, QT dispersion, SVT, and subpulmonary ventricular function were also significant predictors in the most detailed large-population study [51]. LGE CMR, QRS fractionation, and electrophysiology studies provide disease-specific evidence. The usefulness of LGE CMR to predict VT and sudden cardiac death were reported in repaired TOF and AtSO-TGA [21, 33]. QRS fractionation was associated with arrhythmic events in patients with Ebstein's anomaly and with extensive RV fibrosis and dysfunction in repaired TOF [57, 22].

Table 5.3 Usefulness of sudden cardiac death risk stratification tools in adults with congenital heart disease

Domain[a]	Technique[a]	CHD
Cardiac imaging	Global systemic ventricular dysfunction	◎
	Myocardial scar assessment (MRI, SPECT, PET)	○
ECG depolarization abnormalities	QRS duration	◎
	QRS fractionation	○
	Signal-averaged ECG	
Autonomic measures	Heart rate variability	×
	Heart rate turbulence	
	Baroreceptor sensitivity	×
	Imaging: SPECT (MIBG), PET	×
ECG repolarization measures	T-wave alternans	
	QT dispersion	◎
	QRS-T angle	
	QT interval	△
Provocative testing/screening for nonsustained arrhythmias	Electrophysiology study	○ (AtSO-TGA ×)
	PVC/NSVT on ambulatory ECG monitoring	△
Others	SVT	◎
	Subpulmonary ventricle dysfunction	◎

AtSO-TGA transposition of the great arteries after atrial switch operation, *ECG* electrocardiography, *MIBG* [^{123}I] metaiodobenzylguanidine imaging, *MRI* magnetic resonance imaging, *NSVT* nonsustained ventricular tachycardia, *PET* positron-emission tomography, *PVC* premature ventricular contraction, *SPECT* single-photon emission computed tomography, *SVT* supraventricular tachycardia

◎, evidence in sudden cardiac death cases; ○, disease-specific evidence; △, controversial evidence; ×, no evidence or negative evidence

[a]The tools listed refer to those evaluated in a previous study of sudden cardiac death risk stratification in adults with left ventricular dysfunction (non-congenital heart disease) [55]

The ventricular stimulation test in an electrophysiology study was reported as a useful predictor of clinical VT and sudden cardiac death in repaired TOF but not in AtSO-TGA [58, 37]. A signal-averaged ECG, QT interval, and ambulatory ECG monitoring provided controversial evidence, and autonomic measures gave no evidence as predictors for sudden cardiac death in ACHD [51, 59]. There are substantial discrepancies between the hemodynamic condition and autonomic nervous activity because postoperative CHD patients had denervated hearts and restrictive smaller lungs due to multiple open-heart surgeries [60].

The sensitivities of these risk stratification tools in our 33 ACHD patients with sudden cardiac arrest are shown in Fig. 5.2. Among these, ECG findings had relatively high sensitivities, and detailed data are shown in Fig. 5.3. These tools, especially ECG findings, are relevant in predicting sudden cardiac death in ACHD; however, their sensitivities are far from excellent. Prevention of sudden cardiac death in ACHD patients may require more detailed individual evaluation than is typically considered necessary.

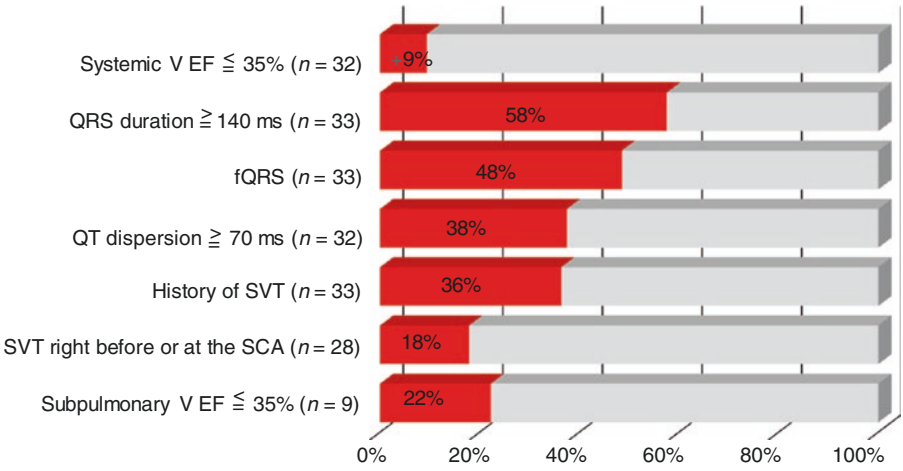

Fig. 5.2 Sensitivities of the risk stratification tools for predicting sudden cardiac death in our 33 adult congenital heart disease patients. Thirty-three adult congenital heart disease patients (≥15 years old) experienced sudden cardiac arrest from September 1983 to January 2016 and were followed up at the National Cerebral and Cardiovascular Center in Japan. Six patients with aborted cardiac arrests (SCA) were included. Basic cardiac defects were Eisenmenger syndrome in five patients, atrial isomerism heart in five, repaired tetralogy of Fallot in four, repaired tetralogy of Fallot with pulmonary atresia in four, functionally repaired transposition of great arteries in two, repaired double-outlet right ventricle in two, repaired aortic stenosis in two, unrepaired cyanotic congenital heart disease in two, and others in seven. Systemic ventricular ejection fraction (V EF) was measured by echocardiography or cineventriculography, which was performed at the latest follow-up. QRS duration, fragmented QRS complex (fQRS), and QT dispersion were measured by electrocardiography at the latest follow-up. Supraventricular tachycardia (SVT) was defined as any type of sustained SVT. Subpulmonary V EF was measured by the cineventriculography that was performed within 5 years before the SCA. The patients who underwent surgical procedures after the cineventriculography were excluded from the evaluation of subpulmonary V EF

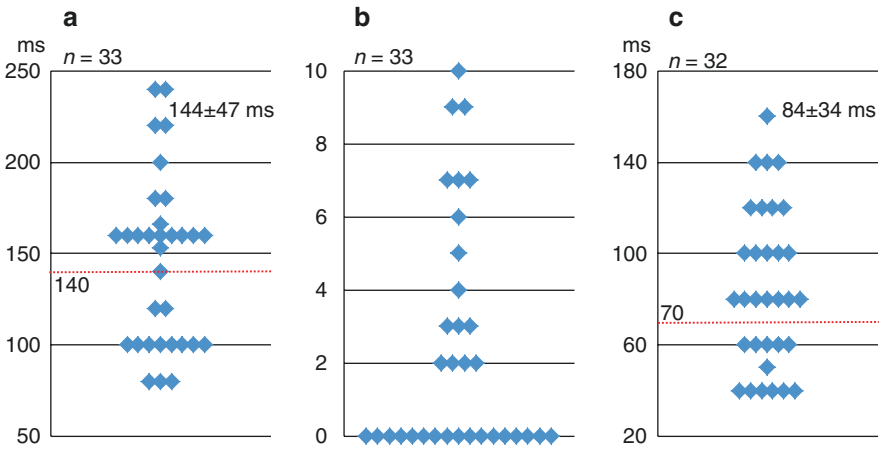

Fig. 5.3 Detailed ECG findings of 33 adult congenital heart disease patients who experienced sudden cardiac arrests. *Panels* a, b, and c show QRS duration, the number of leads showing a fragmented QRS complex, and QT dispersion, respectively. The patient population is the same as that in Fig. 5.1

5.5 Treatment

Disease-specific treatment strategies are essential for rhythm disturbances in ACHD, based on understanding of individual arrhythmogenicities including congenital abnormalities in the conduction system and acquired unique hemodynamic abnormalities.

The first step in treating rhythm disturbance is the prevention of its occurrence by routine clinical practice, including the preservation of a narrow QRS duration, the reduction of atrial and ventricular overload, and the avoidance of myocardial damage. Once an arrhythmia is detected, the hemodynamic and arrhythmogenic factors must be evaluated using various modalities. Data from the hemodynamic assessments are used to decide whether surgery should be carried out to improve the hemodynamic abnormalities, and then the approach to the arrhythmogenic factors should be considered. When patients have bradyarrhythmia or a high risk of sudden death, pacemaker or implantable cardioverter-defibrillator implantation is recommended. Catheter ablation and/or antiarrhythmic drugs alone are only appropriate for patients with unremarkable hemodynamic abnormalities or contraindication of the other treatments.

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Part III

Intervention/Re-intervention Considerations

Perioperative Anesthetic Management of Adult Patients with Congenital Heart Disease

6

Hirotsugu Okamoto

Abstract

In this chapter, perioperative management of patients with congenital heart disease in adulthood including anesthesia is discussed. It is important to provide the safe and careful perioperative anesthetic management by understanding the pathophysiology of each congenital heart disease, the severity of the disease, and the circulatory and respiratory conditions of the patients. Also, it is important to understand the scheduled type of surgical or interventional procedures when managing these patients throughout the perioperative period.

Keywords

Anesthesia • Pulmonary blood flow • Pulmonary vascular resistance • RV dysfunction • LV dysfunction

6.1 General Perioperative Anesthetic Considerations

Because of the diversity of congenital heart disease and the wide spectrum of patient's heart and lungs conditions, careful preoperative evaluation of the patients based on each heart disease and conditions is necessary. For example, it is important to distinguish the patient's symptom coming from whether increased or reduced pulmonary blood flow, coming from whether right or left ventricular dysfunction. Also, the degree of the impairment of the patient's physical status should be evaluated preoperatively using exercise tolerance test, echocardiography, and other

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biochemical and physiological exams. These are listed in two guidelines regarding congenital heart diseases from the Japanese circulation society [1, 2].

During anesthesia, careful management of the patients may be necessary based on their specific heart disease and conditions which are listed in the section of disease-specific considerations. It is advised to use the anesthetic techniques and anesthetic drugs whichever accustomed to or getting used to the anesthesiologists and their institution. Balanced anesthesia technique using midazolam or propofol, fentanyl or remifentanil, and sevoflurane or desflurane is popular in Japan.

Invasive cardiovascular monitoring during anesthesia such as direct arterial blood pressure, central venous or pulmonary artery catheter, and transesophageal echocardiography (TEE) may be required in association with the types of surgery and intervention. In patients at the second- or third-time operation, the preparation for the massive bleeding and ventricular arrhythmia is recommended.

After the surgical procedure, it is important to provide sufficient postoperative analgesia and cardiorespiratory care to the patients at the intensive care unit (ICU). Most of adult patients with congenital heart disease may be transferred to ICU with intubated and artificially ventilated condition. When hemodynamic and respiratory condition is stable, fast track management including rapid weaning from the ventilator and application of recovery protocol is recommended. Especially, in patients after right heart bypass surgery such as Fontan and Glenn procedure, early introduction of spontaneous respiration associated with negative intrathoracic pressure is favorable for hemodynamics. Dexmedetomidine may facilitate early recovery and prevent delirium.

6.2 Disease-Specific Perioperative Anesthetic Considerations

The patients are divided following three groups. First group: the patients underwent complete correction of underlying congenital heart disease in their childhood and now suffering from some of the late complications in their adulthood. Second group: the patients underwent palliative procedure in their neonatal or infantile period and become adults. Third group: the patients grown up to be adults without performing any surgical interventions.

In the first group of patients, discussion will be started from patients received simple closure of either ventricular septum defect (VSD) or atrial septum defect (ASD). In these patients' population, the anesthetic consideration is almost the same as the healthy patients. However, if the patients still have the residual shunt such as VSD and ASD, the risk for the perioperative infectious endocarditis (IE) is still present. Therefore, prophylactic antibiotics are mandatory even scheduled for the dental or minor surgery. The patients with atrioventricular septal defect (AVSD) underwent intracardiac correction in their childhood; residual atrioventricular valve regurgitation (AVVR) is often observed at postoperative period. The right side AVVR causes right ventricular (RV) and right atrium (RA) enlargement due to volume overload. In such patients, systemic venous congestion occurs resulting

splanchnic organ dysfunction. Because intravenous anesthetics and muscle relaxants act longer than usual cases in these patients, postoperative respiratory depression is likely to be occurred. The left side AVVR causes left ventricular (LV) and left atrial (LA) enlargement that may lead pulmonary venous congestion. Therefore, attention should be paid intraoperative fluid overload and perioperative respiratory failure. Either pulmonary valve stenosis (PS) or regurgitation (PR) is often remained in the patients received the correction of tetralogy of Fallot (TOF) in their childhood. In some cases, pulmonary valve replacement is performed in their adulthood for the second-time surgery. Depending upon the patients' cardiopulmonary status, there is a considerable increase in the perioperative risk for hypoxia and RV failure in these patients. In patients with transposition of great arteries (TGA) who received arterial switch operation, peripheral pulmonary stenosis is sometimes developing, especially in case of Lecompte procedure. In contrast, TGA patients received atrial switch operation such as Senning and Mustard procedure, obstruction of either systemic or pulmonary venous return may deteriorate liver function or respiratory function. Therefore, in these patients, careful perioperative respiratory care and precise assessment of liver function are needed. Also, coexisting sinus node dysfunction and other arrhythmia may be exacerbated during surgery.

In the second group of patients who received palliative surgery or staged surgery, patients' group was further divided into subgroups as follows.

First subgroup: patients who is still on the way of palliation (not in a corrective surgery), for example, those underwent only Blalock-Taussig shunt (BTS) or Glenn's procedure. In patients with BTS, pulmonary blood flow depends on mainly arterial blood pressure. Therefore, during anesthesia, systemic hypotension should be avoided using vasopressors. In patients with Glenn's procedure, pulmonary flow depends on hydrostatic pressure difference between the superior vena cava and atrium. Reduced venous return (hypovolemia) and any stimuli increasing pulmonary arterial resistance (light anesthesia, hypoxia, hypercarbia) may cause circulatory collapse.

Second subgroup: patients who have been finished the possible palliative procedure or who have been performed final stage of surgery. Among these patients, Fontan operation or total cavopulmonary connective (TCPC) surgery is most often performed. The same as patients performed Glenn's procedure, keeping pulmonary arterial resistance low and maintaining adequate circulatory volume status are both important considerations throughout the perioperative period. Meticulous hemodynamic care is required when atrioventricular valve regurgitation is associated. Also, in patients received Fontan or TCPC surgery, any types of ventilation increasing intrathoracic pressure, for example, high positive end-expiratory pressure (PEEP), high inspiratory airway pressure should be avoided. If laparoscopic surgery is scheduled, intra-abdominal pressure should be kept as low as possible and steep head-down position may not be allowed in these patients.

The third group of patients remained to be untreated with any surgical intervention including catheter-based therapy. This group of patients are divided in two subgroups such as patients' scheduled cardiac surgery or scheduled noncardiac surgery.

Perioperative considerations for patients undergoing cardiac surgery are discussed based on pathophysiologic manifestations specific to each congenital heart disease.

ASD: most patients with ASD are grown-up without any symptoms. However, as patients getting older, they start suffering from shortness of breath, general fatigue, and other cardiac symptoms, and finally they go to clinics to see a doctor.

In case of ASD with pulmonary hypertension (PH) and RV dysfunction preoperatively, careful induction of anesthesia is required. During anesthesia, monitoring pulmonary artery (PA) pressure using PA catheter is recommended; otherwise, estimation of pulmonary pressure from trans-tricuspid pressure gradient (TRPG) by TEE is recommended. Also, management of pulmonary resistance by infusion of nitrates, phosphodiesterase inhibitor (PDE-I), or inhaled nitric oxide (NO) has to be considered during surgery. Another important perioperative evaluation of adult ASD patient is LV size and function. Because of long-term volume unloading due to shunting blood from LA to RA, LV becomes smaller than normal (hypoplastic LV) in size. In such particular patient, LV volume loading after closure of ASD may lead to LV distension and dysfunction associated with pulmonary edema. If it happens, inotropes and/or LV assist device such as intra-aortic balloon pumping will be needed.

VSD: in adult patients with VSD, there are three conditions of which being operated. First, patients whose VSD is evaluated that not likely to be closed spontaneously during the follow-up period. These patients are at usually low risk for both cardiac surgery and anesthesia.

Second, patients with VSD associated by active IE of any cardiac valves. In these IE patients, cardiac dysfunction due to valvular regurgitation at any infected valve may cause hemodynamic instability. Therefore, careful induction and maintenance of anesthesia will be needed in these cases.

Third, the patients with undiagnosed VSD or with VSD untreated for irreversible pulmonary hypertension. In these patients, right-to-left shunting (R-L shunt) causes cyanosis by increasing pulmonary vascular resistance (Eisenmenger syndrome). Those patients may have systemic complications due to secondary erythrocytosis and RV failure. Cardiac surgery is contraindicated in these patients; however, sometimes noncardiac surgery is scheduled for these patients. If this is the case, during anesthesia, caution should be made not to worsen the R-L shunt that leads further desaturation. Also, it is important to support RV function by using inotropes and by avoiding hypovolemia.

AVSD: an adult patient with complete types of AVSD rarely comes to the operating room except planning for non-cardiac surgery. Long-term exposure of high pulmonary blood flow due to the double shunting both ASD and VSD may have caused Eisenmenger syndrome. Anesthetic consideration is similar to that of patients with VSD-associated Eisenmenger syndrome described above.

In contrast, patient with incomplete type of AVSD is sometimes scheduled for cardiac surgery. During anesthesia, caution should be paid not to further increase small but significantly elevated pulmonary vascular resistance. In addition, worsening of atrioventricular valve regurgitation has to be avoided when it exists.

TOF: it is possible that initial cardiac repair is performed in an adult patient with TOF. In such a case, perioperative management including anesthesia becomes challenging issue. Preoperatively, the degree of cyanosis of the patient with TOF is dependent on pulmonary stenosis (PS), development of pulmonary vascular bed, pulmonary vascular resistance or size of palliative shunt, etc. If patient's SpO2 is below 90%, insufficient airway management during the induction of anesthesia may cause life-threatening hypoxia. Therefore, it is important to give sufficient preoxygenation and provide various airway assist devices. The maintenance of adequate blood pressure is sometimes required to keep pulmonary blood flow and oxygen saturation. Also, in these cyanotic patients with severe PS, abundant collateral circulation including major aortopulmonary connective artery (MAPCA) may cause massive surgical bleeding before establishing cardiopulmonary bypass (CPB). Large bore venous routes and reparation for blood transfusion are required for these patients. At the period of weaning from CPB, inotropes and pulmonary vasodilator are required to treat possible RV failure. Postoperative pulmonary hemorrhage and venous hemostasis are most risky complication after the procedure including simultaneous cryoablation for RVOT. Careful respiratory and circulatory treatment in ICU may be necessary.

Patent ductus arteriosus (PDA): perioperative concerns in an adult patient with PDA arise from the fragility of PDA tissue and long-term PA and LV volume overload. Because of the fragile PDA, simple clipping or surgical interruption is very difficult to perform. Therefore, in such case, surgical intervention is planned under circulatory arrest with systemic hypothermia. Protective strategies for cerebral and splanchnic organs are mandatory in such circumstance.

Ebstein's anomaly: usually, adult patient with Ebstein's anomaly is scheduled for cardiac surgery because of the RV failure associated with severe tricuspid valve regurgitation (TR). Either repair of tricuspid valve or tricuspid valve replacement will be chosen for surgery. In any cases, proper treatment for possible perioperative RV dysfunction and arrhythmia may be required. After the cone procedure, because of the increased risk of tricuspid annulus, narrowing caution should be made to provide the adequate RV volume loading. ASD is not able to close completely in some case in order to maintain blood flow to the left side of the heart. The management of balancing between residual cyanosis and hemodynamic stability has become difficult after the surgery.

Corrected TGA: corrected TGA is one of the complex congenital heart diseases that is scheduled for first-time cardiac surgery in adult. The main problem of this heart disease in adult is the developing systemic ventricular dysfunction which is anatomically RV. Anatomical tricuspid valve regurgitation is often associated and needs to fix. Whichever surgery is performed in this disease, preserving systemic ventricular function throughout the surgery is most important.

Aortic stenosis (AS): most often, congenital AS in adults is due to bicuspid aortic valves. Usually, symptom begins when trans-aortic mean pressure gradient (AoPG) exceeds 20 mmHg. Severe AS patients with AoPG over 40 mmHg, or any AS patients with reduced LV function, careful induction of anesthesia with maintaining systemic vascular resistance may be recommended. After aortic valve replacement

by either surgery or transcatheter, the hypertrophic LV with small cavity is likely to develop postoperative LV failure. Bicuspid aortic valve with aortic stenosis sometime associated with enlarged ascending aorta, which fits operative indication. The application of systemic hypothermia with selective cerebral perfusion or retrograde cerebral perfusion is required to replace enlarged ascending aorta.

Coarctation of the aorta (CoA): severe CoA with PDA is mostly treated before the infantile period. Therefore, adult patients with CoA have simple type such as mild-to-moderate stenosis of the aorta. Surgery is performed under simple cross clamping and end-to-end anastomosis of the aorta without CPB or, in some case, under circulatory arrest with CPB. An extra-anatomical bypass from the ascending aorta to the descending aorta just above the phrenic is applied as a palliative surgery in some case with difficulty of direct repair. Anesthesia is similar to that of aortic surgery except for the patients are sometimes associated with the severe arterial hypertension of the upper extremities and hypotension or hypoperfusion of the lower extremities. Blood pressure monitoring at both pre- and post-stenosis may be preferable. If the CoA patients are associated with VSD, please refer VSD section.

In summary, the anesthetic considerations of congenital heart diseases in adults during surgery are described above. Careful preparation and anesthesia and postoperative care with understanding the disease of the patients and the scheduled surgery may provide the safer perioperative condition.

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Therapeutic Catheter Intervention for Adult Patients with Congenital Heart Disease (ASD, PDA)

7

Teiji Akagi

Abstract

Various types of interventional procedure indicate for adult patients with congenital heart disease. The most common procedure is transcatheter closure of atrial septal defect (ASD). After the introduction of catheter intervention for ASD in the pediatric population, therapeutic advantages of this less invasive procedure were focused on adult through geriatric populations. Currently, two types of devices, such as Amplatzer Septal Occluder and Occlutech Figulla Flex II are available in Japan. The most valuable clinical benefits of this procedure are the significant improvement of symptoms and daily activities, which result from the closure of left-to-right shunt without thoracotomy and cardiopulmonary bypass surgery. These benefits contribute to increase the number of adult ASD device closure candidates who have hesitated over surgical closure. In terms of technical point of view for catheter closure of ASD, the difficulties still exist in some morphological features of defect, or hemodynamic features in the adult population. Morphological features of difficult ASD closure are (1) large (≥30 mm) ASD, (2) wide rim deficiency, and (3) multiple defects. Hemodynamic features of difficult ASD are (1) severe pulmonary hypertension, (2) ventricular dysfunction, and (3) restrictive left ventricular diastolic dysfunction after ASD closure. To complete the catheter ASD closure under these difficult conditions, various procedural techniques have been introduced. These include imaging modalities such as real-time three-dimensional imaging, intracardiac echocardiography, fusion imaging of echocardiography, and fluoroscopic imaging. In adult patients, optimal management for their comorbidities is important issues, which include cardiac function, atrial arrhythmias, respiratory function, and renal function. Management of atrial arrhythmias is a key issue for the long-term outcome in adult patients.

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Keywords
Atrial septal defect • Patent ductus arteriosus • Heart failure • Arrhythmia

The second popular cardiac lesion for interventional procedure is patent ductus arteriosus (PDA). The most adult patients with patent ductus arteriosus can be a treatable condition using Amplatzer Duct Occluder or Amplatzer vascular plug. Although transcatheter pulmonary valve implantation using Melody valve is commonly performed in the US or European countries, this procedure has not been approved in Japan yet. Because the interventional procedures are not complication-free techniques, the surgical backup system is essential for the safe achievement of the procedure. Finally, a team approach including pediatric and adult cardiologists, cardiac surgeons, and anesthesiologists is the most important factor for a good therapeutic outcome.

7.1 Adult Congenital Heart Disease and Catheter Intervention

Remarkable improvement in the survival of patients with congenital heart disease (CHD) has occurred over the past 50 years since reparative surgery has become commonplace. In Japan, it is estimated that there are at least 400,000 adult CHD patients; this number is expected to increase by approximately 9000 patients annually [1–3]. Management of these patients is going to be one of the critical issues even in our daily practice.

On the other hand, some types of CHD have been grown up to adult age without significant symptoms. These include ASD, PDA, and small ventricular septal defect (VSD). However, such stable or less symptomatic condition could not persist throughout their life. The mortality of adult patients whose age over than 60 years gradually increases past few decades [4]. It is well known that the mortality of congenital heart disease dramatically decreased for the past few decades; however especially in adult patients with CHD, mortality has been increasing. The main cause of this phenomenon is that patients with ASD died in the elderly population [5, 6]. Thus, optimal management for elderly patients with ASD is very important for their life.

7.2 Clinical Feature of ASD in Various Aged Population

Atrial septal defect (ASD) accounts for 7% of all congenital heart diseases. There are several different anatomical types in ASD, and the most common type is a secundum defect, followed by defects located in the septum primum, sinus venosus defects, or unroofed coronary sinus [7]. If left untreated, these defects may result in right-sided heart failure, arrhythmia, and pulmonary hypertension. Although surgical closure of ASD is safe, effective, and time tested, it still requires open heart surgery and long hospitalization [8]. Even in the current surgical procedure, complications, which are related surgery or cardiopulmonary bypass, have not disappeared.

Clinical features of ASD are widely varied from pediatric population through adults [9–12]. Majority of these children are asymptomatic and diagnosed by school cardiac screening and physical examination; heart murmur detected by the primary care pediatrician during cardiac echo screening in the newborn period. If defect is smaller than 6 mm, spontaneous closure can be expected during newborn to pediatric periods [9]. Operation is scheduled based on children's body size, usually before the elementary school with very low incidence of mortality rate. Contrary, adult patients of ASD are usually symptomatic. Their heart disease is discovered by palpitation, arrhythmia, or progress of congestive heart failure. In our recent series of adult patients with ASD were newly diagnosed within 3 years before the procedure that means the majority of adult patients could not be diagnosed during the pediatric period under the current medical screening system [13]. In the 1990s Murphy and colleagues reported the natural course of ASD [8]. In this study, survival rate is significantly deteriorated compared to normal population, if patients did not have surgical closure until age of 24 and/or complicated with pulmonary hypertension. However, currently, our patient's background is significantly different compared to such studies; rather numerous adult patients are submerged with asymptomatic condition and occasionally diagnosed at the time of detailed cardiovascular evaluation for atrial arrhythmia, congestive heart failure, or stroke [13].

Although the catheter closure of pediatric or young adult with ASD population has attracted research interest over the last two decades, those of elderly ASD population have yet to be characterized [14]. The extrapolation of studies on younger patients is not appropriate in the geriatric patients. First, elder patients with ASD often acquire comorbid conditions, such as arrhythmia, hypertension, respiratory distress, kidney disease, etc., that always influence on their heart conditions [11, 14]. Second, elder ASD patients may have inherently superior resiliency, milder disease, or balanced physiology in contrast to those not surviving to an advanced age. Therefore, elder or geriatric patients with ASD represent a distinct population for which focused studies are needed.

7.3 Transcatheter Closure of ASD

Transcatheter closure of ASD is associated with low complication rates, short anesthetic times, and short hospitalizations [12]. When conditions are favorable, transcatheter ASD closure has become the treatment of choice rather than surgery in many institutions. Echocardiography, either transesophageal (TEE) or intracardiac, plays a significant role in the guidance of these procedures and in the assessment of the final result. Research efforts are ongoing to examine other imaging modalities, such as CT or MRI, as a means of three-dimensional (3D) imaging prior to transcatheter ASD closure. Up to date, Amplatzer Septal Occluder (St. Jude Medical, St. Paul. MN) is widely used in the world. Since February 2016, new ASD closure device, Occlutech Figulla Flex II, is approved in Japan (Fig. 7.1). Figulla Flex II is softer than Amplatzer Septal Occluder; thus it may reduce the device-related complication, such as cardiac erosion [15]. However, no scientific evaluation has been

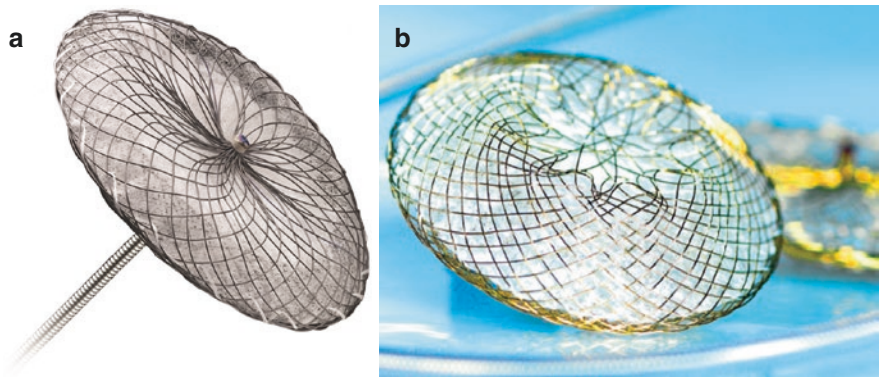

Fig. 7.1 (**a**) Amplatzer Septal Occluder and (**b**) Occlutech Figulla Flex II

performed for statistical evaluation. These devices are suitable for all subtypes of ASD and have successfully closed defects as large as 30–35 mm in diameter. However, the procedural difficulties still exist due to morphological features of septal defect or hemodynamic standpoint.

7.4 Morphological Features of Difficult Transcatheter ASD Closure

It is well known that morphological variations of ASD are frequent, and appropriate patient selection for transcatheter ASD closure is crucial for successful procedure. ASDs are grouped into four major categories: ostium primum, ostium secundum, sinus venosus, and coronary sinus septal defect. Secundum defect is the most common type of ASDs in which the defect involves the region of fossa ovale, and this type is indicated for transcatheter ASD closure. Coronary sinus septal defect is a rare type, in which a communication occurs between the coronary sinus and the left atrium as a result of unroofed coronary sinus. Primum septal defect and sinus venosus defect are indicated for surgical repair. Regarding coronary sinus septal defect, although surgical repair is the standard treatment for this type of ASD, there are some case reports in which transcatheter closure was successful without any conduction disturbance [16].

In patients with secundum septal defect, two crucial parameters, those are the maximal ASD diameter in order to select a device with the appropriate size and the surrounding rim dimensions to optimize the placement of the device, which should be assessed to select patients for procedure. The maximum defect diameter must be less than 38 mm. Most of ASDs have ellipsoidal shape, and it varies during cardiac cycle. The major axis diameter of the defect measured in the phase of ventricular end systole is mandatory for selecting the optimal device size, especially in patients undergone the procedure without balloon sizing or multiple defects. Transcatheter closure of large ASD with a maximal native diameter of >30 mm is still challenging, and alternative special techniques for deployment of the device are usually required. In regard to the classification of surrounding rims, although there are

some differences among studies, distances from ASD to aorta (superoanterior rim), superior vena cava (superoposterior rim), right upper pulmonary vein (posterior rim), inferior vena cava (inferoposterior rim), coronary sinus, and atrioventricular valve (inferoanterior rim) are assessed. The definition of rim deficiency varies among different studies; any rim was considered deficient if its length is <5 mm (Fig. 7.2) [17].

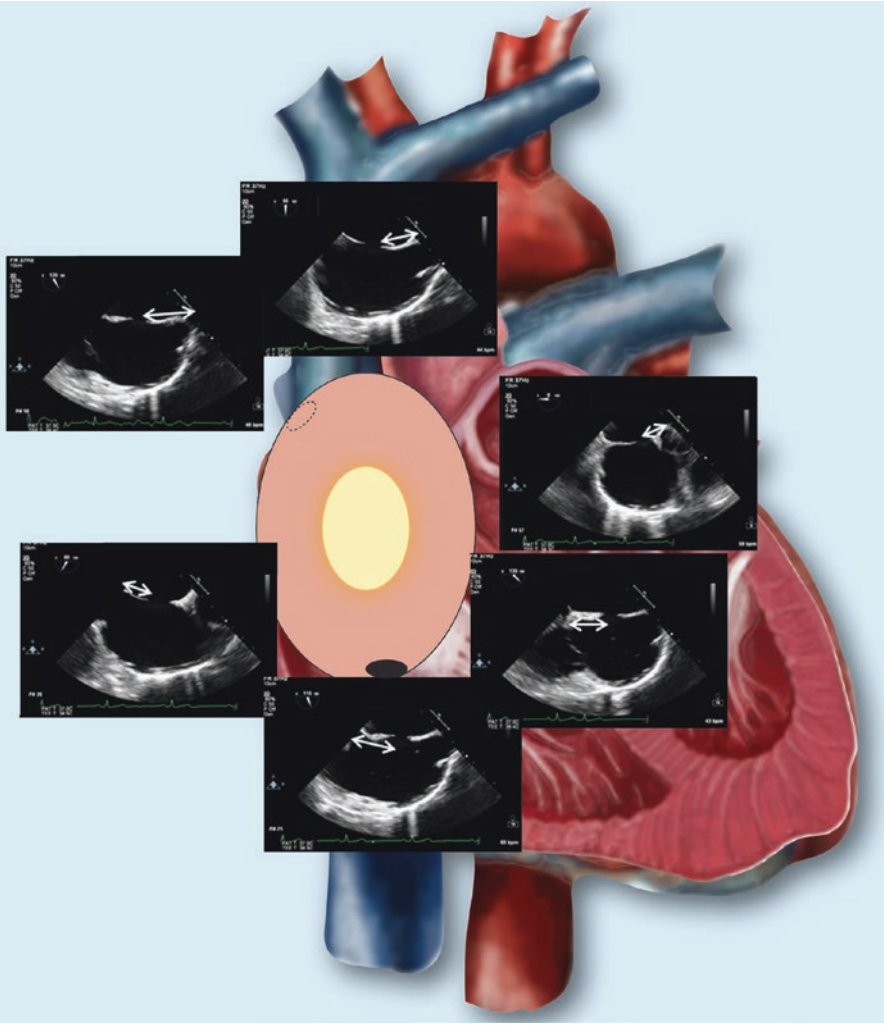

Fig. 7.2 The assessment of surrounding rims using two-dimensional (2D) TEE. Surrounding tissue rims and ASD diameter should be measured in the phase of ventricular end systole with multiple cross-sectional TEE plane. Distances from ASD to aorta (superoanterior rim; 2D TEE view at 0°–30°), superior vena cava (superoposterior rim; 2D TEE view at 90°–120°), right upper pulmonary vein (posterior rim; 2D TEE view at 110°–120°), inferior vena cava (inferoposterior rim; 2D TEE view at 60°–90°), coronary sinus (2D TEE view at 100°–120°), and atrioventricular valve (inferoanterior rim; 2D TEE view at 135°) are assessed. *RUPV* right upper pulmonary vein, *CS* coronary sinus

7.5 Cardiac Erosion and Its Mechanism

In patients with superoanterior rim deficiency, the risk of serious complication, so-called cardiac erosion may increase after the device implantation. Although the definite mechanism of "cardiac erosion" has not been established completely, previous clinical experiences suggested that an aortic rim deficiency and oversized occlusion device might be at highly related with cardiac erosion [18, 19]. However, a large number of cases with an aortic rim deficiency resulted in a successful deployment without complicating cardiac erosion. Morphological factors additional to an aortic rim deficiency should be considered in cases with cardiac erosion.

Atrial septal malalignment is a morphological characteristic frequently encountered in cases with a deficient aortic rim. Surfaces arising from septum primum and septum secundum are different in a defect with malaligned atrial septum resulting in vertical displacement and tight impingement of the right atrial disk toward the right atrium. As the device is deployed against the atrial septum from the left atrium side, the right atrium disk moved toward to the left atrium side after the release. Atrial septal malalignment causes a change in the device axis angle against the aortic root and may be a risk for cardiac erosion in catheter closure of ASD using Amplatzer Septal Occluder (Fig. 7.2). Although the observation of the both side of the disks before and after the release of the device is important, assessment of this situation before the device deployment is difficult. Device deployment against an ASD complicated with a deficient aortic rim can result in a splay of the disks across the aortic root with impingement of the device. Atrial septal malalignment can swell the tight impingement of the device, especially after releasing the cable. Thus, atrial septal malalignment may be a potential risk factor for cardiac erosion [20].

Recently, the instruction for user (IFU) of Amplatzer Septal occluder has been updated especially for avoiding cardiac erosion [19]. That is, the contraindication for defect margins less than 5 mm has been updated to include the inferior vena cava rim, because such defect character tend to be caused of oversized device selection.

7.6 Imaging Modality for Transcatheter ASD Closure

Two dimensional (2D) and color Doppler transthoracic echocardiography (TTE) can demonstrate the presence of ASDs, chamber dilatation, estimated pulmonary artery pressure, shunt ratio, and other coexisting heart disease with high sensitivity and specificity in real time. And the advent of tissue Doppler imaging could facilitate the understanding of cardiac diastolic function in which impaired cardiac function before ASD closure may lead to the development of congestive heart failure after ASD closure especially in elderly patients [20]. However, in terms of accurate assessment of ASD morphology including measurements of maximal diameter and surrounding rims, 2D TTE has sometimes limited ability to visualize ASDs in detail clearly especially in adult patients; thus precise evaluation using transesophageal echocardiography (TEE) are necessary in most ASD patients.

Three-dimensional (3D) echocardiography provides better spatial visualization, and 3D TEE can delineate the 3D structure with high-resolution image. As the

result, 3D echocardiography offers the ability to improve display and our understanding of complex lesions such as valvular and congenital heart disease [19–24]. In addition, although 3D echocardiography was initially based on reconstructed image from serial 2D images, which required cumbersome acquisition and time-consuming offline analysis, recently real-time 3D echocardiography using matrix array transducer has been available in TTE as well as TEE. 3D TTE is a promising modality to provide comprehensible en face image of ASD because of its noninvasiveness, low cost, portability, and wide availability (Fig. 7.3). In terms of patient selection for transcatheter ASD closure, 3D TTE has a potential to provide accurate information of ASD morphology including location, size, and surrounding rims for the treatment both in children and adults. However, there are several limitations of 3D TTE at present such as dependence on the skill of the operator, restrictive echo window especially in elderly patients, and echo dropout in the region of the mid

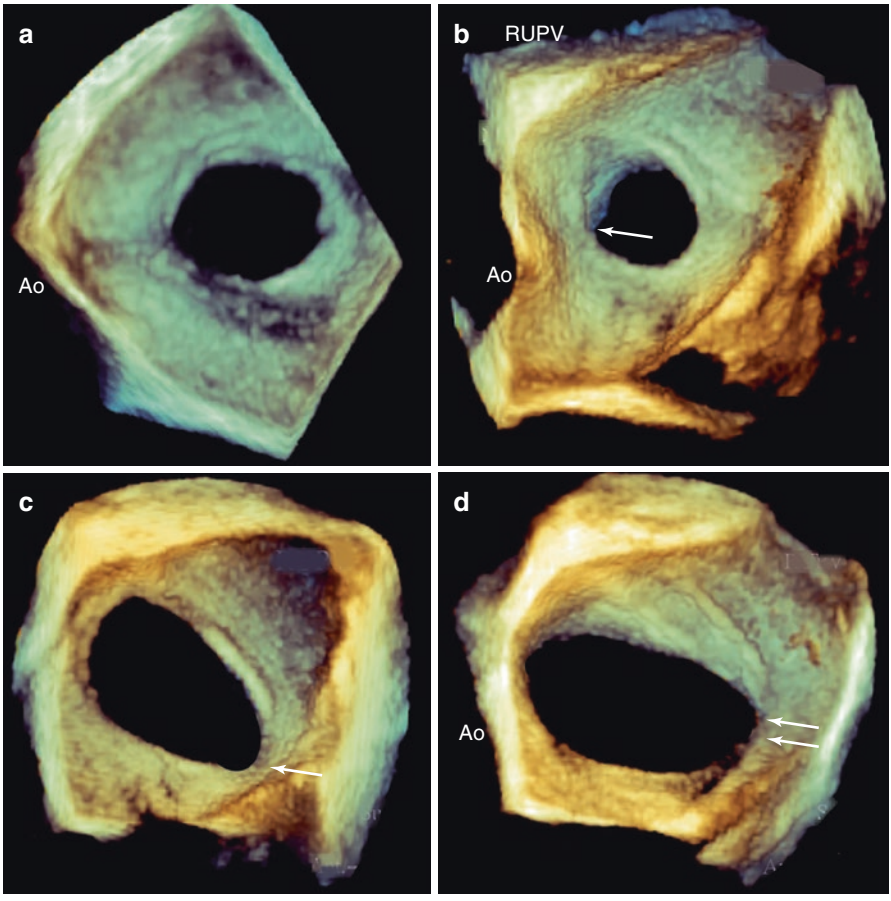

Fig. 7.3 Various shape of ASD visualized by 3D TEE (left atrial en face view). (**a**) Sufficient rim, (**b**) deficient superoanterior rim, (**c**) deficient inferoposterior rim, and (**d**) deficient both superoanterior and inferoposterior rim. *Arrow head* indicates the portion of rim deficiency. *RUPV* right upper pulmonary vein, *Ao* aorta

portion which can lead to false diagnoses of large defects and both lower temporal and spatial resolutions compared to 2D TTE. On the other hand, ASD morphology can be recognized with high-quality en face image using 3D TEE. Real-time 3D TEE allows for the evaluation of various shape of ASD especially in patients with complex-shaped ASD like multiple ASDs (Fig. 7.4) [19, 22, 23]. Nowadays,

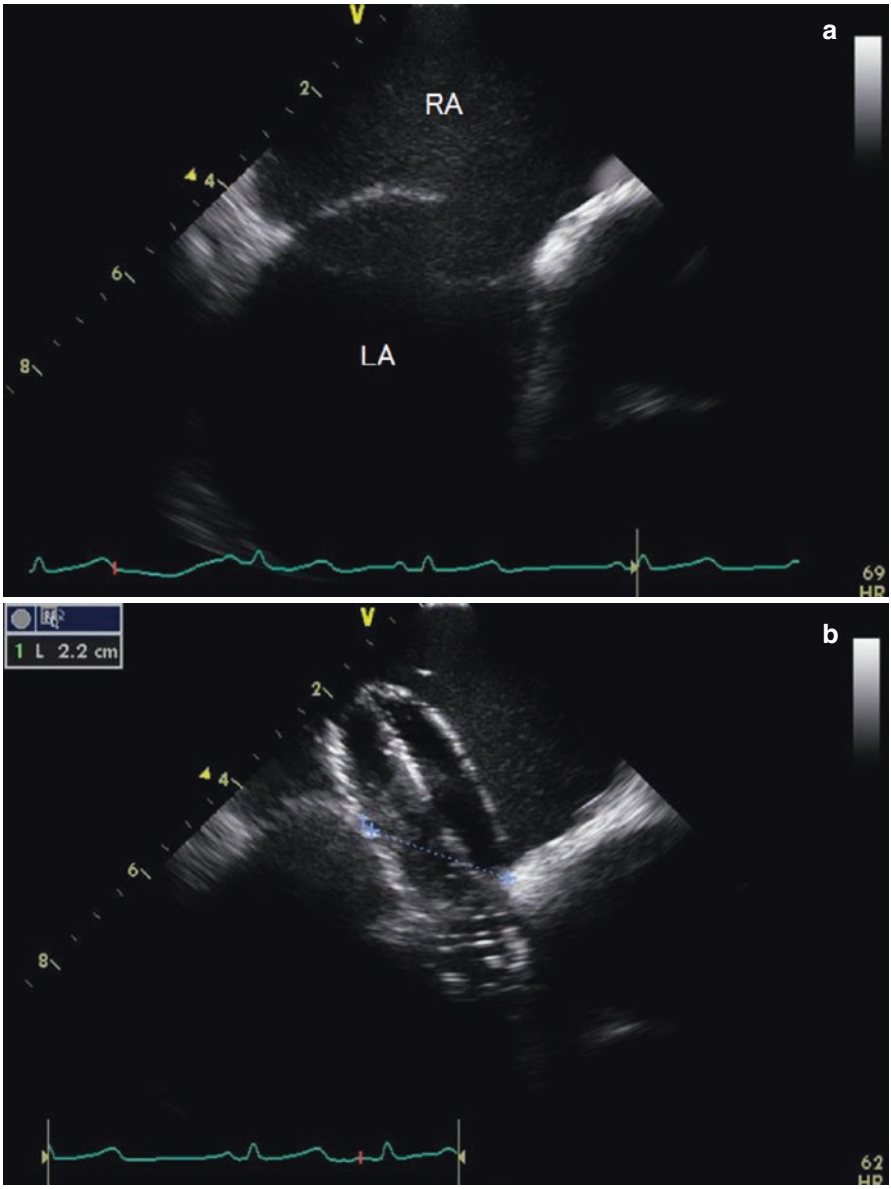

Fig. 7.4 ICE-guided transcatheter ASD closure. (**a**) Short axis view of phased-array ICE demonstrating the anterosuperior rim deficiency before closure. (**b**) Balloon sizing ASD diameter was 22 mm. (**c**) ASD was closed with 22 mm device. *LA* left atrium, *RA* right atrium

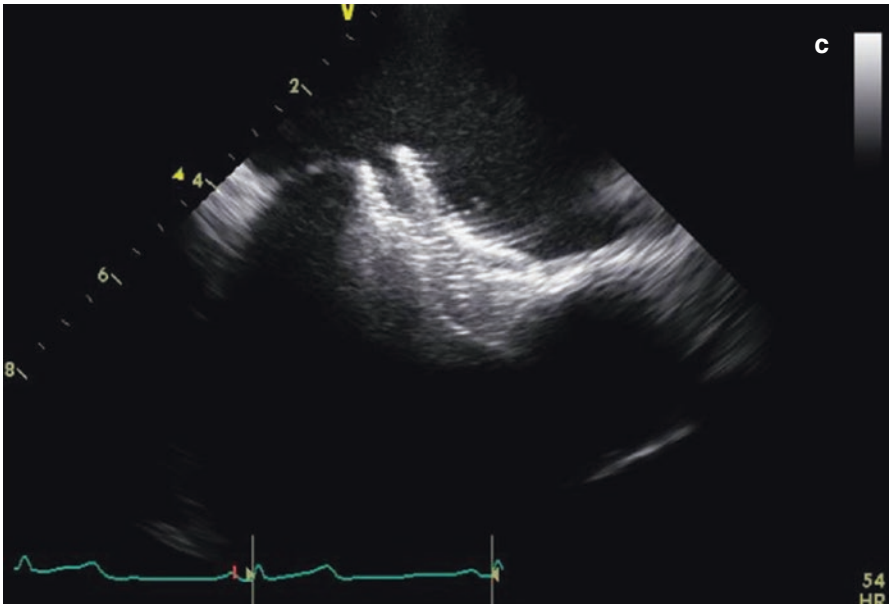

Fig. 7.4 (continued)

intracardiac echocardiography is also available for acceptable echocardiographic guidance for this procedure, especially in simple and small defect (Fig. 7.5).

7.7 Various Closure Technique for Difficult ASD

Various technical modifications were reported for transcatheter ASD closure. These are the modification of delivery sheath, deployment position, or additional material to hold the left atrial disk inside the left atrium, avoiding the left atrial disk slipping into the right atrial side [24].

Rotation of the delivery sheath within the heart, or increasing the curvature of the sheath by remolding outside the body, has been described to improve alignment [25]. Some have advocated deployment of the left atrial disk in the right or left upper pulmonary vein followed by pulling of the sheath into the right atrium to improve the approach to the atrial septum in large defects [26]. Concerns exist in this technique causing injury of the pulmonary vein. A specially designed sheath (Hausdorf sheath, Cook, Bloomington, IN) can be used to help align the left atrial disk parallel to the atrial septum [26–28]. Favorable changes in the approach to the interatrial septum and increased ability to deliver the device have been reported with the Hausdorf sheath [28]. Kutty and colleagues developed a method to modify a Mullins transseptal sheath to enhance delivery [29]. The resulting sheath is straight and has an exit orifice essential in the side of the distal portion of the sheath-a straight, side-hole delivery sheath [29]. The use of a balloon catheter [30] or a long

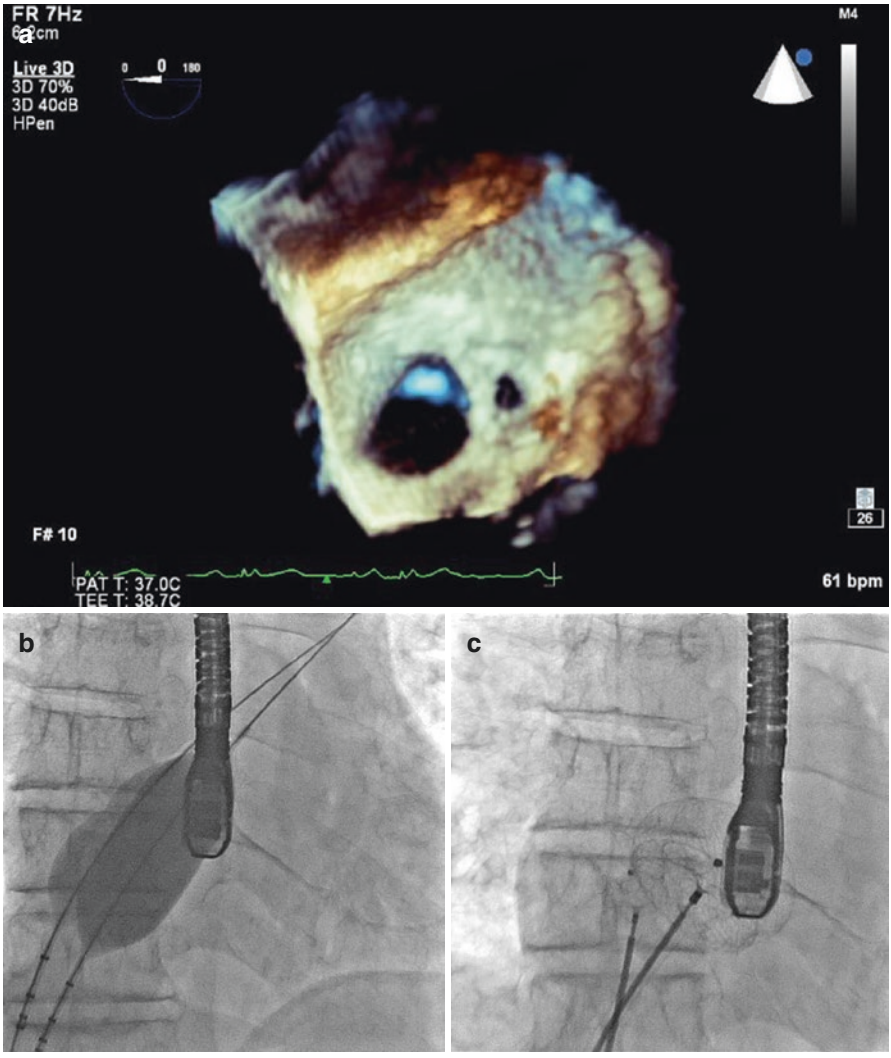

Fig. 7.5 Catheter closure of multiple ASDs. (**a**) 3D-TEE imaging shows isolated two defects; large defect was 24 mm, and small defect was 7 mm. (**b**) Balloon sizing was performed simultaneously both defects. (**c**) A 28 mm and 10 mm devices were deployed

dilator [31] to support the left atrial disk and prevent its prolapse into the right atrium during deployment has been described. Although this technique requires additional venous access, the procedure, especially balloon-assist technique, is relatively simple and less traumatic. Even in the large ASD, high procedure success can be expected. Operators are not required to be familiarized all of these techniques; however, operators should master one or two of different techniques to achieve the procedure successfully for difficult patients or defect anatomy.

7.8 Hemodynamic Features of Difficult Transcatheter ASD Closure

7.8.1 Pulmonary Arterial Hypertension and ASD

Not only morphologically, hemodynamic features have influences on difficulties of transcatheter ASD closure. Candidates for ASD closures have a hemodynamically significant atrial shunt or the presence of right ventricular volume overload and/or clinical symptoms of dyspnea, reduced exercise capacity, or paradoxical embolism. Pulmonary vascular resistance < 5 Wood units.m^2 and the peak pulmonary artery pressure ≤70% of the systemic blood pressure are also important conditions for ASD closure. Although the most of pediatric patients with ASD fulfill these hemodynamic criteria, the incidence of pulmonary artery hypertension significantly increased in adult population. It is well known that the natural course in patients with ASD and pulmonary hypertension is significantly worse than patients without pulmonary hypertension. Thus, closure of ASD in patients with pulmonary hypertension was considered as a high-risk procedure, especially by the surgical closure. However, once transcatheter closure without cardiopulmonary bypass can be performed even in such high-risk patients, several clinical studies have demonstrated the efficacy and safety of ASD closure. Importantly, the more significant reduction of pulmonary artery pressure can be achieved even in severe pulmonary hypertension [32, 33].

Furthermore, the expansion of therapeutic indication is considered under the combination of new pulmonary hypertension-specific medical treatment, such as prostanoids, endothelin receptor antagonists, and phosphodiesterase-5 inhibitors. Even in the initial hemodynamic parameter seems to be untreatable (or contraindication) for ASD closure, catheter closure of ASD may be performed if such pulmonary vascular resistance can be considered as responder for pulmonary artery-specific vasodilators [34, 35]. Long-term follow-up is mandatory especially these high-risk populations (Fig. 7.6).

7.8.2 Management of Elderly Patients with ASD

In the past, surgical correction of ASD in geriatric population has not been indicated positively, because of difficulties of perioperative management and high incidence of comorbidities. Additionally, geriatric patients by themselves did not wish open heart surgery, even if hemodynamic benefit can be expected. However, after the introduction of the transcatheter closure of ASD, the experiences of older or geriatric patients are significantly increasing [11, 14].

In the elderly patients with ASD, hemodynamic features are significantly different from those in children and young adults. Elderly patients with ASD frequently present with hemodynamic abnormalities such as pulmonary hypertension, atrial arrhythmias, and valvular regurgitation, which causes congestive heart failure [14]. The incidence of pulmonary hypertension significantly increase by age in ASD

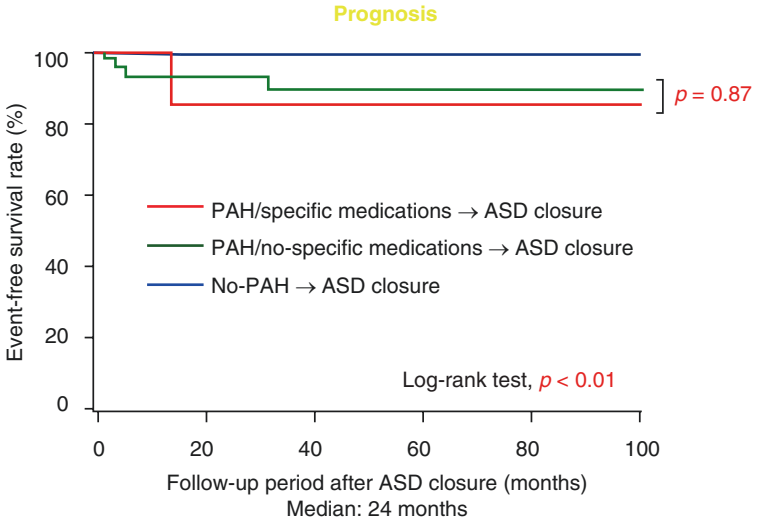

Fig. 7.6 Clinical efficacy of treat and repair strategies in ASD patients with severe pulmonary hypertension: even in patients required PAH-specific medication, long-term event-free ratio is equivalent compared with patients without PAH-specific medication

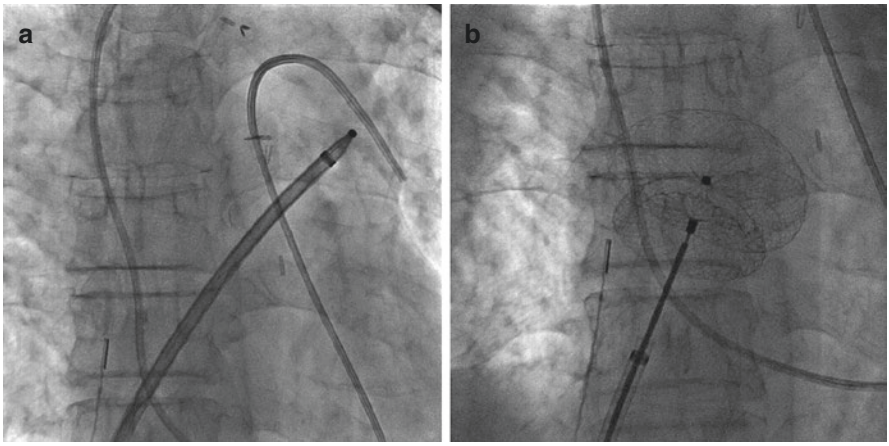

Fig. 7.7 Catheter closure of an 82-year-old patient with large ASD and permanent atrial fibrillation. (**a**) PCW was continuously monitored during the device deployment. In this case, ICE was used as imaging guidance. (**b**) 32 mm device was deployed, and no significant elevation of PCW pressure was observed

patients; the decision of ASD closure is sometimes difficult especially in patients with severe pulmonary hypertension. Moreover, various comorbidities, such as systemic hypertension, chronic obstructive pulmonary disease, coronary artery disease, chronic kidney disease, and left ventricular diastolic dysfunction often complicate the clinical features in this population (Fig. 7.7). Left ventricular diastolic

dysfunction, which is also seen as part of normal aging and frequently occurs in elderly individuals with hypertension or increased arterial stiffness, may cause acute congestive heart failure after ASD closure [13]

In our institution, approximately 10% of cases of transcatheter closure of ASD were patients whose aged older than 70 years. Most of these patients had at least one major comorbidity, including systemic hypertension, stroke, coronary artery disease, and atrial fibrillation. More than half of the patients were being treated with a diuretic for congestive heart failure, and 30% of the patients had a history of hospitalization due to heart failure. Majority of patients complicated with symptoms of heart failure are classified as NYHA functional class more than class II [14].

Previous studies have suggested that the development of acute congestive heart failure is due to abrupt elevation in left ventricular preload following transcatheter ASD closure, especially in elderly patients with impaired left ventricular systolic or diastolic function [13]. In our experience, despite the fact that our patients had impaired left ventricular diastolic function estimated by decreased e' and increased E/e' as well as various comorbidities, acute congestive heart failure after the ASD closure has not developed. We speculate pre- and periprocedural anticongestive medication was very important and effective for preventing congestive heart failure after ASD closure in elderly patients [14]. Additionally, we routinely monitored pulmonary capillary wedge pressure (PCWP) during the procedure to avoid the acute congestive heart failure caused by ASD closure in elderly patients. If mean PCWP increased >10–15 mmHg from the baseline value during balloon occlusion of the defect (test balloon occlusion), or PCWP increased >20 mmHg, we judge such ASD closure would develop pulmonary edema, and the procedure should be abandoned. Especially in patients who had a history of heart failure, we considered them to be hemodynamically high-risk patients. Creation of fenestration hole in the device may avoid the abrupt hemodynamic change after the transcatheter closure of ASD. However, the optimal fenestration size has not been evaluated, and the experiences are still limited.

Although the majority of elder patients were complicated with various comorbidities, high procedural success rate can be expected even in this aged population. Also, significant improvement of NYHA functional class was observed after closure even though about 30% of the patients in this study had a history of hospitalization for congestive heart failure. No patient required additional hospitalization for congestive heart failure during the follow-up period after device closure (Fig. 7.8).

Atrial arrhythmias are the most commonly seen comorbidity in adult patients with ASD. In our experiences, approximately one third of patients whose age over than 60 years old, or half of patients whose age over than 70 years, are complicated with atrial fibrillations. Previously, we reported the clinical benefits of catheter closure of ASD in patients with permanent atrial fibrillation [36]. Even if patients complicated with atrial fibrillation, the resolution of left-to-right shunt contributes significant improvement of clinical symptoms of these patient. Although, strict anticoagulation treatment is required even after the ASD closure, transcatheter closure of ASD should be considered even if patients with permanent atrial fibrillation without age limitation (Fig. 7.8). If patients complicated of symptomatic paroxysmal or

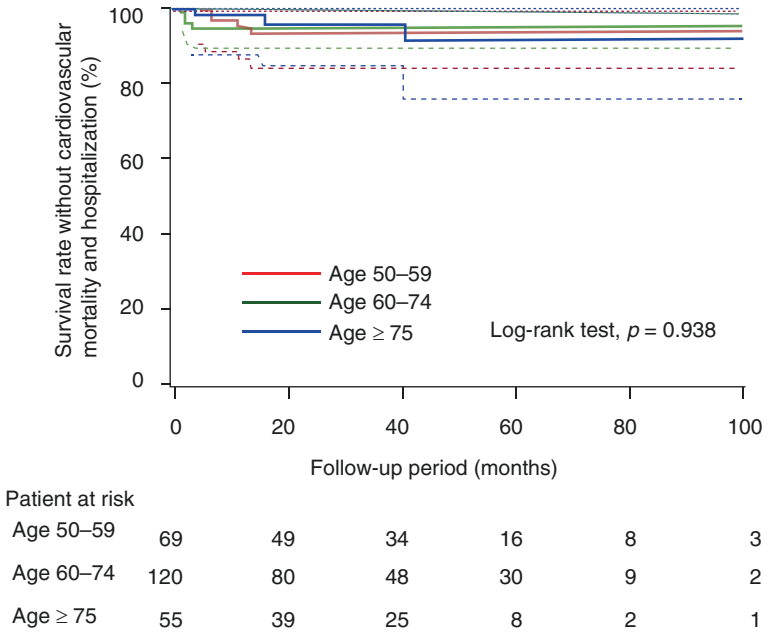

Fig. 7.8 Long-term outcome after catheter closure of ASD in adult patients. Even in the geriatric population, excellent long-term outcome can be expected. Age at procedure is not affected by the long-term outcome

persistent atrial fibrillation, catheter ablation such as pulmonary vein isolation should be indicated prior to the catheter closure of ASD. In our institution, pulmonary vein isolation is going to indicate in patients whose age younger than 75 years, symptomatic paroxysmal or persisted atrial arrhythmias, and left atrial dimension >50 mm. Transcatheter ASD closure is scheduled when sinus rhythm persists >3 months after the ablation. Although the experiences are still limited, this collaboration between electrophysiological and interventional procedures can contribute the new therapeutic strategies in patients with ASD and atrial arrhythmias.

7.9 Future Direction of Transcatheter Intervention for ASD

Transcatheter closure of ASD using currently available devices has been established as safe and effective medical treatment for the most of patients with ASD. Although some specific anatomical features are not suitable for this procedure, remaining patients are probably treatable by cardiac surgery. On the other side, complications due to this procedure, especially cardiac erosion, are still observed in a certain number patients. The mechanism of cardiac erosion has not been clarified completely; some erosion occurred even long-term after the procedure. Thus, the longitudinal follow-up after this procedure is essential. Other important interests, such as device-induced late atrial arrhythmias, atrioventricular valve regurgitation, and reaction remodeling of myocardial tissue should be checked in the future.

The target of this procedure has been expanded from pediatric population to adults, including geriatric population. In this regards, the collaboration between adult and pediatric cardiologist has to be conducted for the total therapeutic management in this procedures.

7.10 PDA and Catheter Intervention

7.10.1 Clinical Features of Adult Patients with PDA

In general, majority of patients with PDA are diagnosed and treated in neonates or children; unrepaired patients with PDA are considered to be relatively rare situation. However, even in nowadays, adult patients with PDA are not rare. Compared to pediatric patients, adult PDA patients are usually symptomatic, such as shortness of breath or palpitation, which is caused by congestive heart failure. In such adult patients, medical treatment is not enough for resolving of heart failure; closure of PDA is considered as the essential treatment. However, surgical closure of PDA in adults is not a simple procedure compared with pediatric patients. Long-term persisted left ventricular volume overload could cause atrial arrhythmias and mitral or aortic valve insufficiency. Morphology of ductus arteriosus is also different form pediatric population. Conical shape of ductus is the most common type in pediatric patients; however in adults, short and tubular or window shape of ductus is frequently seen. Also adults PDA has calcification and fragile of the PDA wall. Such morphological features make surgical closure of adult PDA difficult. In fact, the majority of adult patients with PDA are required of cardiopulmonary bypass and mid-sternum thoracotomy.

In this regard, clinical implication of transcatheter closure of PDA seems to be very high in adult patients.

The indication of PDA closure in adult patients is same as pediatric patients. Catheterization including descending aortography is the essential for the accurate morphological and hemodynamic diagnosis of PDA; the latest three-dimensional CT or MRI imaging is quite valuable for decision-making of therapeutic strategies for interventional procedures.

7.10.2 Catheter Intervention of PDA

In the past, coil occlusion of PDA is only available for therapeutic option of catheter closure of PDA in Japan [37]. Cook detachable coil or 0.052 inch Gianturco coil was used for interventional procedure. Although this modality was effective in patients with small PDA (usually less than 3 mm), complete closure of moderate or large PDA was always difficult. Multiple coil implantations contributed to the procedure's success in this condition; however, multiple coil implantation required technical skills and higher complication rate, such as coil migration or hemolysis [38].

Recently, Amplatzer Duct Occluder (ADO) was introduced for catheter intervention for PDA and contributes high success rate and low complication rate even in

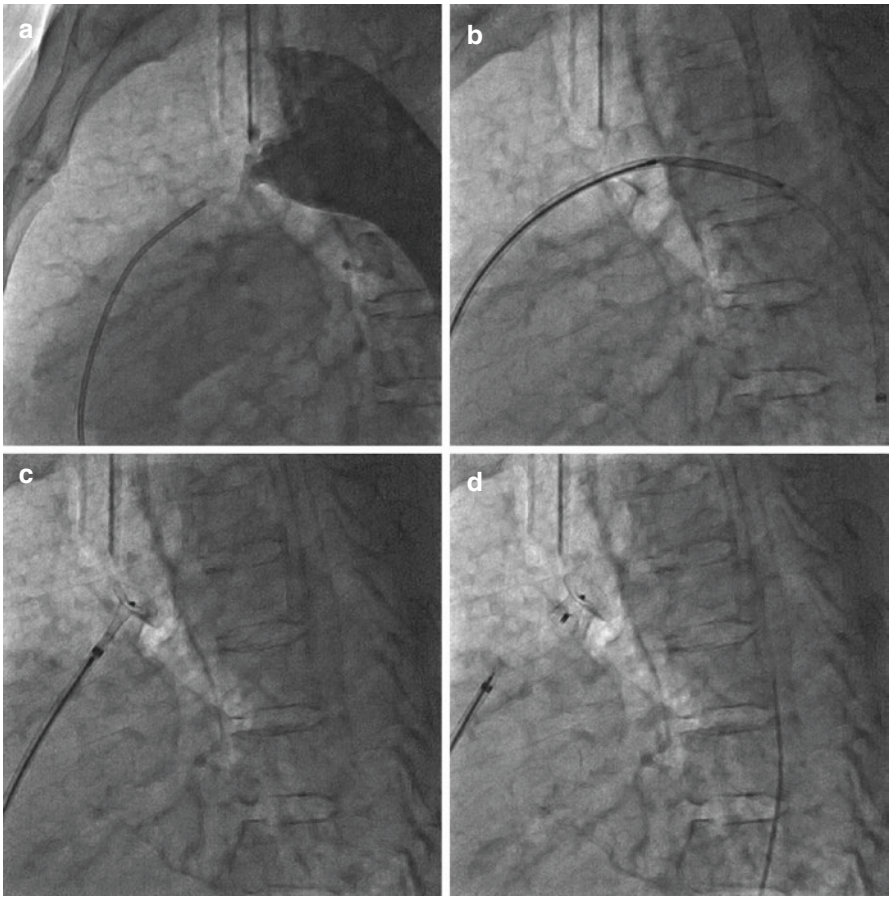

Fig. 7.9 Catheter closure of adult PDA. (**a**) Aortography demonstrated 4.5 mm PDA. (**b**) Amplatzer Duct Occluder was advanced to the descending aorta passing through the ductus. (**c**) 8 mm device was deployed from the aorta. (**d**) Device was placed stable position, and ductus was completely closed

moderate or large PDA [39]. The cylindrical, slightly tapered device has a thin retention disk 4 mm larger in diameter than its body to ensure secure positioning in the ductal ampulla. As similar of Amplatzer Septal Occluder, polyester fibers sewn into the device induce thrombosis and rapid complete occlusion (Fig. 7.9). Various diameter of the device are available, from 4 mm to 12 mm. ADO introduced from femoral vein using six French long sheath. Device can be repositioning and retrieving until detachment. Device was selected >2 mm larger than narrowest PDA diameter, thus using this device, PDA up to 10 mm diameter can be closed safely. Compared with coil occlusion, ADO is a very effective and safe procedure even in adult patients with short or tubular PDA. Although several studies reported that hemolysis caused by residual shunt can occurred after the procedure, the most of

those cases resolved naturally within a few days after the intimal proliferation around the device [40].

7.10.3 Future Direction of Catheter Intervention for ACHD

In Europe and North America, there are many other kinds of devices for congenital heart disease, including device for ventricular septal defect [41], pulmonary valve [42], covered stent [43], patent foramen ovale [44], etc. Unfortunately, we cannot introduce such devices in Japan at this moment. However, if these interventional procedures can perform safely, it must be great benefit not only for pediatric patients but also adult patients with congenital heart disease. Rather, such interventional procedure tend be focused on adult patients. Key issues for expanding such new interventional procedures are collaboration between pediatric cardiologists, adult cardiologists, and cardiovascular surgeons. Pediatric cardiologists have better knowledge of congenital heart disease itself, especially anatomy, however, not enough experiences for age-related complication such as arrhythmias, hypertension, etc. For safe and effective procedure outcome in adult patients with congenital heart disease, the optimal management of comorbidities is very important. In this regard, adult cardiologist has to conduct the total therapeutic strategies in these patients; if possible, the establishment of adult congenital heart disease specialist in each institution, which involved these interventional procedures, is the most desirable direction optimal patient's care.

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Repaired Tetralogy of Fallot

8

Yukihisa Isomatsu and Munetaka Masuda

Abstract

Along with surgical and pharmacological innovation, operative mortality of tetralogy of Fallot (TOF) repair has been improved dramatically. The more patients with TOF repair reach their adulthood, the more problems have been revealed particularly in the twenty-first century. To grasp the current overview after TOF repair, recent understanding about TOF is briefly described in section "Introduction." Pulmonary valve regurgitation and pulmonary valve replacement in patients with repaired TOF is explained in section "Pulmonary Regurgitation and Its Assessment." More attentions, in the recent era, are paid to the unfavorable effects of pulmonary valve regurgitation which theoretically causes right ventricular volume overload. Considering the deleterious effects of pulmonary valve regurgitation on the right ventricle, timing and indication of pulmonary valve replacement for repaired TOF has been a major concern during this decade and is described in section "Indication and Timing of Pulmonary Valve Replacement" (PVR). Selection of the prosthetic valve for pulmonary valve replacement is another concern, and our surgical policy regarding prosthesis selection is discussed in section "PVR and Selection of Prosthesis." Surgical technique of pulmonary valve replacement including each procedure is illustrated in detail in section "Surgical Technique." In the final section, "Tricuspid Regurgitation After TOF Repair," we proposed our surgical concept of doing simultaneous tricuspid annuloplasty at the time of pulmonary valve replacement in patients with repaired TOF.

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Repaired tetralogy of Fallot • Pulmonary valve regurgitation • Pulmonary valve replacement • Tricuspid valve regurgitation • Adult congenital heart disease (ACHD)

8.1 Introduction

Along with the introduction of cardioplegia mainly in the 1970s, with the advent of prostaglandins by 1980, and also with the accumulation of precise anatomical findings mainly in the 1980s, operative results after tetralogy of Fallot (TOF) repair has been improving noticeably since Lillehei et al. performed the first open-heart repair for TOF in 1954 [1]. The operative mortality of TOF repair in Japan has decreased from more than 10% in 1975 [2] to 4.1% in 1997 [3] and 1.4% in 2013 [4].

The more patients with TOF repair reach their adulthood, the more problems have been revealed particularly in the twenty-first century. The major adverse cardiovascular events (MACE) have been reported to be not rare in patients with repaired TOF [5–9]. The care givers who are working at the field of treatment for adult congenital heart disease (ACHD) should have knowledge and information because various types of MACE may occur.

8.1.1 Recent Understanding About TOF

It is nowadays well known that long-term survival after repair is good [10]. According to the longer follow-up studies, several medical problems have become apparent: (1) exercise intolerance and ventricular dysfunction, (2) arrhythmia and sudden cardiac death, (3) pulmonary valve regurgitation, (4) tricuspid valve regurgitation, and (5) right ventricular (RV) and left ventricular (LV) failure [5–9, 11–15].

Residual pulmonary stenosis, ventricular septal defect, and aortic regurgitation/dilatation (mentioned in Chap. 13) are also the concern.

8.1.2 Exercise Intolerance and Ventricular Dysfunction

RV dysfunction in patients with repaired TOF leads to exercise intolerance and is associated with ventricular tachycardia and sudden cardiac death (SCD) [16]. Exercise testing is helpful to decide the timing of pulmonary valve replacement (PVR) because RV dysfunction may obvious only during exercise and biventricular electromechanical dyssynchrony may worsen [14]. RV volume overload may negatively affect the function of both RV and LV due to their interdependence (ventricular-ventricular interaction) [17].

8.1.3 Arrhythmia and Sudden Cardiac Death

High-grade ventricular arrhythmias (sustained monomorphic ventricular tachycardia >30 s in duration) will be identified in about 10% of patients [18], and atrial reentrant tachycardia will develop during extended follow-up in more than 30% of patients [19]. Most SCD events in patients with repaired TOF appear to be due to sustained ventricular tachycardia and not a few SCD events in them due to rapidly conducted atrial tachycardia [20]. Risk factors for ventricular tachycardia and SCD are as follows [14]:

1. Older age at time of repair (>20 years of age)
2. Prior large palliative shunts
3. Prolonged QRS duration on electrocardiogram (>180 ms)
4. Compromised LV systolic and/or diastolic function [5]
5. Severe RV enlargement

Surgical PVR alone, to date, does not have a major impact on the risk reduction for ventricular tachycardia, at least when performed in TOF adults with a long-standing hemodynamic burden [14]. Reverse remodeling and ventricular tachycardia reduction might be feasible if surgery is performed earlier in the disease course [21].

8.2 Pulmonary Valve Regurgitation and Its Assessment

The “right ventricle” has been considered to be well tolerable to volume overload mainly caused by pulmonary valve regurgitation. As an example to explain this recognition, there is a paper describing the longevity of RV-PA conduit by one of the authors of this chapter [22]. Their indication for conduit replacement, which 82 of 366 patients underwent, was pulmonary stenosis in all but three patients with infective endocarditis. There were no patients who underwent conduit replacement because of pulmonary regurgitation alone although mean RVEDV before replacement was 130–145% of normal by conventional cineangiogram. It was presumably due to that the major concern of TOF repair in the 1970s–1980s was the sufficient release of the right ventricular outflow tract obstruction even if the competence of the pulmonary valve may be sacrificed to some extent. However, the more patients with TOF repair in their infancy reach 30–40 years old, the more attentions are paid to the unfavorable effects of pulmonary valve regurgitation which inevitably causes “right ventricle” volume overload. Those effects decrease exercise performance and increase lethal ventricular arrhythmia and sudden cardiac death.

On the historical background of TOF repair described above, transannular patch has been employed widespread since then and is employed even now in some situations. For example, we often do transannular patching instead of preserving the pulmonary valve when the Z-value of the pulmonary valve estimated by UCG is less

than −2.0 to −2.5. In this transannular patch technique, the fibrous continuity of two (or three, uncommon) cusps of the pulmonary valve is disrupted anatomically whether a transannular patch has an artificial monocusp valve or not. In consequence the coaptation between pulmonary cusps is lost, and the pulmonary valve regurgitation inevitably happens as postoperative sequelae.

The transatrial/transpulmonary approach may offer improved intermediate-term RV function and a lower risk for arrhythmias [23]. Although pulmonary valve sparing techniques have logical advantage of long-term pulmonary valve competence, there has been no definitive longitudinal data in terms of pulmonary valve regurgitation from comparison of other surgical approaches, such as conventional infundibulotomy with or without a preserved pulmonary valve.

8.2.1 Indication and Timing of Pulmonary Valve Replacement (PVR)

Considering deleterious effects of pulmonary valve regurgitation on the right ventricle, timing and indication of pulmonary valve replacement (PVR) for repaired TOF has been a major concern during this decade. Symptomatic exercise intolerance, clinical arrhythmia onset, and right heart failure were advocated as indications for PVR [15, 24]. Several studies showed PVR after the emergence of these symptoms did not produce RV reverse remodeling and improved clinical symptoms [25–28]. It means that PVR not performed until those symptoms clinically emerge is somewhat late. Therefore, objective indicators are searched.

Since 2003–2005, cardiac magnetic resonance (CMR) has been recognized as a gold standard method to quantify the degree of PR and also to evaluate residual anatomic and hemodynamic abnormalities [29, 30]. It is based on the fact that CMR has reproducibility and accuracy compared with the conventional imaging modality, such as echocardiography, cardiovascular computed tomography, and cardiac angiography [31, 32].

Although this does not reach the consensus regarding cutoff value, right ventricular end-diastolic volume index (RVEDVI) is regarded as a convincing indicator of pulmonary valve regurgitation. According to the Canadian Cardiovascular Society guidelines (2010), progressive RV enlargement (RVEDVI > 170 mL/m^2) was one of indications for PVR [12]. In the guidelines by the European Society of Cardiology (2010), it was described that normalization of RV size after re-intervention becomes unlikely as soon as the RVEDVI exceeds 160 mL/m^2 [13]. No specific RVEDVI figure as a cutoff value was indicated in the American College of Cardiology and American Heart Association guidelines (2008) [11]. The Japanese Circulation Society released guidelines of management and re-intervention therapy in patients with congenital heart disease long term after initial repair in 2012. They described RVEDVI < 150–170 mL/m^2 and RVESVI < 82–90 mL/m^2 may be a borderline for RV remodeling after PVR [33].

We, at present, make RVEDVI > 150–160 mL/m^2 a central feature of PVR.

8.2.2 PVR and Selection of Prosthesis

A prosthetic valve is usually used for PVR in adult patients with repaired TOF. Homograft, which is popular material at the pulmonary position in the Western countries, is not a realistic alternative because of its unavailability in Japan.

Regarding the selection of prosthesis as of 2016, we believe stented bovine pericardial valve with antimineralization treatment is the choice of valve in the right side of the heart based on the following reasons:

1. Longer durability in the right side (low pressure system) is theoretically expected than placed in the left side of the heart.
2. Transcatheter implantation of pulmonary valve prosthesis, which is not available in Japan to date, can be performed in patients with PVR by bioprosthesis. It cannot be performed after PVR using with a mechanical valve because of its structure.
3. According to Abbas and Hoschtitzky, there is no apparent evidence about superiority of biological valve at the pulmonary position [34]. Regarding the freedom from redo PVR until 5–10-year duration, no significances exist between bovine pericardial valve and stented porcine valve in the literatures. However, considering good long-term (15–20 years) results of redo PVR free rate particularly in Japanese patients [35, 36], stented bovine pericardial valve is an encouraging option. Furthermore, antimineralization and patient-prosthesis mismatch might be key factors for durability of biological valves [37, 38], and thus stented bovine pericardial valve with antimineralization treatment is our choice.

Deliberating the hemorrhage complications caused by anticoagulation with warfarin or quite frequent thromboembolic episodes of the mechanical valve at the right side of the heart, we think PVR using with a mechanical valve is an exceptional alternative (e.g., left-sided mechanical prosthesis).

8.2.3 Surgical Technique

Under general anesthesia with a patient in a supine position, a second or third time median sternotomy is carefully made. The right femoral vein and the left femoral artery, when necessary, are exposed for cannulation. Substernal and pericardial adhesion is carefully dissected. Meticulous care is required during dissection when RVOT aneurysm exists. After cardiopulmonary bypass was initiated with ascending aortic cannulation with dispersion tip, bicaval direct cannulations, and left heart venting through the right upper pulmonary vein to the left ventricle, the patient is cooled on (rectal temperature 34–35 °C). After aortic cross-clamping, cardiac arrest is obtained by cold-blood cardioplegia from the antegrade coronary perfusion and retrograde perfusion thereafter (every 15–20 min).

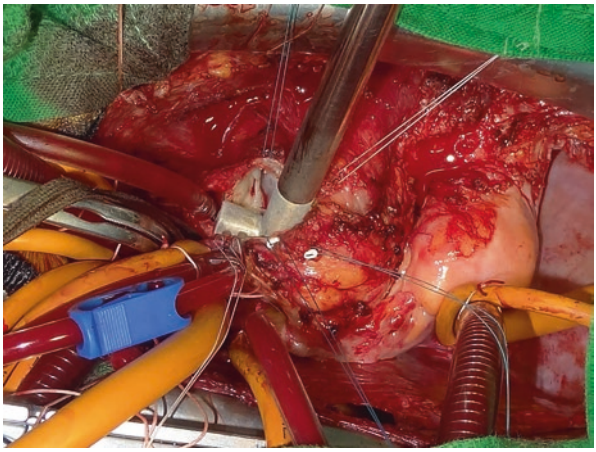

Fig. 8.1 Cryoablation is performed at the infundibular septum which is often the origin of the ventricular arrhythmias

Cryoablation, if necessary, is performed for ventricular arrhythmias related to RV dilatation and/or previous operative scar. Cryoablation is usually placed around the previous right ventriculotomy and at the infundibular septum (Fig. 8.1) which is often the origin of the ventricular arrhythmias. Following the right atriotomy, residual VSD is examined through the tricuspid valve and residual VSD (if present) is closed. A longitudinal incision is then made from the main pulmonary artery (PA) beyond the native pulmonary valve to the RVOT when transannular patch is used or to the native pulmonary valve when transannular patch is not used. Previous transannular patch is removed except for the remnant for suturing a new patch. Handmade strips with glutaraldehyde-treated autologus pericardium (if available) or xenopericardium are used to reinforce the suture line after RVOT aneurysm is excised. The thickened or degenerative bicuspid (most of cases) pulmonary valve is removed. When choosing the size of a bioprosthesis, care should be taken not to underestimate the valve size because patient-prosthesis mismatch is more likely to occur in biological valve than in mechanical valve. On the other hand, the use of oversized valve may result in compression of the left main trunk of the coronary artery; therefore selection of the valve size is crucial. At first eight to ten mattress sutures are placed at the native pulmonary valve ring and then placed at the cuff of a stented bovine pericardial bioprosthesis. At the transitional portions between the native pulmonary wall and the prosthetic patch, one end of the pledgetted suture is passed from the outside of the native tissue, and another end of this suture is passed from the patch to avoid the perivalvular leakage (Fig. 8.2), so that the pledget locates astride both the native tissue and the patch. To do this maneuver easily, in addition, either end of suture between the native pulmonary ring and the bioprosthesis cuff is left untied. At this time, we usually place two pairs of monofilament suture between the native tissue and the prosthetic patch for the purpose of fitting them tightly to prevent hemorrhage.

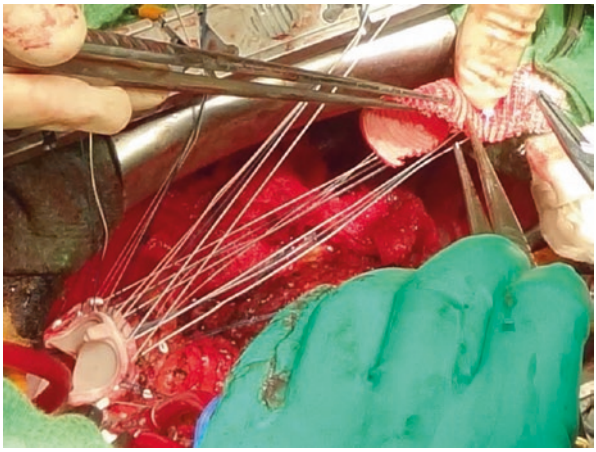

Fig. 8.2 To avoid the perivalvular leakage, one end of the pledgetted suture is passed from the outside of the native wall, and another end of this suture is passed from the patch (just this stitch) at the transitional portions between the native pulmonary wall and the prosthetic patch, so that the pledget locates astride both the native tissue and the patch

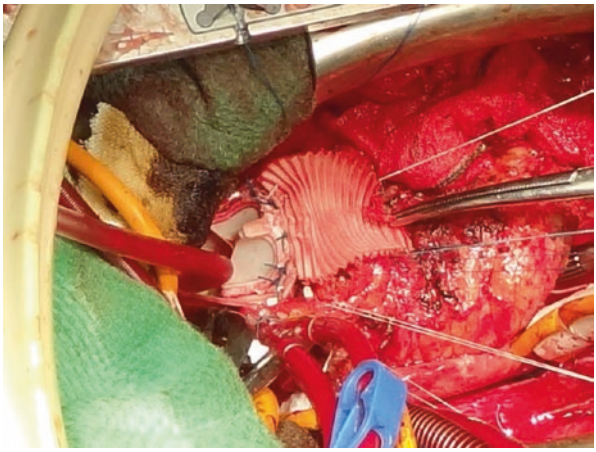

Fig. 8.3 Two pledgetted sutures at the transitional portions (described at Fig. 8.2) and the four mattress sutures passed from the outside of the patch and then through the bioprosthesis cuff are all tied finally

Thereafter, the three or four mattress sutures are passed from the outside of the patch (approximately one-third of a vascular prosthesis) and then through the cuff of this bioprosthesis. Finally, the remaining sutures are all tied (Fig. 8.3). Strut orientation is recommended at the 6-10-2 o'clock positions to avoid the obstruction of the left or right PA orifices by relatively tall stent of the bioprosthesis. Positioning of the bioprosthesis should be posteriorly angulated toward the downward pulmonary arteries, resulting in efficient hemodynamics and less of a tendency toward development of an aneurysmal pulmonary artery [39]. The patch is sutured to the main pulmonary artery and the right ventricular portion to complete the new entire RVOT. Tricuspid annuloplasty is finally performed using the tricuspid ring (Fig. 8.4).

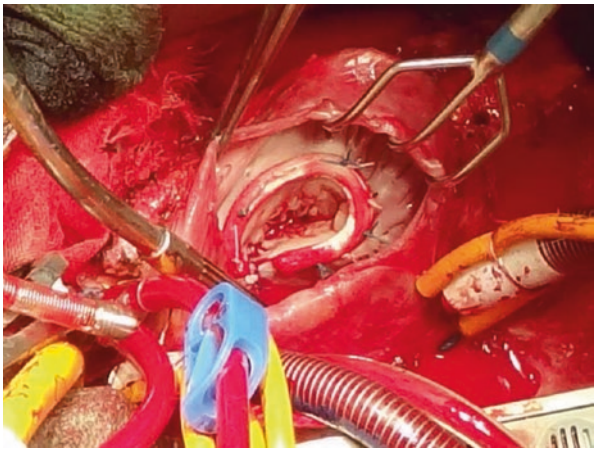

Fig. 8.4 Tricuspid annuloplasty is performed using the tricuspid ring including edge-to-edge repair between anterior and septal leaflets anticipating the less possibility of tricuspid valve regurgitation in the future

8.3 Tricuspid Valve Regurgitation After TOF Repair

The positive role of the additional prophylactic tricuspid annuloplasty is unclear. Only two papers described regarding the need for tricuspid annuloplasty at the same time of PVR [40, 41]. The former stated tricuspid valve function improved to a similar degree with or without annuloplasty. The latter concluded concomitant tricuspid annuloplasty should not be considered based on tricuspid annular dilation alone. However, considering that tricuspid regurgitation may be secondary to RV dilatation not only from pulmonary valve regurgitation but from a structural valve abnormality related to the VSD patch at initial repair [14], we usually do tricuspid annuloplasty (including edge-to-edge repair between anterior and septal leaflets) in anticipation of the less possibility of tricuspid valve regurgitation even at the time of initial repair. We, like many other surgeons, use the three-dimensional tricuspid ring in adult patients because tricuspid regurgitation recurs in the long term after conventional Kay or DeVega procedure.

Conclusion

Pulmonary valve regurgitation, its assessment and indication, and surgical technique of pulmonary valve replacement for patients with repaired tetralogy of Fallot are mainly described in this chapter.

There have been several other issues, such as more sensitive indicators peculiar to each patient who require a pulmonary valve replacement, the essentially limited longevity of bioprostheses, the effectiveness of cardiac resynchronization therapy for patients who have biventricular dysfunction, and the need of implantable cardioverter-defibrillator.

Aortopathy (or aortic root dilatation), which is often observed in adult repaired TOF patients, is described in another chapter in this textbook.

Longitudinal and careful follow-up using developing (sometimes breakthrough) methods is mandatory to obtain a better quality of life as well as a longer life expectancy in repaired TOF patients.

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Post-RV-PA Conduit Repair

9

Yutaka Imoto, Tomoyuki Matsuba, Hideaki Kanda, and Yoshiya Shigehisa

Abstract

Reconstruction of the right ventricular outflow tract with extracardiac conduits facilitated the complete repair of complex cardiac malformations such as pulmonary atresia with VSD, transposition of the great arteries with VSD and left ventricular outflow tract obstruction, and truncus arteriosus. Commonly used conduits now are the valved conduits with various materials and designs: homograft, stented xenograft, stentless xenograft, autologous tissue conduit, and expanded polytetrafluoroethylene conduit. Early results are excellent in these conduits; however, conduit reoperation is unavoidable in the mid or long term due to conduit obstruction, valve regurgitation, infectious endocarditis, formation of aneurysm or pseudoaneurysm, somatic outgrowth, and so on. Among all, conduit obstruction is the most frequent cause of conduit explantation. Operative indication for conduit obstruction is usually based on the pressure gradient across the conduit or right ventricular systolic pressure, but it is important to perform the reoperation before the development of right ventricular failure. Reoperation is performed under cardiopulmonary bypass; the old conduit is removed, and the distal and proximal ends of a new conduit are anastomosed to each position. There is a variety of conduit types used in reoperation as in the first implantation, but it still remains unclear which conduit should be appropriate. Relatively larger sized conduit can be used in the reoperation compared to the first operation, which may offer a longer durability. Percutaneous pulmonary valve implantation

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is a less invasive alternative for the treatment of conduit dysfunction and may avoid polysurgery and reoperative procedure-related complications, but it is not approved in Japan at this point of time.

Keywords
Right ventricular outflow tract • RV-PA conduit • Pulmonary atresia • Reoperation

9.1 Introduction

Conduit reconstruction of the right ventricular outflow tract (RVOT) continues to play an important role in the surgical treatment of a broad spectrum of complex congenital heart defects. Over the decades, many types of conduits with various materials, designs, and sizes have been developed, and excellent early results have been obtained after corrective surgery using these conduits. However, durability of conduit is still a problem, and the late outcome is affected by the hemodynamic consequences of conduit failure and the need for conduit reoperation. In this chapter, types of RV-PA conduits, durability, and mechanism of conduit failure are summarized along with the considerations for conduit reoperation.

9.2 RV-PA Conduit Repair

9.2.1 Definitive Diagnoses in the Patients Who Undergo RV-PA Conduit Repair

Definitive diagnoses in the patients who may undergo right ventricle-to-pulmonary artery (RV-PA) conduit operation are listed in Table 9.1. They are categorized into subgroups: (1) pulmonary atresia or stenosis associated in other cardiac lesions, (2) truncus arteriosus, (3) absent pulmonary valve syndrome, and (4) other conditions

Table 9.1 Definitive diagnoses and operative procedures in which RV-PA conduit is used

(i) Pulmonary atresia or stenosis • PA-VSD with or without MAPCAs • TGA-III • ccTGA
(ii) Truncus arteriosus
(iii) Absent pulmonary valve syndrome
(iv) Miscellaneous • Ross procedure (aortic stenosis or regurgitation) • Yasui procedure (interruption of the aortic arch, severe aortic stenosis, and ventricular septal defect)

PA-VSD pulmonary atresia with ventricular septal defect, *MAPCAs* major aortopulmonary collateral arteries, *TGA-III* complete transposition of the great arteries with ventricular septal defect and pulmonary stenosis, *ccTGA* congenitally corrected transposition of the great arteries

requiring surgical procedures in which autologous pulmonary valve is used as a substitute for an aortic valve. Rastelli procedure was first reported in 1969 [1], which was performed in a patient with transposition of the great arteries (TGA), ventricular septal defect (VSD), and subpulmonary stenosis; intracardiac route from the left ventricle to the aortic valve was created, and RV outflow tract was constructed with valved conduit (Fig. 9.1). Similar surgical procedure is performed in patients with VSD and pulmonary atresia; it is also known as "extreme Fallot" or "Fallot with pulmonary atresia." In special type of this subgroup, pulmonary atresia with major aortopulmonary collateral arteries (MAPCAs) is known as concomitant anomaly, in which multiple peripheral pulmonary arteries originate directly from the descending aorta or from the arch vessels. Unifocalization of all the MAPCAs is mandatory to carry out the Rastelli procedure. In congenitally corrected transposition of the great arteries (ccTGA) with pulmonary atresia, definitive repair is achieved by "conventional Rastelli procedure" (Fig. 9.2a) or "double switch with Mustard-Rastelli procedure" (Fig. 9.2b). A valved conduit is interposed between the anatomical LV (pulmonary ventricle) and the pulmonary artery in the former procedure and between the anatomical RV and the pulmonary artery in the latter. RV-PA conduit is used in total correction of truncus arteriosus unless direct anastomosis of the pulmonary artery to the RV is selected (Fig. 9.3). Absent pulmonary valve syndrome is characteristic of severe pulmonary regurgitation and extremely dilated pulmonary arteries, which results in airway obstruction. Since perfect valve competence against high pulmonary resistance is required in this condition, valved conduit is preferred rather than *a monocusp patch repair* in which *a long incision is made*

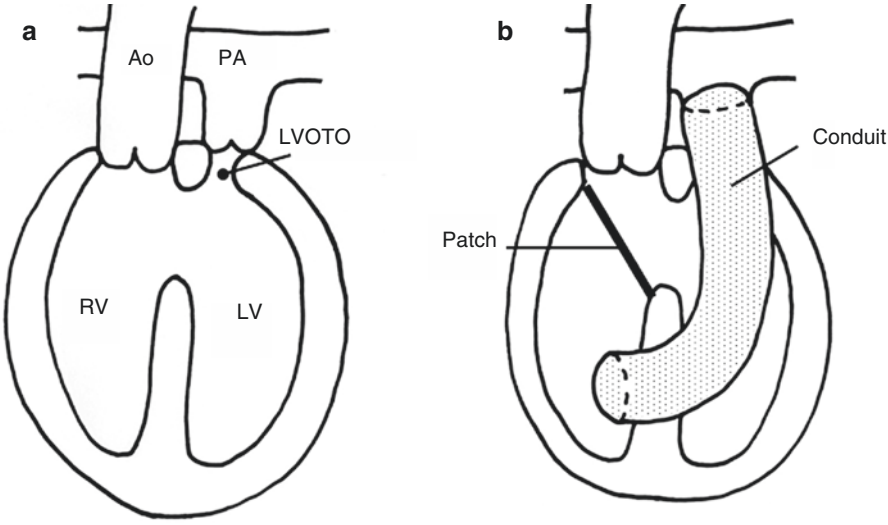

Fig. 9.1 Rastelli procedure for TGA-III. Transposition of the great arteries (TGA), ventricular septal defect (VSD), and left ventricular outflow tract obstruction (LVOTO) are seen (**a**). The VSD is closed with a patch to make a connection between the left ventricle and the aortic valve, and RV-PA conduit is reconstructed (**b**). *Ao* aorta, *PA* pulmonary artery

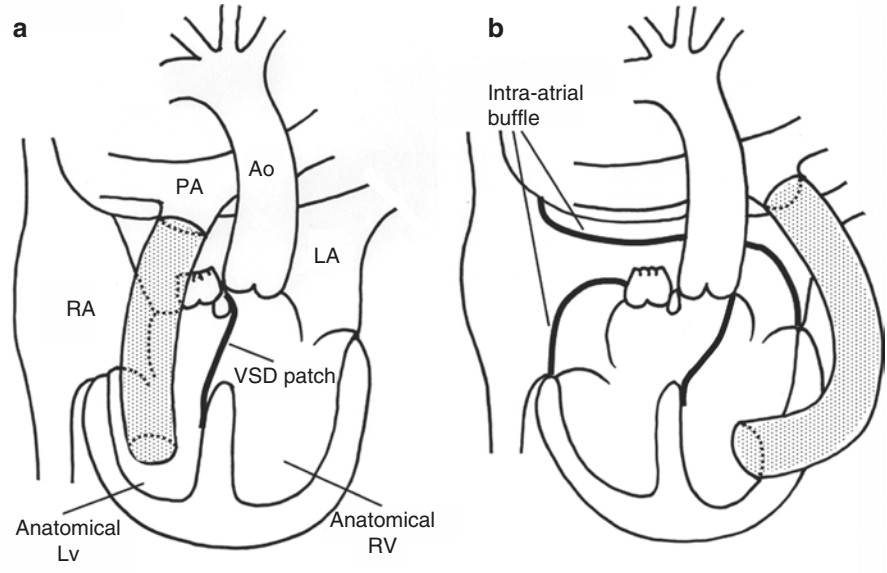

Fig. 9.2 Conduit repair for ccTGA with pulmonary atresia. Two types of definitive repair are shown: "conventional Rastelli procedure" (**a**) and "double switch with Mustard-Rastelli procedure" (**b**)

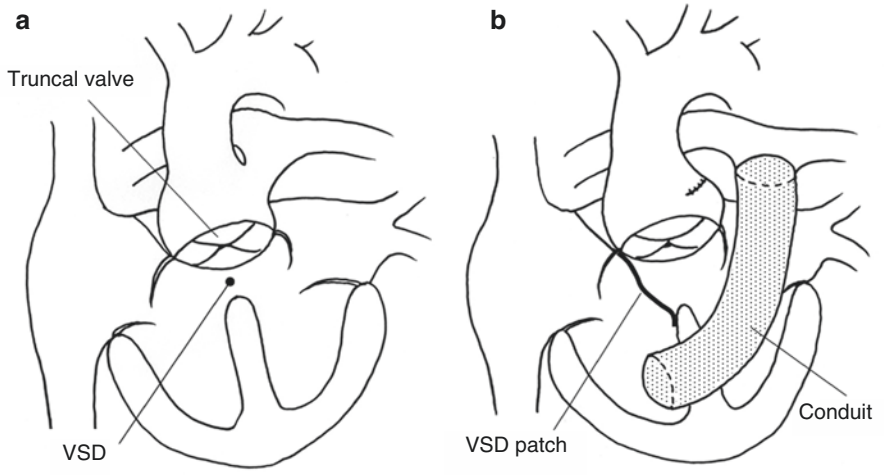

Fig. 9.3 Rastelli procedure for truncus arteriosus. Truncal valve overrides the interventricular septum (**a**). In total correction, the VSD is closed, and RV-PA conduit is interposed between the RV and the distal pulmonary artery, which was excised from the truncal artery (**b**)

across the pulmonary valve and a transannular patch with a simple cusp attached inside is anastomosed.

In Ross procedure [2], aortic valve replacement is performed with a pulmonary autograft, and a valved conduit is used as a substitute for it (Fig. 9.4). Yasui procedure [3] offers an innovative technique for complex cardiac anomalies with

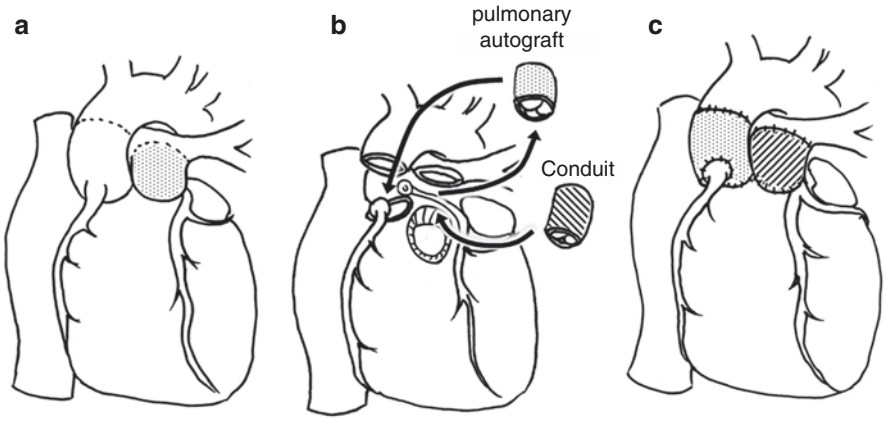

Fig. 9.4 Ross procedure. (**a**) Preoperative appearance of the heart. (**b**) Pulmonary autograft is harvested, and aortic valve replacement is performed with it. The right ventricular outflow tract is reconstructed with some type of conduit. (**c**) Postoperative appearance

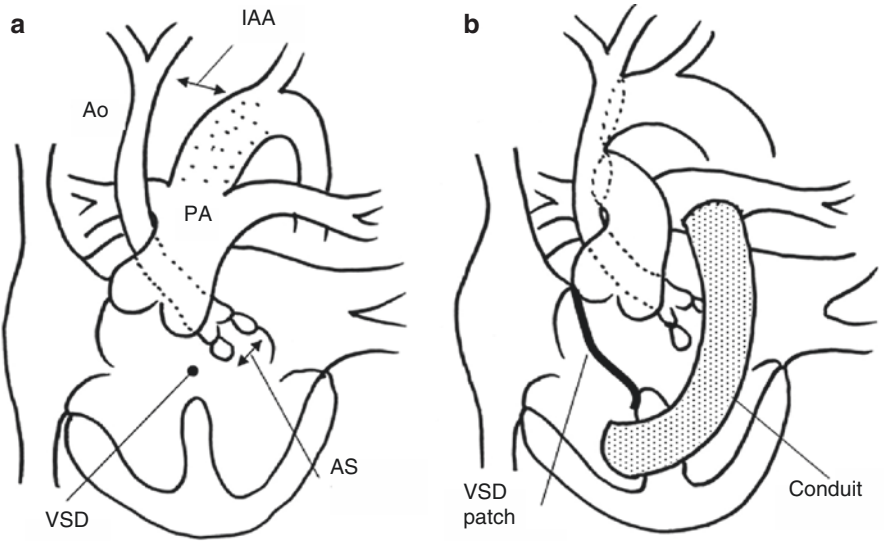

Fig. 9.5 Yasui procedure. Preoperative diagnoses are complex cardiac anomalies of interruption of the aortic arch, VSD, and severe aortic stenosis (**a**). The pulmonary valve is used as a main semilunar valve for systemic outflow tract; therefore an extracardiac valved conduit is needed instead (**b**). *IAA* interruption of the aortic arch, *AS* aortic stenosis

interruption of the aortic arch, VSD, and severe aortic stenosis, where the aortic valve is too small to be used as a systemic semilunar valve. The pulmonary valve is included in the left ventricular outflow tract (LVOT) as a substitute of the aortic valve, and right ventricular outflow tract (RVOT) is reconstructed with a valved conduit (Fig. 9.5).

9.2.2 Conduit Type and Durability

Various types of conduit for reconstruction and reoperation in RVOT have been developed over the years. Most of them are valved conduits and are divided into five categories: (1) homograft conduit (pulmonary and aortic), (2) stented xenograft conduit, (3) stentless xenograft conduit, (4) autologous tissue conduit, and (5) expanded polytetrafluoroethylene valved conduit.

9.2.2.1 Homograft

Use of homograft was first reported by Ross and Somerville [3] in the RVOT reconstruction of *tetralogy of Fallot and pulmonary atresia* in 1965 and is gold standard in the western countries [4]. In Japan, the use of homograft is not popular because of the shortage of donors.

Mechanism of conduit failure includes conduit stenosis, conduit regurgitation, aneurysm formation, and infectious endocarditis. The majority of the conduit replacements were due to conduit stenosis, valvular stenosis mainly due to leaflet calcification, distal anastomosis stenosis, sternal compression, and somatic outgrowth [5–9]. Conduit stenosis was responsible for failure in 53% of patients, technical issues accounted for 30%, and only 8% failed as a result of somatic outgrowth [10]. Durability of homograft conduit is related to patient age and homograft size. Infants showed a disappointing rate of freedom from conduit failure (42%) in comparison with older children (87%) at 5 years [4]. Smaller conduits are generally related to earlier reoperation, but extremely oversized conduit may fail more rapidly due to external compression of the conduit by the closed sternum, valve distortion, and insufficiency with sternal compression or distortion of distal PAs from the oversized conduit [11].

9.2.2.2 Stented Xenograft

Clinical use of stented xenograft started in the 1970s; porcine valve within a woven Dacron graft as represented by Carpentier-Edwards porcine-valved conduit® (Edwards Lifesciences, Irving, CA, USA) (Fig. 9.6a) and Hancock porcine-valved conduit® (Medtronic, Minneapolis, MN) (Fig. 9.6b).

Schiralli et al. [12] reported excellent longevity of Carpentier-Edwards porcine-valved conduit used in the RVOT reconstruction; freedom from reoperation was 70.3% at 8.2 years. The increase in transconduit gradient over time was inversely proportional to conduit size, but the patients receiving large sized conduits (25 and 30 mm) demonstrated no gradient development over this follow-up period. They concluded that Carpentier-Edwards porcine-valved conduit showed excellent longevity at intermediate-term follow-up. Belli et al. [13] reported that freedom from reoperation in Hancock porcine-valved conduit was 98% at 1 year, 81% at 5 years, and 32% at 10 years. They concluded that the Hancock valved conduit is a safe and reliable conduit.

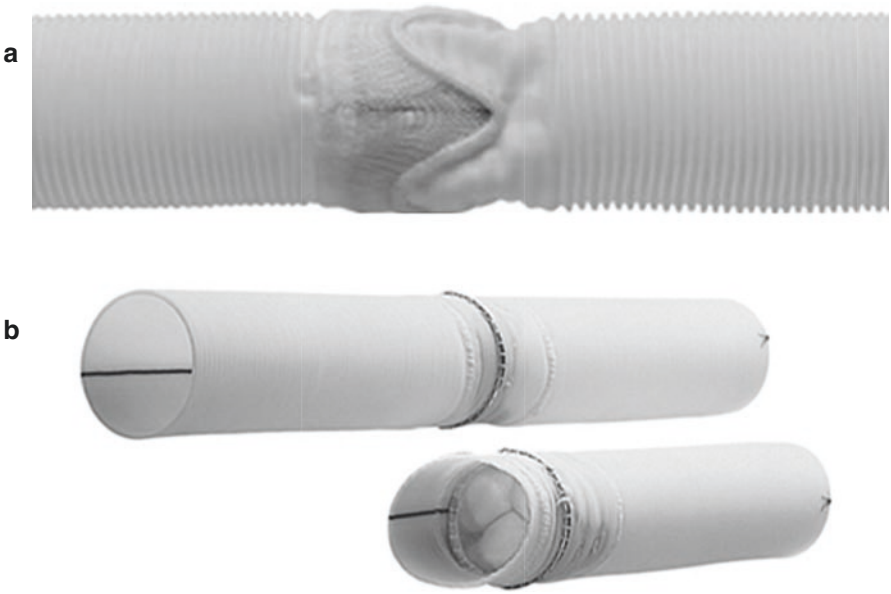

Fig. 9.6 Stented xenograft valved conduits. Carpentier-Edwards porcine-valved conduit® (Edwards Lifesciences, Irving, CA, USA) (**a**) and Hancock porcine-valved conduit® (Medtronic, Minneapolis, MN) (**b**) are shown

9.2.2.3 Stentless Xenograft

Medtronic Freestyle® stentless porcine bioprosthesis (Medtronic, Inc., Fridley, Minnesota, USA) (Fig. 9.7), a representative stentless xenograft valved conduit, is derived from a porcine aortic root. It is extensively used in the aortic position, and the report of its use as a RVOT conduit has first published in 2001 [14]. Dunne et al. [15] reported satisfactory short-term outcomes, including functional status and freedom from reintervention based on the meta-analysis of 13 observational studies, including 334 patients with a mean follow-up of 34 months (range 10–98 months); structural valve deterioration occurred in 4.8%, and reintervention was required in 1.1%.

Contegra® (Medtronic, Minneapolis, MN) is a bovine jugular vein graft comprised of a trileaflet venous valve with three natural sinuses (Fig. 9.8). This conduit is stored in buffered glutaraldehyde and is available in sizes from 12 to 22 mm and has been widely used recently [16]. The main advantages of this conduit are use of natural tissue as raw material, unlimited availability, sufficient length at both inflow and outflow, and a favorable in vitro hemodynamic performance due to an effective orifice area [17]. Mery et al. [18] reported that Contegra was associated with a significantly lower incidence of reintervention and replacement compared with

Fig. 9.7 Stentless xenograft valve. Medtronic Freestyle® stentless porcine bioprosthesis (Medtronic, Inc., Fridley, Minnesota, USA)

Fig. 9.8 Bovine jugular vein graft containing a trileaflet venous valve, Contegra® (Medtronic, Minneapolis, MN). Sufficient lengths are available at both inflow and outflow (**a**). Natural continuity between valve and conduit is noted (**b**)

homograft and porcine heterograft; overall freedom from reintervention in Contegra at 5, 10, and 15 years was 73%, 45%, and 26%, respectively. Morales et al. [19] reported excellent midterm results of Contegra; 3-year freedom from severe conduit regurgitation was 81%, and freedom from severe conduit stenosis was 100%. Excellent morphology and hemodynamics, and better durability in a medium-term follow-up, were reported with Contegra conduit [20, 21]. In contrast, Göber et al. [17] do not recommend routine use of this material, because of the unpredictable incidence of supravalvar stenosis. Other problems in Contegra have also been reported: high risk of infectious endocarditis, pseudoaneurysm formation at the distal anastomosis, aneurysmal dilatation, extensive intimal proliferation at the level of distal anastomosis, diffuse stenosis by tissue ingrowth, conduit kinking, and compression [18, 19, 22–25]. Freedom from conduit dysfunction and failure were significantly related with younger age, conduit size, and original diagnosis (truncus arteriosus) [18].

9.2.2.4 Autologous Tissue Conduit

Handmade autologous pericardial conduit is also used as an RV-PA conduit. Schlichter et al. [26] reported excellent durability of fresh autologous pericardial conduit with bileaflet valve (Fig. 9.9) in the 54 survivors of RVOT reconstruction who were followed up from 5 to 15 years; freedom from reintervention at 5 and 10 years was 92% and 76%, resulting in 100% at 10 years for conduits larger than 16 mm at the time of implantation. Isomatsu et al. [27] reported that freedom from late events (conduit replacement or late death) was 88.5% at 5 years and 85.4% at 10 years in autologous pericardial valved conduit. Younger age at operation and postoperative pressure ratio from right to left ventricle were predictors of conduit longevity. They recommended autologous valved conduit in RVOT reconstruction when direct anastomosis is not suitable.

9.2.2.5 ePTFE Valved Conduit

Expanded polytetrafluoroethylene (ePTFE) valved conduit is very popular as RV-PA conduit in Japan. One of the reasons for this is that the domestic supply of homograft conduits is extremely rare. There are several types of handmade ePTFE valved conduit: ePTFE trileaflets composed in autologous pericardial roll, in Dacron tube, or in ePTFE tube with bulging sinuses [29, 30]. Ando and Takahashi [31] reported their follow-up results of ePTFE valved conduit composed in Dacron tube; freedom from conduit explantation was 88%, freedom from PR (≤ mild) was 75%, and the pressure gradient across the conduit was 18.1 mmHg at 7 years. Koh et al. [32] compared late results of conduits

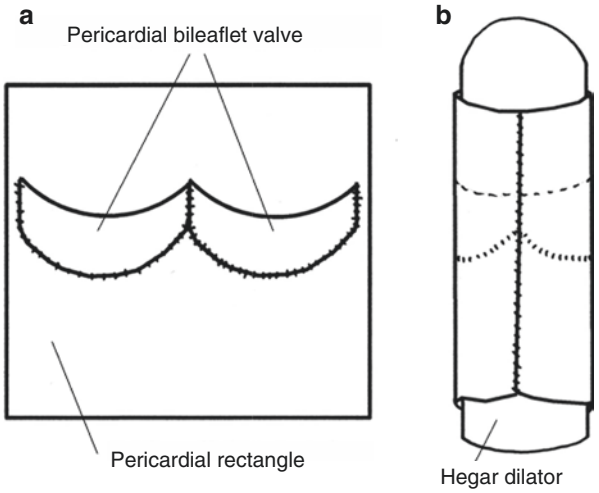

Fig. 9.9 Autologous tissue conduit with bileaflet valve. Two leaflets were sutured onto the rectangular patch; all of them were autologous pericardium (**a**). The pericardial rectangle with the cusps is wrapped around the Hegar dilator and closed with double running suture (**b**). From the reference [28]

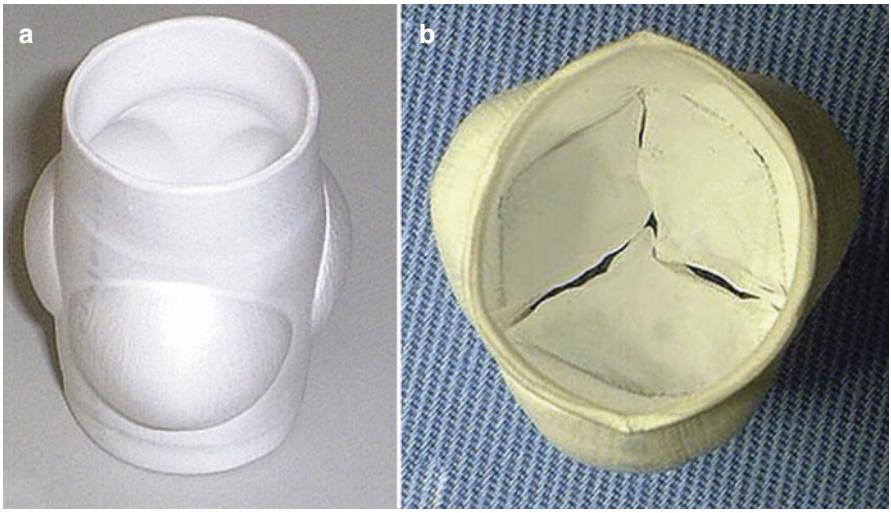

Fig. 9.10 ePTFE valved conduit with bulging sinus. View from outside (**a**). View from above; fan-shaped valves that are anastomosed at the edge of the bulging sinuses and tightly sealed (**b**). From the reference [30]

containing ePTFE trileaflets and whole heterologous pericardial trileaflet conduits; all trileaflet conduits have been free from calcification or important obstruction over a follow-up period up to 7 years. In general, glutaraldehyde-fixed heterologous pericardium was found to have a prominent inflammatory reaction, with calcification and shrinkage. In contrast, ePTFE trileaflet conduit is expected to provide flexible valve behavior along with favorable durability, and when ePTFE leaflets became nonfunctional, they adhered to the conduit wall and became fixed in the open position without resulting in significant obstructive deterioration. Whole ePTFE trileaflet valved conduit with bulging sinuses showed excellent midterm results (Fig. 9.10). Freedom from reoperation at 10 years was 95.4%, and pulmonary insufficiency was mild or nonexistent in 95.0% of the patients. The pressure gradient between the right ventricle and the pulmonary artery was 14.0 ± 13.2 mm Hg [26, 29]. In addition to the good compatibility of the material [33], they believe that the combination of bulging sinuses and fan-shaped valve leaflets contributes to the excellent long-term results of this conduit; bulging sinus generates vortex flow which improves closing property of the valve, and a fan-shaped leaflet makes ideal coaptation. In the comparison with various types of RV-PA conduits (homografts, ePTFE valved conduits, Medtronic Hancock bioprosthetic valved conduits, non-valved ePTFE tubes, and others) for biventricular repair, Shinkawa et al. [34] reported that the significant factors for the freedom from conduit reoperation were age, preoperative diagnosis, conduit size, and conduit material. The freedom from conduit reoperation at 5 years was best in ePTFE valved conduits (92.1%).

9.3 Conduit Reoperation

9.3.1 Indications for Conduit Reoperation

Conduit reoperation is indicated for conduit obstruction (calcification or thickening of the leaflets, pseudointimal peel formation), valve regurgitation (laceration, perforation, or shrinkage of the leaflets), infectious endocarditis, formation of aneurysm or pseudoaneurysm, somatic outgrowth, and so on. Among all, conduit obstruction is the most frequent cause of conduit explantation [28, 35–37].

Operative indication for conduit obstruction is usually based on the pressure gradient across the conduit or RV systolic pressure. According to Mohammadi et al. [38], their indication is either (1) conduit pressure gradient (65–70 mmHg) or (2) RV/LV pressure ratio (≥0.8). Dearani et al. [39] reported less value criteria of pressure gradient, 40–50 mmHg. Homann et al. [40] adopted the conduit exchange before the clinical signs of right ventricular failure, when the conduit pressure gradient exceeds 40–50 mmHg. Sano et al. [36] also emphasized the importance of timing of conduit replacement before the appearance of right ventricular failure.

9.3.2 Surgical Procedure in Conduit Reoperation

9.3.2.1 General Consideration in Reoperated RV-PA Conduit

It is well known that the ascending aorta in the patients with pulmonary atresia is larger than normal and is frequently associated with anterior shift. As a result, it adheres firmly to the posterior aspect of the sternum in reoperated cases. Re-sternotomy thus accounts for a high risk of aortic injury and is sometimes fatal as a result of uncontrollable hemorrhage even after commencement of cardiopulmonary bypass. Injury of coronary arteries is another fatal complication as the coronary arteries are buried in the scar tissues and are sometimes difficult to be recognized. Preoperative evaluation by contrast computed tomography or magnetic resonance imaging is very important to prevent these disastrous complications [41].

After establishing cardiopulmonary bypass, the old conduit is removed, and the distal and proximal ends of a new conduit are anastomosed on each side using continuous sutures. Cardiac arrest is not always required unless other procedures such as closure of the residual shunt or left side intracardiac procedure are needed. Electrically induced ventricular fibrillation may be used. In case of pulmonary branch stenosis repair, it must be repaired using a patch of xenograft pericardium or ePTFE before implantation of a new conduit.

9.3.2.2 Surgical Technique and Intervention in Conduit Reoperation

There are a variety of conduit types used in reoperation, as in the first implantation: homograft, stented xenograft, stentless xenograft, and handmade ePTFE conduit. It is still unclear which type of conduit should be chosen in the reoperation. Valveless tube with different materials had been used before, but their use is now limited,

since right ventricular dysfunction from severe PR on long term is well acknowledged [42]. Usually, larger-sized conduit can be used in the reoperation compared to the first operation, which may lead to longer durability.

In Japan, stented xenograft valve incorporated in Dacron tube had been a standard conduit for reoperation for a long time, but ePTFE conduits with trileaflets are likely the most popular conduits used recently; however, there are no official statistics on the difference. Intermediate-term result of this conduit is excellent, although much longer follow-up is mandatory to decide longevity of the conduit.

In addition to the usual conduit replacement, special techniques may be indicated in the reoperation. In "peel technique" first introduced by Mayo group [43], a new conduit was constructed with the conduit bed as a posterior wall and a patch of xeno-pericardium, Dacron, or ePTFE as the roof of the conduit. In most cases of the original series, the conduit had no valve inside, but an ePTFE monocusp is embedded as a modified method. Cerfolio et al. [44] reported satisfactory long-term results which they attributed to the merit of autologous tissue included in the route. Contrary to their results, Mohammadi et al. [38] reported frequent restenosis with this technique; the discrepancy between the results might be due to difference in operative age and conduit size.

Percutaneous pulmonary valve implantation (PPVI), also called as transcatheter pulmonary valve implantation or transcatheter valve-in-valve implantation, is a less invasive alternative for the treatment of RVOT dysfunction which was first performed by Bonhoeffer et al. [45] in 2000. A stented bovine jugular vein valve crimped over a balloon catheter is delivered to the conduit and positioned. PPVI may avoid repeated operations with re-sternotomy, cardiopulmonary bypass, cardiac arrest, and resulting postoperative cardiac failure and is increasingly adopted as the standard procedure in Europe and North America, although not officially approved in Japan. Melody® valve (Medtronic Inc., Minneapolis, Minnesota) is a bovine jugular vein valve with bare-metal platinum-iridium stent (Fig. 9.11a). It is

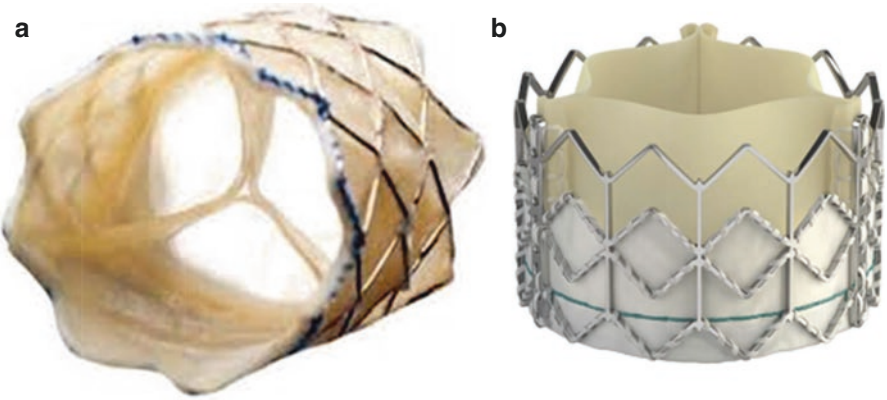

Fig. 9.11 Prosthetic valves for percutaneous pulmonary valve implantation. (**a**) Melody Valve® (Medtronic Inc., Minneapolis, Minnesota). (**b**) Edwards Sapien Pulmonic transcatheter heart valve® (Edwards Lifesciences, Irvine, California)

available in diameters of 16 and 18 mm, which can be expanded to 18 or 20 mm and 18, 20, or 22 mm, respectively. The Edwards Sapien Pulmonic transcatheter heart valve® (Edwards Lifesciences, Irvine, California) is a trileaflet bovine pericardial tissue valve with stainless steel stent (Fig. 9.11b). It is available in 23, 26, or 29 mm diameters [46]. Double valve replacement for the pulmonary and tricuspid valves using transcatheter valve-in-valve implantation technique was reported in a patient with transannular patch repair of Fallot [47]. He had already undergone reoperations: pulmonary valve replacement with homograft (twice) and tricuspid valve replacement preceded by valvuloplasty. Percutaneous valve-in-valve implantation technique may avoid polysurgery and surgical complications generated from the reoperative procedures and will make a paradigm shift in the treatment of cardiac anomalies with pulmonary atresia and the related diseases in which RV-PA conduit is mandatory.

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Repaired Complete Transposition of the Great Arteries

10

Kosuke Yoshizawa and Keiichi Fujiwara

Abstract

Complete transposition of the great arteries (d-TGA) is a common congenital heart disease. The surgical strategy for d-TGA has changed from the atrial switch operation to the arterial switch operation. This chapter describes the postoperative concerns regarding these two switch operations as well as details of the management of adult patients with repaired d-TGA. Long-term complications after the atrial switch operation include intra-atrial baffle-related problems, arrhythmias, right ventricular (systemic ventricular) failure, and tricuspid regurgitation. Transcatheter reintervention for baffle leaks or obstructions has been reported as effective. Right ventricular failure is common, and reintervention options for this are cardiac resynchronization therapy, arterial switch conversion, and cardiac transplantation. Atrial arrhythmias after the atrial switch operation are frequent. Catheter ablation and/or pacemaker implantation is indicated for some patients; however, the approach is complex. In recent years, the arterial switch operation has been the surgical option of choice. This procedure has the advantage of maintaining an almost normal anatomy. Long-term sequelae after the arterial switch procedure include pulmonary artery stenosis, coronary artery complications, and aortic valvular dysfunction. When pulmonary artery stenosis is severe, surgical repair should be performed. Sequential coronary angiography can reveal coronary stenoses in asymptomatic patients. The fate of the neo-aortic valve has been a major concern. In conclusion, there remain a number of concerns regarding repaired d-TGA patients; regular follow-up and appropriate timing of reinterventions are important.

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Complete transposition of the great arteries • Adult congenital heart disease • Atrial switch operation • Arterial switch operation • Long-term complications

10.1 Introduction

Complete transposition of the great arteries (d-TGA; the "d" refers to the dextroposition of the bulboventricular loop) is defined as atrioventricular concordance and ventriculoarterial discordance and is characterized by the aorta arising from the morphological right ventricle and the main pulmonary artery arising from the morphological left ventricle (Fig. 10.1a). It is the second most common congenital heart disease that results in cyanosis (5–7% of congenital heart disease). Senning [1] reported the first successful case of the systemic and pulmonary venous switching using a right atrial wall and an atrial septum in 1959. In 1964, Mustard [2] reported a new procedure of systemic and pulmonary venous switching using a pericardial baffle in an atrium. Between the 1960s and mid-1980s, the physiological type of repair (Fig. 10.1b), which uses a venous switching technique at an atrial level, was the surgical treatment of choice. In patients with this repair, however, the morphological right ventricle functions as a systemic ventricle. In 1975, Jatene et al. [3] reported the first successful use of the arterial switch operation (Fig. 10.1c). Since then, several technical modifications, along with surgeons' experience, have resulted in the standardization of this operation. Currently, the arterial switch procedure is the standard care for d-TGA in neonates.

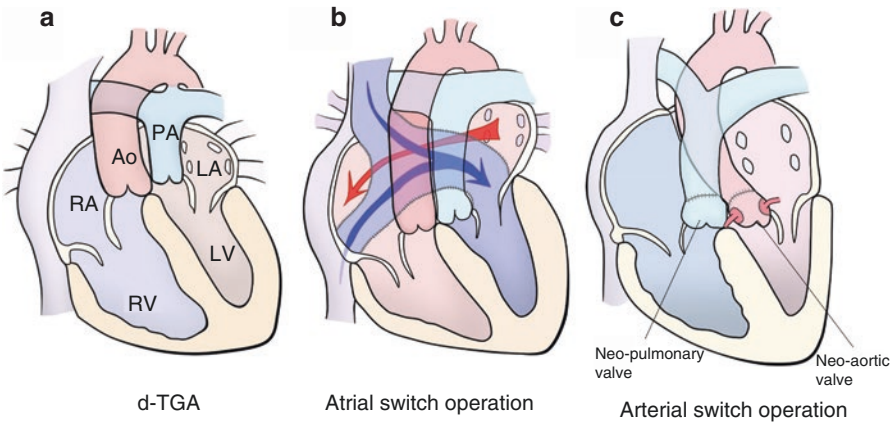

Fig. 10.1 (**a**) Schema in a patient with d-TGA. (**b**) After the atrial switch operation, blood from the superior and inferior vena cava was redirected to the mitral valve and pulmonary venous blood to the tricuspid valve in the atrium. (**c**) The arterial switch operation is often referred to as an anatomical correction, giving almost normal hemodynamics to a patient with d-TGA. *RA* right atrium, *RV* right ventricle, *Ao* aorta, *PA* pulmonary artery, *LA* left atrium, *LV* left ventricle

This chapter discusses the postoperative concerns regarding these operations and the management of adults with repaired d-TGA. Details of the Rastelli procedure and other procedures for d-TGA with left ventricular outflow tract obstruction are described in Chap. 9.

10.2 Atrial Switch Operation

Since the mid-1980s, atrial switch procedures have been superseded by arterial switch procedures, which means that patients with Mustard or Senning repairs will disappear over the next 40 years [4]. In recent years, the atrial switch operation has been adopted only as part of the double switch operation for corrected transposition of the great arteries. Many patients who underwent the atrial switch operation survived to adulthood, even beyond 40 years of age. The survival rates of the Senning and Mustard procedures have been reported as similar. Long-term complications include intra-atrial baffle-related problems, arrhythmias, right ventricular (systemic ventricular) failure, and tricuspid regurgitation (TR) [5, 6]. Indications for reintervention after the atrial switch operation are summarized in Table 10.1.

10.2.1 Intra-atrial Baffle-Related Complications

Intra-atrial baffle-related problems include baffle leaks and obstructions. Khairy et al. [7] reported that baffle-related complications occur in as many as one in five adult survivors. These complications account for majority of the reoperations, but the mortality risk of reoperations has been reported to be high, at 36% [8]. Recently, catheter techniques for treating baffle leaks and obstructions have been reported.

Table 10.1 Indications for reintervention after the atrial switch operation

Complications	Indications	Procedures
Baffle leaks	• Large shunt • Tachyarrhythmias • Presence of endocardial pacemaker	• Surgery • Transcatheter procedures
Baffle obstruction	• High pressure gradient (10–15 mmHg) • Symptoms (SVC syndrome, PLE) • Pacemaker implantation	• Surgery • Transcatheter procedures
Systemic right ventricular failure	• Resistant to medical therapy	• CRT • Retraining of left ventricle • Transplantation
Tricuspid valve regurgitation	• Severe regurgitation	• Valve repair • Valve replacement • Pulmonary artery banding

SVC superior vena cava, *PLE* protein-losing enteropathy, *CRT* cardiac resynchronization therapy

10.2.1.1 Baffle Leaks

Intra-atrial baffle leaks result in left-to-right shunts such as a patent fossa ovalis. Most of the leaks are small but multiple and are often visualized only by transesophageal echocardiography. Baffle leaks are best imaged using agitated saline injection performed during a transesophageal echocardiogram [9]. Three-dimensional transesophageal echocardiography can provide practical information regarding orientation in patients with complex anatomy [10].

A large shunt is an absolute indication for a transcatheter or surgical closure [11–13]. Even in patients with small baffle leaks, the risk of paradoxical embolus and cerebrovascular events may increase if the patient has tachyarrhythmias or an endocardial pacemaker [11].

Although surgical repair of the atrial baffle has previously been reported, catheter interventions may be safer and more effective [12, 14]. An atrial septal occluder is usually used for the closure of baffle leaks [12, 15–17]. Daehnert et al. [15] described the widely varying positions of the baffle leaks, which result in atypical occluder positions compared to native atrial septal defects. Precise position assessment using transesophageal echocardiogram in conjunction with fluoroscopy is important.

Using a covered stent has been reported as a method for simultaneously eliminating baffle leaks and obstructions [18, 19]. Recently, stent-graft devices (such as the Gore excluder® device) have been used; these are commercially available for use in patients with abdominal aortic aneurysm [20, 21].

10.2.2 Baffle Obstruction

Obstruction of the systemic venous pathway is one of the most common complications following the atrial switch operation. The superior limb is most commonly affected at 37–44% of the cases [11, 22]. Obstruction of the superior vena cava can result in chylothorax [23] and superior vena cava syndrome [24]. Inferior baffle obstruction may cause protein-losing enteropathy [25–27]. Although pulmonary vein obstruction is less common, it can occur both early and late in the postoperative period [28]. These obstructions can be imaged by transthoracic echocardiography [29]. The baffle obstruction should be assessed by transesophageal echocardiography [30], angiography, computed tomography (CT), or magnetic resonance imaging (MRI) to visualize anatomical details.

Although reintervention should be considered in symptomatic patients, asymptomatic patients for whom future pacemaker placement is planned should also be treated to prevent further stenosis of the venous pathway. Indications for reintervention for venous stenosis are still under debate. Some reported cases have suggested that a high pressure gradient (>10–15 mmHg) or the presence of symptoms (e.g., superior vena cava syndrome or protein-losing enteropathy) are indications [26, 27]. Insignificant baffle obstruction in asymptomatic patients with normal cardiac function can also be a risk factor for sudden death [31].

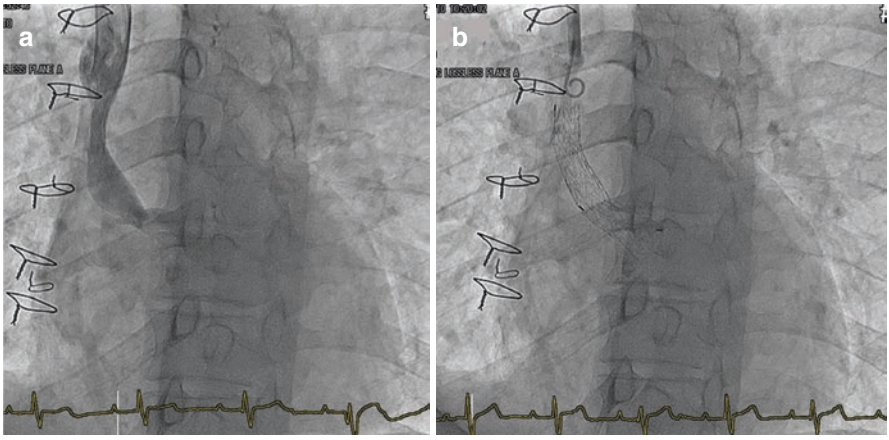

Fig. 10.2 (**a**) Angiography showing stenoses of the superior vena cava and the baffle. (**b**) A Gore excluder® device was implanted

Although surgical reintervention methods have been reported [13, 32], catheter techniques have also been introduced for this complication. Balloon angioplasty has demonstrated effectiveness in the short term but has a high incidence of restenosis of up to 40% [33]. Stent implantation is therefore recommended [34, 35]. As patients with baffle obstruction frequently have concomitant baffle leaks, a covered stent can be used as simultaneous treatment for both the baffle obstructions and leaks [20, 21]. Figure 10.2 shows an angiogram of the placement of a Gore excluder® device for the superior vena cava and baffle stenoses.

Laser lead extraction is necessary before the transcatheter procedure in patients with an atrioventricular block and endocardial pacemaker [21].

10.2.3 Systemic Right Ventricular Failure

Morphological right ventricular failure has been recognized in the long term after the atrial switch operation [36]. The mechanism for this is not well understood. One possible mechanism results from the structural difference between the left and right ventricles [37]. The left ventricle has a limited nontrabeculated area and two papillary muscles, whereas the right ventricle has an infundibulum without significant trabeculation. The longitudinal arrangement of cardiomyocytes in the right ventricle may be a morphological cause of the inability to compensate for high volume and pressure, and myocardial fibrosis [5], myocardial ischemia [38], and ventricular–ventricular interaction [39] have been described as reasons. The association of TR and/or arrhythmias can lead to progressively deteriorating ventricular dysfunction.

MRI and echocardiography are useful tools for evaluating right ventricular function. Although cardiac MRI is the gold standard for this assessment [40], it cannot

be used in patients with pacemakers. Echocardiography is a more commonly used modality, but its usefulness of evaluation on right ventricle is limited by the shape of right ventricle and the expertise of the echocardiographer. The myocardial performance index has been used to evaluate heart failure after an atrial switch procedure [41]. More recently, Diller et al. [42] reported that a reduction in global longitudinal strain is a good predictor of adverse clinical outcome in these patients.

Medical management using angiotensin-converting enzyme inhibitors [43, 44], angiotensin receptor blockers [45], aldosterone antagonists [46], and beta-adrenergic receptor blockers [47] has been reported and discussed, but left ventricular failure management principles cannot be applied to right ventricular failure [44]. When these medical management methods are not effective, heart failure should be treated by reintervention. Options for this include cardiac resynchronization therapy (CRT), arterial switch conversion with retraining of the left ventricle (i.e., pulmonary artery banding), and cardiac transplantation.

CRT using biventricular pacing has been shown to be beneficial in patients with left ventricular failure, whereas the efficacy of CRT in patients with right ventricular failure has not yet been established. Particularly for patients with associated congenital heart disease, the benefit of CRT is still unclear [48]. Although there have been no large clinical studies, some promising reports have described CRT as improving hemodynamics in adult congenital heart disease with a systemic right ventricle [49, 50]. If the coronary sinus is accessible from the systemic veins, the systemic right ventricular lead may be placed entirely transvenously [51]; the alternative would be the implantation of epicardial leads with thoracotomy. In our institution, two patients with Mustard repair underwent the replacement of a CRT device, and in one of them we took a hybrid approach involving the implantation of leads. After the light atrium and left ventricular leads had been placed percutaneously, the right ventricular lead was placed with thoracotomy. Pacing site selection and setting the CRT (e.g., A-V delay, V-V delay) remain complex. There has been a reported case of a patient with Mustard repair who underwent upgrading from a single-chamber pacemaker to CRT, and functional evaluation revealed improved cardiac performance in DDD mode with broad QRS [52]. This result seems to indicate that the data derived from CRT in structurally normal left ventricular failure are not reliable for the treatment of right ventricular failure with congenital heart disease.

Retraining of the left ventricle and conversion to the arterial switch protocol was introduced by Mee in 1986 [53]. Some reports have described successful outcomes in young patients [54]. Poirier et al. [55] reported that being >12 years old at the time of the operation was a risk factor for mortality. In some adult cases, the left ventricle cannot respond to the increased afterload, and then biventricular failure occurs. In general, retraining of the left ventricle for conversion to the arterial switch operation cannot be an option in adults. Conversely, the increased afterload may result in a rightward “septal shift” and an improvement of tricuspid valve coaptation. The regression of TR after pulmonary artery banding has been observed in some patients [56, 57]. A similar mechanism may explain the superior prognosis in patients with congenitally corrected transposition of the great arteries (ccTGA) with pulmonary stenosis

compared with ccTGA without pulmonary stenosis [58]. Whether pulmonary artery banding provides effective palliation has yet to be determined.

Orthotopic heart transplantation should be considered for patients with systemic right ventricular failure not amenable to medication or the surgical options described above. Irving et al. [59] described their experience of cardiac transplantations in the adult population with congenital heart disease and reported that 22% of transplants were performed in d-TGA following atrial switch. In the same report, 88% in the d-TGA patients survived at the early period of the cardiac transplantation, and only one death at 7 years was described.

10.2.4 Tricuspid Valve Regurgitation

Mild TR is very common in adult patients who underwent Mustard or Senning procedures. Moderate-to-severe TR is found in more than 20% of the adult survivors [60]. Etiologies of these TRs include structural abnormalities of the valve itself, iatrogenic lesions during the Rashkind balloon atrial septostomy [61] or prior ventricular septal defect repair, and functional regurgitations secondary to the right ventricular dysfunction. In d-TGA patients, intrinsic abnormality of the tricuspid valve is very rare [62, 63]. Szymański et al. [60] analyzed 42 patients with d-TGA after the atrial switch operation and classified their TRs into the following three distinct types based on their causes: predominant annular dilatation (type I), valve prolapse (type II), and valve tethering (type III). These authors reported that the most common type was tricuspid valve tethering (44%). In addition to a mechanism similar to functional mitral regurgitation, a right-to-left septal shift may contribute to the tethering. Beta-adrenergic receptor blockers have been suggested as medications for functional TR [64]. If TR becomes severe, tricuspid valve repair or replacement may be required.

The surgical option, i.e., replacement or repair of the tricuspid valve, is still controversial [65]. This valve can be approached via the right atrium. Tricuspid valvuloplasty is often performed with the technique of annuloplasty using a ring. The recurrence rate of TR after these repairs is reported to be up to 37% [65]. Although tricuspid replacement is required either when the quality of the leaflets is insufficient or when recurrence occurs, the results can be disappointing, with little improvement in hemodynamics [66, 67]. Pulmonary artery banding may be a better option as previously described, although currently there is insufficient data demonstrating favorable survival after this procedure. Patients with symptomatic right ventricular failure associated with TR may ultimately require cardiac transplantation.

10.2.5 Arrhythmias

Long-term bradyarrhythmias and tachyarrhythmias are common in patients after the atrial switch operation [68]. Bradyarrhythmias are generally induced by the sick sinus syndrome (SSS); Gellat et al. [69] reported that SSS was found in 23% at

5 years and 60% at 20 years of survivors following the atrial switch operation. These may be caused by damage during the initial operation or the interruption of right atrial blood flow. Pacemaker implantation is required when SSS occurs; however, some considerations around pacemaker implantation need to be taken into account. In the presence of an intra-atrial baffle leak, the risk of systemic thromboemboli will be more than twofold with transvenous leads implantation [70]. The patency of the baffle route should be assessed before implantation. In patients who have stenosis of the superior vena cava or the superior baffle, a catheter intervention before implantation or epicardial pacing may be necessary. Finally, consideration of the potential benefit of CRT is important for the prevention of subsequent right ventricular failure.

Atrial tachyarrhythmias are found in up to 25% of patients, and intra-atrial reentrant tachycardia (IART), also referred to as atrial flutter, is the most frequent type of arrhythmia [7, 69]. IART has been reported to be a probable marker for sudden death [71], and atrial arrhythmias may be a surrogate marker for ventricular dysfunction [72]. Pacemaker implantation may be considered not only in the setting of bradyarrhythmias but also of tachyarrhythmias to facilitate aggressive medical therapy.

Catheter ablation is indicated for patients with recurrent symptomatic or drug refractory atrial arrhythmias. Traditional ablation procedures are limited by the anatomic complexity in these patients. Most IART circuits are similar to typical atrial flutter in a heart with a normal structure, but the cavotricuspid isthmus is partitioned into two distinct regions by the atrial baffle. The tricuspid valve is not directly accessible from the systemic venous route because of this partition; therefore, another approach is required such as access via a baffle leak, a transbaffle puncture [73], or a retrograde aortic approach using remote magnetic navigation [74]. A transbaffle puncture under transesophageal echocardiographic guidance is safe and effective [73, 75]. El-Said et al. [76] reported their 18-year experience with 16 patients who had previously undergone the atrial switch operation and suggested that transbaffle puncture was a safe technique with no residual shunt at follow-up. Although good results of a retrograde approach have also been reported [74], this brings the potential risk of damage to the atrioventricular valve, and it is impossible in the presence of a mechanical valve. Magnetic navigation technology is still only available in a few institutions in Japan, but the reduction in radiation exposure with this technique is particularly important.

10.3 Arterial Switch Operation

Since the first introduction of the arterial switch operation for d-TGA by Jatene in 1975 [3], techniques and management for the care of neonatal congenital heart disease have improved. In 1984, Castaneda et al. [77] reported successful results in newborns with d-TGA and demonstrated the capacity of the left ventricle in a neonate to take over the systemic circulation. The transition in surgical strategy from

atrial switch to arterial switch procedures was mostly completed by the early 1990s. These days, it is usually performed in the first month of life for all forms of d-TGA without left ventricular outflow tract obstruction.

Losay et al. [78] reported one of the largest studies of arterial switch procedures, which found that the survival rate at 10 and 15 years was 88% and that there were no deaths after 5 years in the 1095 survivors. Because the perioperative outcome of the arterial switch operation has been reported to be good [79–81], the focus has shifted from mortality to long-term complications and exercise performance [82, 83]. The arterial switch procedure has the advantage of maintaining an almost normal anatomy and avoiding incisions and suture lines in the atrium. However, the technique involves translocating the aorta and the pulmonary artery and detachment of the coronary arteries in the neo-aorta. It is a delicate operation, and long-term sequelae after the procedure include pulmonary artery stenosis, coronary artery complications, and aortic valvular dysfunction. These complications may require surgical or transcatheter reintervention.

10.3.1 Supravalvular Pulmonary Artery Stenosis

Pulmonary artery stenosis is the most commonly encountered long-term complication in patients after the arterial switch operation [81, 84, 85], with the incidence reported to range from 3% to 30% [86]. Various causes have been reported, with the technique for the reconstruction of the pulmonary artery possibly being one of the most important factors. Although the direct anastomosis technique reported by Pacifico et al. [87] has the advantage of reconstruction without any artificial materials, the tension at the direct anastomotic site is higher than that for anastomosis with a patch [85]. After the Lecompte maneuver [88], the left pulmonary artery is likely to be narrow. Presence of the ductal tissue has also been suggested to be a cause of pulmonary artery stenosis [86].

Echocardiography, angiography, and CT are used to assess the degree of pulmonary artery stenosis. Catheterization should be performed to measure the right ventricular pressure. Patients with symptoms, severe stenosis of the branch pulmonary artery, or right ventricular systolic pressure >50 mmHg may require reintervention [5].

The reintervention-free rate for right outflow obstruction reported by Willams et al. [89] was 83% at 10 years. In the same report, 55% of 62 reinterventions were surgical, and the remaining 45% were percutaneous. Catheter intervention techniques, such as balloon angioplasty and stent implantation, have been reported for dilating branch pulmonary artery stenosis [90, 91]. Torres et al. [92] described 18 cases of iatrogenic aortopulmonary communication after catheter interventions, with nine patients requiring surgical closure of the communication. An inner vascular image by CT and an intraoperative photograph are shown in Fig. 10.3. When the obstruction is severe, which leads to a high pressure gradient, surgical repair is more clinically efficacious than a percutaneous procedure [80].

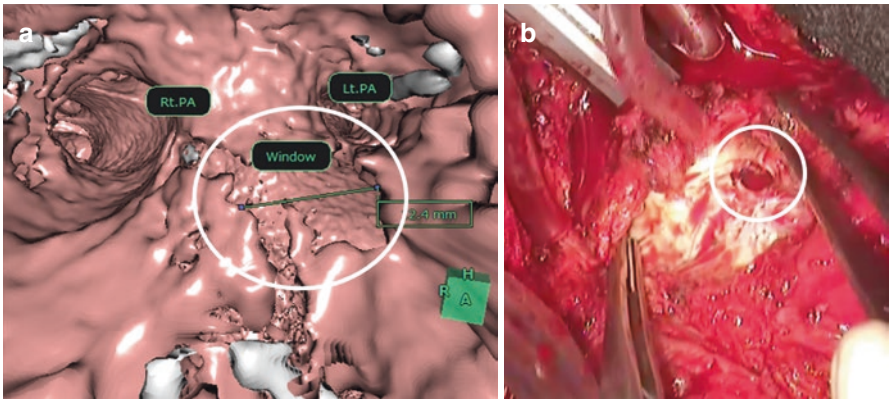

Fig. 10.3 (**a**) An inner vascular image by CT shows a view of aortopulmonary communication from the pulmonary artery. (**b**) An intraoperative photograph; the white circle indicates a window to the aorta. The aortopulmonary communication was repaired with a heterologous pericardium patch. *Rt.PA* right pulmonary artery, *Lt.PA* left pulmonary artery, *Window* aortopulmonary communication

10.3.2 Coronary Artery Stenoses or Obstructions

In the arterial switch procedure, reimplantations of coronary arteries should be performed; this is not required in the atrial switch procedure. Some problems related to replaced coronary arteries may occur both early and long term postoperatively. Perioperative coronary complications have a significant impact on the results of the operation [93–95]. A meta-analysis by Pasquali et al. [96] revealed that intramural or single coronary artery patterns were significant risk factors for operative mortality. The incidence of late coronary artery stenosis or obstruction after the arterial switch operation has been reported to be 3–7% [97–100]. Although coronary artery stenosis or obstruction has been reported to be a risk factor for sudden death [97, 101], most patients with late coronary artery stenosis are asymptomatic. It is possible even for the total obstruction of the coronary artery to be found in asymptomatic patients [98]. The richness of retrograde coronary perfusion from collateral arteries or cardiac denervation [102] is one of the mechanisms for this asymptomaticity.

Anatomical kinking, extrinsic compression, stretching, and intimal proliferation are possible causes of reimplanted coronary stenosis or obstruction [98]. Studies in animals [103] and humans [104] have described the normal growth of aorta–coronary anastomoses after the arterial switch operation. Intracoronary ultrasound assessment has revealed proximal intimal thickening in 89% of patients in the long term following the arterial switch operation [105], and this change may be related to the occurrence of late coronary ostial stenosis.

Noninvasive modalities, such as electrocardiogram, echocardiography, and exercise testing, have low sensitivity for coronary stenosis after the arterial switch operation [99, 106]. Although selective coronary angiography is the most accurate means for assessing the patency of reimplanted coronary arteries, the indication for

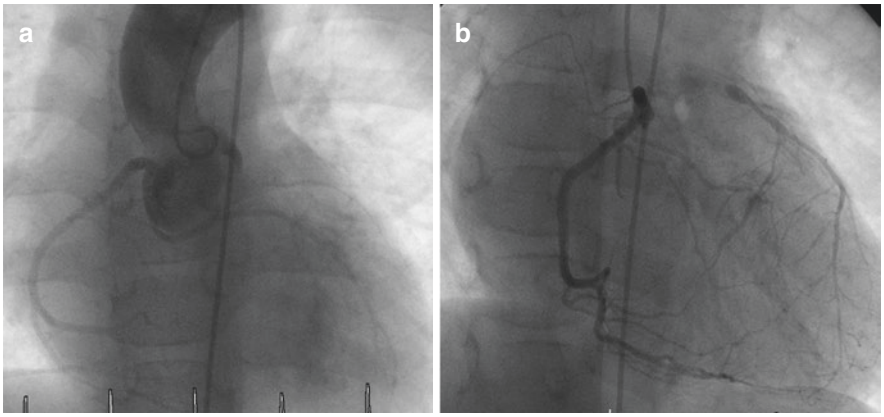

Fig. 10.4 (**a**) Coronary angiography in a d-TGA patient after the arterial switch operation. The reimplanted right coronary artery and circumflex artery were patent, and the ostium of the left descending artery was totally occluded. (**b**) The left descending artery was found with flow of collateral arteries from the right coronary artery and circumflex artery. This patient was asymptomatic and was treated with a coronary artery bypass graft

this invasive examination has not been determined because most patients with coronary stenosis or obstruction after the arterial switch operation are asymptomatic as previously mentioned. Angiography for an asymptomatic patient with ostial occlusion of a reimplanted left descending artery is shown in Fig. 10.4. Legendre et al. [99] recommended sequential selective coronary angiography at 5, 10, and 15 years following the operation. However, noninvasive techniques for the assessment of coronary stenosis have been developing. Multislice CT is one alternative modality for detecting ostial stenosis in patients after the arterial switch operation [107]. Coronary assessment using MRI has an advantage over other non-X-ray techniques; however its diagnostic accuracy remains unsatisfactory because of its low spatial resolution [108]. Scintigraphy with exercise or dynamic positron emission tomography with N-13 ammonia during pharmacologic vasodilation is used to assess the physiological significance of coronary artery stenosis [109]. Even in asymptomatic patients with good hemodynamic condition, a continuous follow-up of the coronary arteries after the arterial switch operation is of major importance. In patients with severe coronary stenosis or obstruction, treatment should be undertaken to prevent sudden death.

Surgical or transcatheter procedures are options for the treatment of coronary stenoses. Coronary artery bypass grafting (CABG) and ostial patch angioplasty are surgical options. It is important to select the appropriate type of revascularization procedure to be performed in each case [110]. In most reported cases with CABG, internal thoracic artery (ITA) was used for the bypass graft [111, 112], and excellent midterm results have been reported after CABG with ITA in a young population [113]. CABG with bilateral ITAs has also been reported [110, 114]. ITAs are live grafts with growth, and their long-term patency is expected. The other surgical option is ostial patch plasty of the coronary artery. Segmental stenosis of a coronary artery

ostium in the absence of calcification is indicated for this procedure. An autologous pericardium has been used in many cases to enlarge ostial stenosis [115]. A saphenous vein patch or polytetrafluoroethylene patch has also been used in some cases [116]. A simple ostial stenosis can be repaired by onlay patch enlargement from the main coronary stem to the adjacent aortic wall. In a patient with a single coronary ostium, modified coronary ostial angioplasty that employed a single, "pantaloon"-shaped autologous pericardial patch has been reported [110]. The coronary artery pattern and the relationship between the aorta and the pulmonary artery should be assessed preoperatively. To allow adequate exposure of the aortic root, the pulmonary trunk should be transected under some anatomical conditions. Percutaneous balloon dilation of the ostial stenosis is not effective [117]. Although percutaneous stenting may be effective, implantation of a stent in the ostial position of a coronary artery or in a young population can be potentially harmful. The sequential redilation of stents may be needed, and in patients with stent implantation in the coronary ostium, a subsequent surgical ostial patch plasty may be difficult or impossible. The redilation of stents in congenital heart disease is reported to be safe and effective [118]. Both bare-metal stents and drug-eluting stents can be used for the implantation. An antithrombosis prophylaxis is essential after stenting.

10.3.3 Neo-aortic Valve Insufficiency

The fate of the neo-aortic valve, which is the native pulmonary valve, after the arterial switch operation has been a major concern since the operation was introduced. Neo-aortic valve insufficiency has been reported with prevalences varying between 0.3% and 55% [78, 84, 119–121]. Although the incidence of reintervention for neo-aortic valve insufficiency has been reported to be low [111, 122], the insufficiency has been described as following a time-dependent progression [123]. Reinterventions for neo-aortic insufficiency may become more frequent in the near future.

The etiology of neo-aortic insufficiency has been reported to be multifactorial [118, 123]. Possible risk factors include prior pulmonary artery banding (two-stage anatomical repair), the presence of a left ventricular outflow tract obstruction [124], the presence of a ventricular septal defect [122, 123], and the trapdoor type of coronary reimplantation [121]. It has been shown that the pulmonary valvular leaflets are able to mechanically tolerate the systemic pressure in patients following the Ross procedure. Neo-aortic dilatation is one of the associated concerns; however, some authors have reported no correlation between neo-aortic insufficiency and root dilatation [121, 124, 125].

Neo-aortic valve insufficiency can easily be found by transthoracic echocardiography [119]. Patients with severe incompetence should be referred for surgical reintervention before left ventricular dysfunction occurs [123].

Suggested surgical treatment options for neo-aortic insufficiency include various repair techniques [126], neo-aortic valve replacement [127], and the Ross operation [128]. In the young population, valve replacement should be avoided. Serraf et al. [111] reported the application of various techniques, such as annuloplasty [129] and

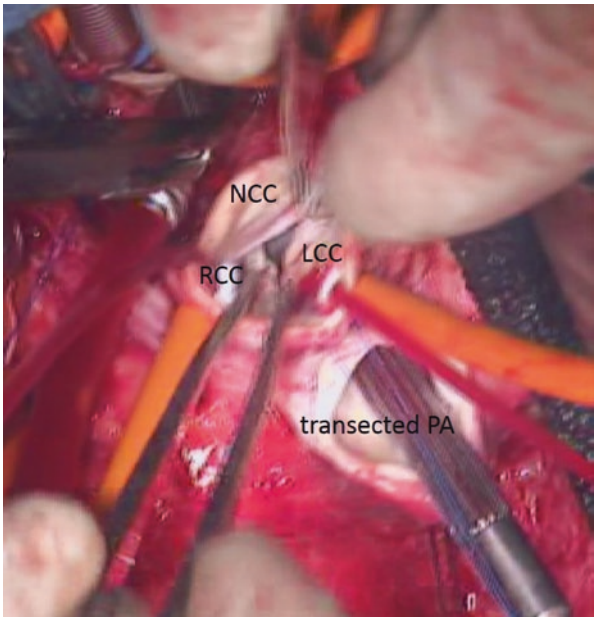

Fig. 10.5 Neo-aortic cusps were inspected after the main pulmonary trunk was transected. The right coronary cusp was dysplastic. The cusp was enlarged with an autologous pericardial patch. *NCC* noncoronary cusp, *RCC* right coronary cusp, *LCC* left coronary cusp, *PA* pulmonary artery

commissuroplasty [130], to neo-aortic valve repair. Transection of the main pulmonary trunk may be necessary to approach the neo-aortic root. Figure 10.5 shows an intraoperative photograph of one of our cases of neo-aortic valve repair after the arterial switch operation. When the neo-aortic root dilatation is concomitant, the Bentall operation or valve-sparing reimplantation technique [131] should be employed.

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Congenitally Corrected Transposition of the Great Arteries

11

Kiyozo Morita

Abstract

Congenitally corrected transposition (ccTGA) is a rare cardiac malformation, characterized by the combination of discordant atrioventricular and ventriculo-arterial connections, accompanied by other cardiovascular malformations in the majority of cases. The clinical presentation and the age of onset of ccTGA largely depend on the presence and severity of associated malformations. Currently, most patients who underwent a surgical repair in childhood survive to reach adulthood with or without postoperative residual lesions or late complications to be repaired, while there is also a considerable population of unoperated patients in adulthood. The correct diagnosis is often made for the first time in adulthood, because of a symptom of heart failure or incidentally when an ECG, chest X-ray, or echocardiogram is performed for other reasons. With advancing age, ccTGA even in the setting of no associated malformations can often lead to progressive systemic atrioventricular (AV) valvar regurgitation and the systemic right ventricular dysfunction late in adulthood, which might be the most important and common manifestation for adult ccTGA. The physiological repair, the anatomical repair, or the tricuspid valve replacement can be indicated to adult unoperated patients, as well as the redo operation for the late postoperative complication after the initial intracardiac repair. This chapter deals with the specific morphological features, which relates to the natural and unnatural history of this disease, and the indication and procedures of the interventional approaches for both unoperated and postoperative patients.

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11.1 Introduction: Overview of ccTGA in Adulthood

Congenitally corrected transposition (ccTGA) is a rare cardiac malformation accounting for approximately 0.5–1.0% of congenital heart disease, characterized by the combination of discordant atrioventricular (AV) and ventriculo-arterial (VA) connections, accompanied by other cardiovascular malformations in more than 90% of cases [1]. The clinical presentation and the age of onset of ccTGA largely depend on the presence and severity of associated malformations.

Adults with ccTGA categorize to the unoperated and operated patients. Currently, most patients who underwent a surgical repair in childhood survive to reach adulthood with or without postoperative residual lesions or late complications to be repaired, while there is also a considerable population of unoperated patients in adulthood.

Some patients may be diagnosed in childhood but not require operation. In a majority of adult ccTGA, however, the correct diagnosis is made for the first time in adulthood, because of a symptom of heart failure or incidentally when an ECG, chest X-ray, or echocardiogram is performed for other reasons. With advancing age, ccTGA even in the setting of no associated malformations can often lead to progressive atrioventricular (AV) valvar regurgitation and the systemic right ventricular dysfunction late in adulthood, which might be the most important and common manifestation for adult ccTGA. Therefore, ccTGA is a unique entity among a variety of complex congenital heart malformations, in which the initial surgical intervention (i.e., intracardiac repair for associated anomaly, tricuspid valve replacement, and the cardiac resynchronization therapy: CRT) can be definitely indicated to adult unoperated patients, as well as the redo operation for the late postoperative complication.

This chapter deals with the specific morphological features, which relates to the natural and unnatural history of this disease, and the indication and procedures of the interventional approaches for both unoperated and postoperative adult ccTGA patients.

11.2 Anatomical Type and Associated Lesions

11.2.1 Definition and Anatomical Type

ccTGA is a complex congenital anomaly with a wide spectrum of morphological features and clinical profiles. The underlying malformation is the combination of discordant atrioventricular and ventriculo-arterial connections (“duplicated discordance”) and results in normal physiology despite the presence of the transposition of the great arteries.

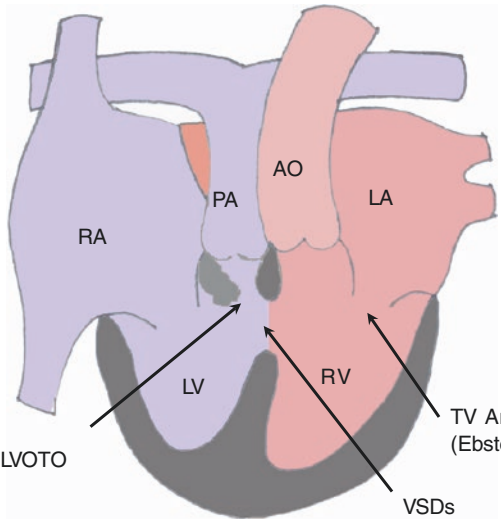

Fig. 11.1 Congenitally corrected transposition of the great arteries (ccTGA). Definition and associated malformations: the combination of discordant atrioventricular and ventriculo-arterial connections ("duplicated discordance") results in normal physiology despite the presence of the transposition of the great arteries

Thus, the morphologically right atrium is connected to a morphologically left ventricle across the mitral valve, which gives rise to the pulmonary artery. The morphologically left atrium is connected to the morphologically right ventricle across the tricuspid valve, which gives rise to the aorta (Fig. 11.1).

The most common anatomical arrangement is situs solitus with L-looping of the ventricles and the aorta anterior and leftward of the pulmonary artery (S,L,L) in 95 percent of cases [2], while situs inversus with D-looping of the ventricles and the aorta anterior and rightward (I,D,D) is also seen in the other 5% of ccTGA cases.

The majority of cases of ccTGA have any associated anatomical abnormalities. The most common lesions include ventricular septal defect (VSD) in 60–80% of patients, the left ventricular outflow tract obstruction (LVOTO) or pulmonary stenosis/atresia (PS/PA) in 40–50% of patients, and abnormalities of the morphologically tricuspid valve in up to 90% of patients with Ebstein's anomaly in 50% [3–5]. The isolated ccTGA without associated malformation is seen only 1% of cases (Fig. 11.1).

11.2.2 Associated Malformations

11.2.2.1 Ventricular Septal Defect (VSD)

The majority of VSDs are perimembranous, located below the pulmonary valve, with the posterosuperior margin of the defect formed by an extensive area of fibrous continuity between the leaflets of the pulmonary, mitral, and tricuspid valves, most characteristically in this anomaly. Often the perimembranous defects become at least partially obstructed by aneurysmal membranous atrioventricular (AV) septum tissue or the straddling tricuspid valve tissue. Other types of defects are also described including doubly committed subarterial (conal) defects, muscular defects, and AV canal type defects.

11.2.2.2 Left Ventricular Outflow Track Obstruction (LVOTO)

The LVOT obstruction may comprise subpulmonary stenosis and/or pulmonary valve stenosis. Pulmonary atresia (PA) can also be seen. The subpulmonary stenosis is often related to the presence of a fibromuscular shelf on the septum, muscular hypertrophy, tunnellike hypoplasia, or an aneurysmal dilation of fibrous tissue derived from the interventricular component of the membranous septum or an accessory mitral or tricuspid valve tissue.

11.2.2.3 Lesions of the Morphologically Tricuspid Valve

The tricuspid valve has been reported to be abnormal in the great majority of ccTGA patients. There is a wide spectrum of severity. Ebstein's anomaly of the systemic AV valve also occurs but is different from the typical right-sided Ebstein's anomaly, only characterized by the septal and posterior leaflets displaced inferiorly toward the cardiac apex [6]. It is rare to find the large "sail-like" deformity of the anterosuperior leaflet, as seen in the setting of concordant atrioventricular connections. And the atrialized portion of the RV inflow is also relatively small.

Another morphological variation is straddling of the tricuspid valve, with overriding the ventricular septum in the presence of VSD. The morphologically mitral valve also straddles and overrides, often in combination with double outlet right ventricle [7].

11.2.3 The Atrioventricular Conduction System in ccTGA: Clinical and Interventional Considerations [1, 8, 9]

With the arrangement of AV discordance, there is reversed offsetting of the attachments of the leaflets of the atrioventricular (the morphological mitral and tricuspid) valves to the septum, with the mitral valve on the right side attached appreciably higher than the tricuspid valve on the left side at the crux of the heart. Almost always there is fibrous continuity between the leaflets of the pulmonary and mitral valves in the roof of the right-sided morphologically left ventricle. The pulmonary outflow tract is deeply wedged between the atrial septum and the mitral valve, thus deviating the atrial septum away from the ventricular inlet septum. Consequently, this gap of septal malalignment is occupied by an extensive membranous septum [1] (Fig. 11.2).

Due to this malalignment of the atrial and inlet ventricular septum, the regular atrioventricular node, which is located at the apex of the triangle of Koch in the base of the atrial septum, is anatomically impossible to connect to the atrioventricular bundle in ccTGA with situs solitus {SLL} arrangement. Instead, the anterior AV node is located beneath the ostium of the right atrial appendages at its junction with the anterior atrial wall and is positioned above the lateral margin of the area of pulmonary to mitral fibrous continuity. The anterior AV node gives rise to a penetrating bundle (PB) through fibrous trigone, and the non-branching bundle (NBB) or the His bundle encircles pulmonary valve anteriorly and descends onto the anterior part of the trabecular septum on the right side (morphologic LV) surface of the septum. (with intimately close relationship to the anterosuperior edge of pm VSD, if present). And then the NBB bifurcates into a cord-like right bundle branch (RBB), which extends leftward to reach the morphologically right ventricle. The fanlike left

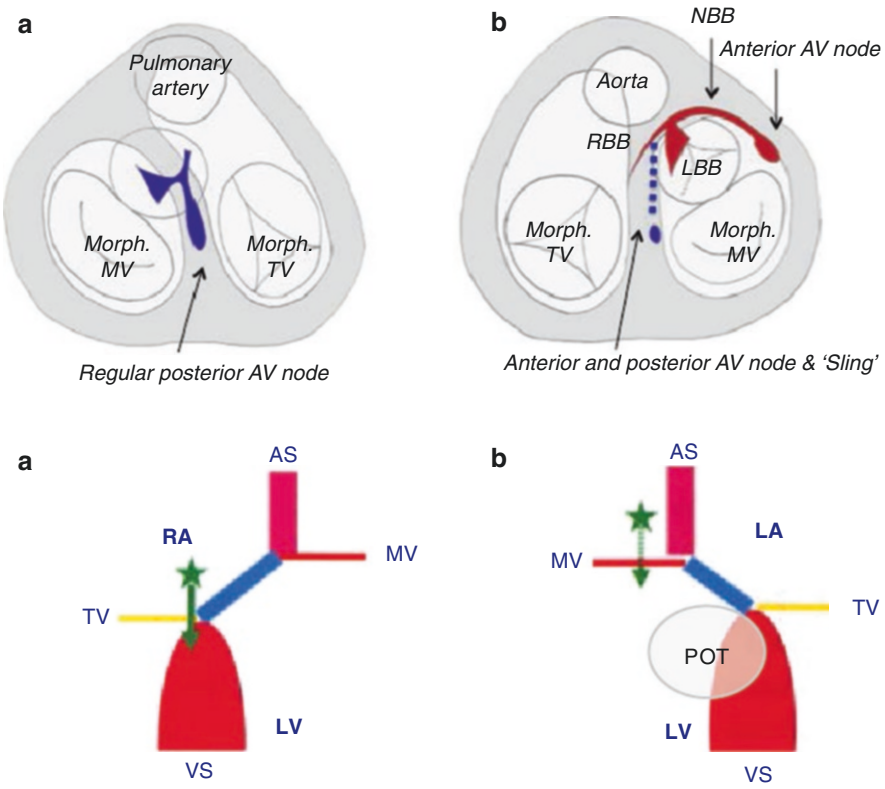

Fig. 11.2 The atrioventricular conduction system in ccTGA. (**a**) Normal heart and (**b**) ccTGA in situs solitus. *AS* the atrial septum, *VS* the ventricular septum, *TV* tricuspid valve, *MV* mitral valve, *AVS* the atrioventricular septum, *POT* the pulmonary outflow tract

bundle branch (LBB) cascades down the smooth surface of the morphologically left ventricle (Fig. 11.2). This abnormal course of the conduction system is of crucial significance to the surgeons in the presence of a ventricular septal defect or subpulmonary obstruction (Fig. 11.3).

In contrast, the normal AV conduction bundle from regular posterior AV node is present in situs inversus, which arrangement of ccTGA is associated with better alignment of the atrial and inlet septum with less "wedging" of the pulmonary outflow tract. Furthermore ccTGA in situs inversus and the other variations may have the dual AV node with possible sling, resulting in the occurrence of reentrant supraventricular tachycardia [10, 11].

11.2.3.1 Clinical Implications of Abnormal Conduction System

The long penetrating and non-branching bundle in ccTGA are vulnerable to fibrosis with advancing age. This makes the conduction system somewhat tenuous, with a progressive incidence of complete AV block.

Other conduction disturbances described include sick sinus syndrome, atrial flutter, reentrant atrioventricular tachycardia due to a dual AV node, and an accessory pathway along the atrioventricular junctions.

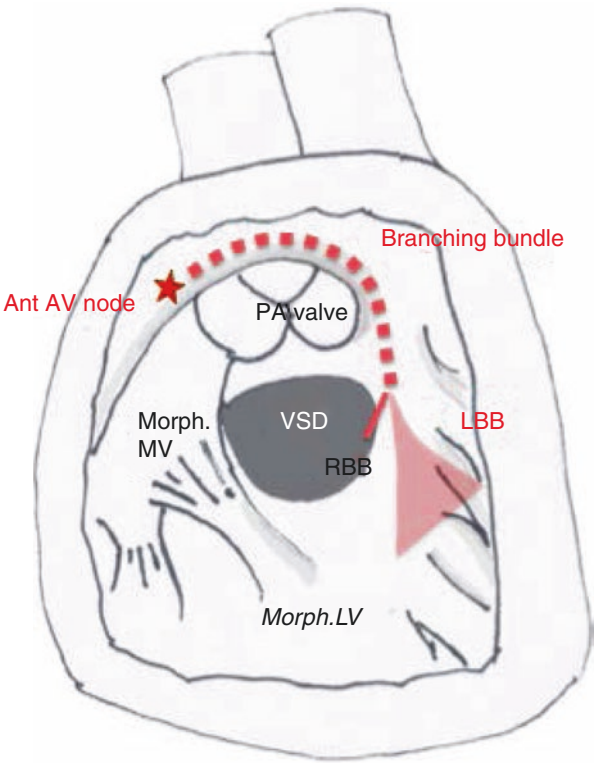

Fig. 11.3 The relationship of the abnormal course of the AV conduction bundle to the pulmonary valve and a ventricular septal. From the left ventricular view

11.3 Overview of Surgical Intervention

11.3.1 Surgical Management Strategies

11.3.1.1 Physiological Repair vs Anatomical Repair

Figure 11.4 depicts the classification and modifications of surgical procedure for ccTGA: *Physiological repair* vs *anatomical repair*. Until recently, patients with associated abnormalities underwent conventional physiological repair. The goal of the operation is to repair the cardiac defects by closing VSD, repairing the tricuspid valve, and reliving LVOTO, while leaving the morphologically right ventricle as the systemic ventricle. The physiologic approach is straightforward but has the shortcomings over time. After this type of repair, the RV remains the systemic ventricle, and long-term results of this type of surgical repair are disappointing with the late occurrence of the right ventricular dysfunction, tricuspid valve regurgitation, and complete heart block. Because of this poor prognosis over the long term, there is an increasing trend toward achieving anatomical correction.

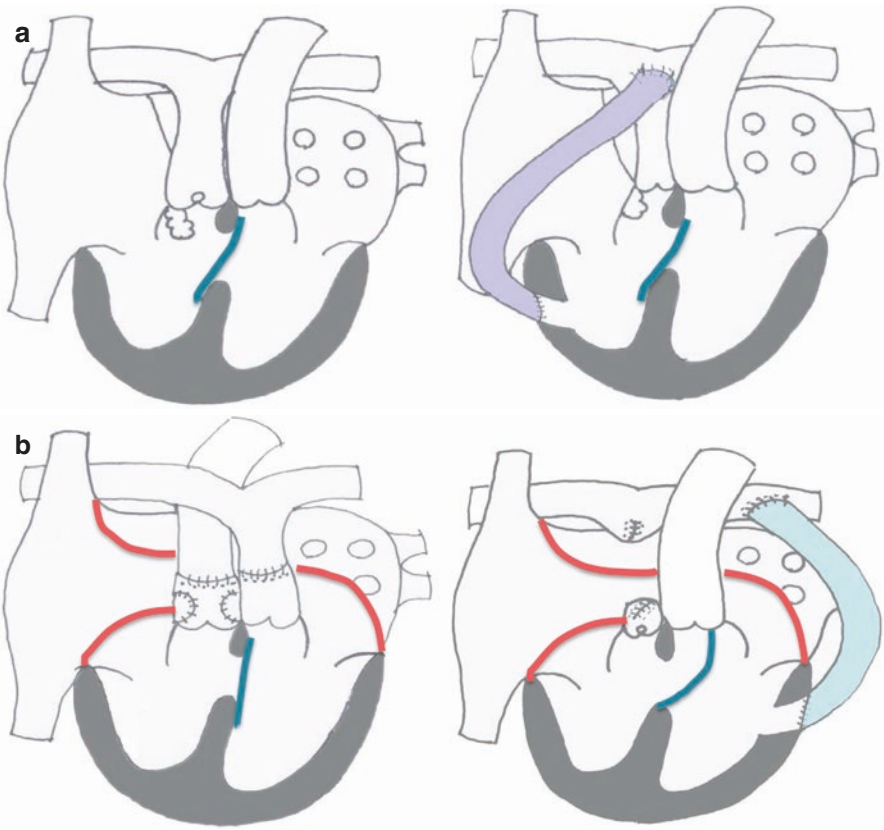

Fig. 11.4 The classification of surgical procedure for ccTGA: *Physiological repair* (**a**) vs *anatomical repair* (**b**). (**a**) (1) VSD closure (2) LVOTO relief using LV-PA conduit (conventional Rastelli) with VSD closure (**b**) (1) The double switch operation (DSO) (2) The Rastelli–Senning/Rastelli–Mustard Operation

The concept of the anatomical correction is the rerouting of the pulmonary venous return to the morphologically left ventricle and aorta and the systemic venous return to the morphologically right ventricle and pulmonary arteries, thus restoring a normal anatomic pattern of circulation. This can be achieved by the combination of atrial switch operation and either arterial or intraventricular switch operation. Anatomic correction for ccTGA is tailored to the patients' specific anatomies: (1) the arterial–atrial switch procedure or the double switch operation (DSO) for patients with normal LVOTO regardless of the presence of VSD and (2) the Rastelli–atrial switch procedure [the Rastelli/Senning or the Rastelli/Mustard] for patients with an unrestrictive VSD and LVOTO (pulmonary atresia or severe subpulmonary stenosis). Current surgical strategies for ccTGA in relation to the anatomical types are shown in Fig. 11.5.

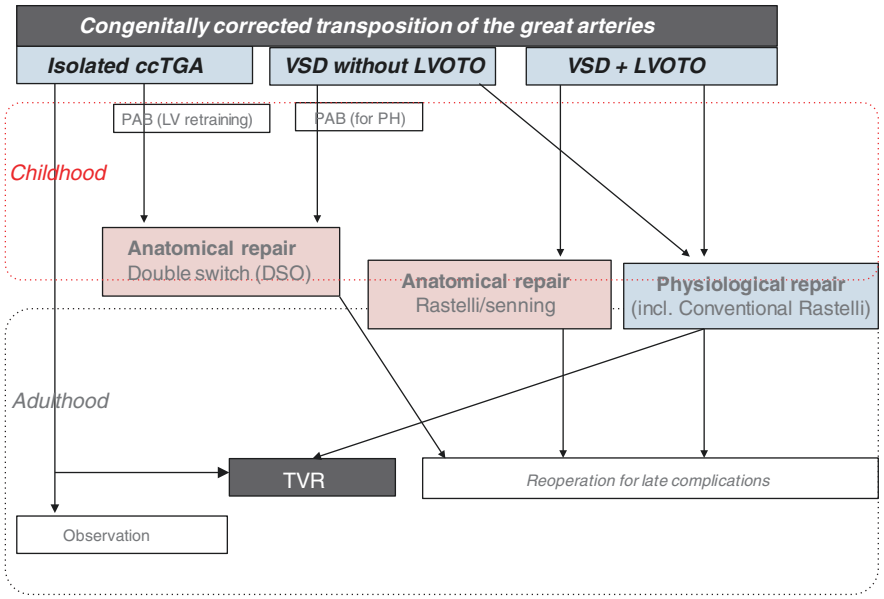

Fig. 11.5 Current surgical strategies for ccTGA in relation to the anatomical types

Despite anatomical repair may improve long-term prognosis, this operation represents major and technically challenging surgical procedures. The physiological repair may be still indicated to a certain group of patients with associated lesion who are contraindicated to anatomical repair.

11.3.1.2 Operative Indication for ccTGA

In general the diagnosis of ccTGA is not in itself an indication for surgical correction. The operative indication should be based on the hemodynamic impact of the associated lesions and the potential of the systemic RV to fail. Definitive indication includes the patients with heart failure due to a large VSD or a VSD with significant LVOTO/PS. When a VSD is present, the indications for operation will be determined by its hemodynamic impact (i.e., Qp/Qs, pulmonary arterial pressure, and pulmonary resistance), as well as the specific morphology of the defect itself. In the presence of pulmonary stenosis the indication for surgery is dictated by the severity of the obstruction (i.e., transpulmonary pressure gradient >50 mmHg) and the degree of cyanosis, hypoxemia, and polycythemia. Other major indications for surgery include the severity and progression of tricuspid valve regurgitation (TR). Replacement of the morphologically tricuspid valve is usually recommended, if the regurgitation is more than grade 2/4 at the time of intracardiac repair of other lesions [12]. Systemic AV valve replacement is relatively common in the adult age.

If the decision is made to achieve the anatomic correction in order to retain anatomically normal physiology to avoid the future deterioration of the systemic RV and TR, the timing and strategies of surgery are always difficult decision, especially in asymptomatic patients with the isolated ccTGA or with hemodynamically

well-balanced lesions. Most centers would not recommend a prophylactic double switch operation for patients without associated abnormalities in whom the RV and tricuspid valve function are normal. Instead, pulmonary arterial banding (PAB) is indicated to the isolated ccTGA to retrain the LV for the subsequent anatomical correction in childhood, especially in patients with the presence of significant TR or RV dysfunction. Some centers consider the anatomical repair is their institutional first choice for the patients who have a balanced systemic and pulmonary blood flow due to VSD and pulmonary stenosis without clinically significant cyanosis to treat [13].

11.3.1.3 PAB for Retraining the Left Ventricle in Isolated ccTGA for DSO [14–16]

In the isolated ccTGA without associated abnormalities, LV pressure will be at pulmonary artery pressure; thereby the LV should be retrained in younger children by the placement of a pulmonary artery band (PAB) to increase LV pressure for DSO. This strategy is thought to be particularly required in pediatric patients with significant tricuspid regurgitation. Some report proposed the early prophylactic pulmonary artery banding in neonate with isolated ccTGA considering the future application of DSO.

In childhood the LV can be successfully retrained using a strategy of progressive pulmonary artery banding in order to provide an increased pressure load on the LV and promote LV hypertrophy. The possible predictors for a successful LV retraining include an LV systolic pressure of at least 70–80% of systemic pressure in childhood or 100% in adolescence and an LV wall thickness or LV mass index that is equivalent to that in a systemic LV. One of the best predictors of failure of retraining is age, with most successfully retrained patients being <10 years of age [17].

11.3.1.4 Pulmonary Artery Banding as a Definitive Palliation

Pulmonary artery banding intended to train the LV has been shown simultaneously to reduce the tricuspid regurgitation and subsequently to improve the RV dysfunction [18]. As regards the mechanism of this phenomenon, it has been speculated that an increase in the LV to RV pressure ratio also may reduce the degree of TR by the shift of the interventricular septum toward the RV [18, 19]. Recently Cools et al. [20] proposed PAB as "open-end" palliation for systemic RV dysfunction and progressive tricuspid regurgitation in 14 patients aged 0.9–14.9 years. Whether this strategy will be applied to adults with isolated ccTGA remains to be seen.

11.4 Clinical Manifestation in Adulthood

11.4.1 Clinical Manifestation of Adult Unoperated ccTGA and the Timing of Diagnosis

The adult with ccTGA presents in various ways, and the clinical course is quite variable depending on the presence and severity of associated lesions. If there are no associated defects, or well-balanced circulation due to the combination of the lesions, the patient will typically be asymptomatic early in life. Diagnosis can be

made later in adulthood, when patients present with complete heart block or congestive heart failure, or incidentally when an ECG, chest X-ray, or echocardiogram is performed for other reasons.

According to the report from the Mayo Clinic adult congenital heart disease database from 1986 to 2000 of the unoperated adult (≧18 years old) with ccTGA, the correct diagnosis was first made at the age older than 18 years old in 66% of patients, 17% of whom were more than 60 years old at the time of diagnosis [21]. And more strikingly, adult patients with unoperated ccTGA are often misdiagnosed in adulthood and are referred late with the presence of symptomatic systemic AV valve (SAVV) regurgitation, significant right ventricular dysfunction, and AV block. Beauchesne et al. reported that 53% of adult unoperated patients had advanced systemic ventricular dysfunction at the time of referral, and, often, they have had severe SAVV regurgitation ≧3/4 in 59% of them [21] and therefore were deemed as "referred late."

11.4.2 Natural History

The natural history of patients with ccTGA is largely dictated by the function of the systemic RV and by the presence or absence of associated abnormalities.

In general, ccTGA is known to have an unfavorable natural history. Most patients with lesions will develop progressive RV dysfunction, relatively early in life, and may not, in great majority, live over 50 years of age. A single center database review from the Toronto Congenital Cardiac Centre for Adults of 131 patients with ccTGA showed a mortality rate of 21% in patients >18 years of age, with a mean age at death of 33 years. Several studies documented an increasing incidence of cardiac failure with advancing age; this late consequence is extremely common by the fourth and fifth decades. A multicenter study conducted by the International Society for Adult Congenital Cardiac Disease of 182 patients with adult ccTGA (≧18 years old) has demonstrated that by the age of 45 years, 67% of patients with associated lesions and 25% of patients without significant associated lesions had congestive heart failure [22].

In contrast, in the setting of ccTGA without any other associated anomalies, the ventricular function is adequate to maintain a "normal" physical activity into adulthood [23, 24]. Some patients, but very rare, may survive to the seventh and eighth decades when no associated anomalies exist being discovered as a chance finding at autopsy [25, 26].

11.4.2.1 Mechanism of Systemic Right Ventricular Failure

The exact mechanism of SV failure is unknown but may relate to microscopic structural features and fiber orientation of the RV myocardium. The morphologically RV lacks the helical myocytic arrangement, essential to the twisting or torsion of the ventricle, and thus being unable to sustain the demands of a systemic ventricle, unlike LV [27].

Other possibilities include coronary perfusion mismatch, because the cardiac hypertrophy caused by the pressure overload on the morphological right ventricle

may surpass the coronary artery oxygen supply, which comes mainly from the right coronary artery. A high incidence of myocardial perfusion defects with regional wall-motion abnormalities and impaired ventricular contractility has been reported [28]. Systemic ventricular dysfunction is also caused by volume overload due to AV valve regurgitation or complete AV block.

11.4.2.2 The Left-Sided Morphologically Tricuspid Valve

The natural history of the left-sided morphologically tricuspid valve is variable. The valve tends to remain competent during the first decade of life but slowly becomes progressively incompetent during the second to fifth decades of life. If there is an Ebsteinoid malformation of the valve, the regurgitation can be seen at birth. In the majority of patients, the SAVV is morphologically abnormal, and with time, there is increasing regurgitation. Beauchesne et al. [21] reported that adult unoperated ccTGA obtained prevalence of systemic valvar regurgitation of 59%, and 68% of them underwent systemic AV valve replacement.

11.4.2.3 Rhythm Abnormality: Complete Atrioventricular Block and Atrial Tachyarrhythmias

Approximately one-tenth of infants born with congenitally corrected transposition have complete heart block [29, 30]. In patients born with normal cardiac conduction, the risk of developing heart block over time increases by 2% per year until it reaches a prevalence of 10–15% by adolescence and 30% in adulthood [31].

Around two-fifths of adult patients, nonetheless, will have normal cardiac conduction throughout their lives. As time passes, the PR interval prolongs, until complete heart block becomes manifest [2].

11.4.2.4 Impact of Atrial Situs on Natural History

Oliver et al. [32] reviewed the long-term outcome of 38 adult ccTGA patients (≧18 years old) to compare the natural history of two anatomic arrangements, situs inversus vs situs solitus, and concluded that the natural prognosis was significantly better in situs inversus than that in situs solitus. Ebstein-like anomaly or spontaneous complete atrioventricular block was rare, and late complications are uncommon in patients with ccTGA with situs inversus. It has been speculated that the good septal alignment in ccTGA with situs inversus might preclude of AV conduction disorders and tricuspid valve abnormalities.

11.4.3 Unnatural History of Operated Patients

11.4.3.1 Long-Term Outcome and Complications After the Physiological Repair

Long-term results of this type of surgical repair are disappointing [33, 34]. Hraska et al. [33] reported the outcomes of 123 patients with ccTGA who underwent a variety of surgical procedures. The 10-year survival after physiological repair was only 67%, and systemic RV dysfunction occurred in 44% of patients. Freedom from RV dysfunction was approximately 40% at 15 years with factors predicting RV

dysfunction being Ebstein's anomaly, tricuspid valve replacement, and postoperative complete heart block.

As regards the impact of the individual procedures, Bogers et al. [35] reviewed the long-term outcome of Rastelli-type and non-Rastelli-type physiological repairs for ccTGA. Actuarial survival at 20 years was 62% for the non-Rastelli group and 67% for the Rastelli group. Freedom from reoperation was 47% at 20 years in the non-Rastelli group and 21% at 19 years for the Rastelli group. Tricuspid valve regurgitation was more often seen in the non-Rastelli group, whereas redo operations were performed predominantly in the Rastelli group mainly for conduit obstruction.

The impact of preoperative TR is crucial in the physiological repair, and it has been documented that when no tricuspid valve regurgitation is present preoperatively, a survival rate of 72% at 30 years can be reached with the physiological repair [36].

11.4.3.2 Long-Term Outcome and Complications After the Anatomical Repair: The DSO and the Rastelli/Senning Procedure

Series of the DSO and the Rastelli/Senning procedure have been published by several groups in large centers with early mortality currently of 0–10% and long-term survival at 10 years of 80–95% [14, 36–41]. Another factor to be considered for interpreting the outcome of anatomical repair is the learning curve for such complex operations and the recent progress in technical modification.

As regards the type of anatomical repair (the DSO vs Rastelli/Senning), more recently it has been reported that the long-term outcome of the DSO was more favorable than the other with an excellent reoperation-free survival, and this procedure should be considered as the optimal procedure of choice [38, 39]. Hiramatsu et al. [38] reviewed 90 patients with ccTGA from 1983 to 2010 underwent the Rastelli–Senning/Mustard procedure (group I) and the DSO (group II). Although survival, including hospital and late mortality at 20 years, was similar (75.7% in group I vs. 83.3% in group II), freedom from reoperation was 77.6% in group I vs. 94.1% in group II. Similarly, Gaies et al. [39] demonstrated that the 10-year survival was superior in the patients who underwent the DSO compared to the Rastelli–Senning.

In contrast, the outcome of the Rastelli/Senning operation for ccTGA with LVOTO and VSD has been improved with the technical modification and the improvement in the materials for extracardiac conduit. For patients with pulmonary stenosis and restrictive VSD, additional DKS anastomosis seems to be an effective approach to avoid postoperative systemic ventricular outflow tract obstruction and surgical heart block, as reported by Hoashi et al. [13].

The Complication of the Anatomical Repair

There is a definite incidence of late occurrence of various complications relating to anatomical repair. The complications after the atrial switch include sinus nodal dysfunction, supraventricular arrhythmias, and problems with the atrial baffle obstruction. If the ventricular switch is used, the left ventricular outflow obstruction due to the stenosis of VSD or intracardiac rerouting baffle, aortic regurgitation, or RV-PA

conduit obstruction and regurgitation can occur. After the DSO, coronary arterial obstruction or stenosis, aortic valvar regurgitation, and pulmonary arterial stenosis may be evidenced.

Outcome of Retraining the Morphological Left Ventricle for Isolated ccTGA

In the isolated ccTGA, during childhood, the subpulmonary LV has been successfully retrained using a strategy of multi-staged PAB in order to provide an increased pressure load on the LV and promote LV hypertrophy. Recent studies documented that the failure rate of LV training before anatomical repair from 0 to 20% is mainly due to LV dysfunction. One of the best predictors of failure of retraining is age, with most successfully retrained patients being <10 years of age [14, 16, 17]. Devaney et al. [16] reported that the two oldest patients, aged 12 and 14 years, had LV failure necessitating removal of the band PAB among 15 patients who underwent PAB for the LV retraining. Poirier et al. demonstrated that the success rate was only 20% in patients older than 12 years old, whereas 62% of the patients less than 12 years old successfully completed LV retraining [17]. Therefore, surgical retraining of the LV is an option in children but not in adults due to unfavorable outcomes. LV retraining is even a challenging task in older children.

LV Dysfunction After DSO

Systolic dysfunction of the LV is relatively common after the double switch procedure [15, 40, 41]. In a retrospective, single-institution study of a total of 113 ccTGA patients, Murtuza et al. [41] demonstrated that freedom from death, transplantation, or poor LV function at 10–14 years was significantly lower in the DSO compared to the Rastelli–Senning group, despite the better actuarial survivals at 10 years in the former group. Quinn et al. [15] reported that patients requiring LV retraining prior to the DSO may be more at risk of developing significant LV dysfunction (6 of 11 patients: 55 %) than patients whose the left ventricle remains at systemic pressure at birth (6 of 33 patients 16 %).

LV dysfunction has been also noticed by several groups, regardless of the proceeded PAB to retrain LV, and is attributed to various factors including complete AV block, aortic regurgitation, and mitral regurgitation [41, 42]. LV function in patients who did not have a large left to right shunt preoperatively demonstrated to be better than in the group who had a large VSD or patent ductus arteriosus as a cause of LV preparedness [40].

The occurrence of LV dysfunction indicates that the DSO is still fraught with imperfections. The Rastelli group apparently more often required conduit revisions but has otherwise performed well.

11.4.3.3 Anatomical vs Physiological Repair

As regards the benefit of the anatomical repair in the actuarial survival rate, Shin'oka et al. [36] reported that there were no statistical differences in the long-term survival rates between the physiological and anatomic surgical repairs. Nevertheless, the outcome of the physiological repair was much worse in patients with significant preoperative TR (the survival at 30 years: 71.9% without TR vs 19.1% with TR). In

contrast, results of the anatomical repair were favorable even for patients with significant TR (71.8% 30 years), and, therefore, the anatomical repair should be a procedure of choice for those patients with significant TR. Conversely, the physiological repair still remains a viable option with an acceptable long-term survival when patients do not have significant TR before their operation.

In 2010 Lim et al. [43] analyzed 167 patients with ccTGA who underwent biventricular repairs and demonstrated the superiority of anatomical repair compared to the physiological repair in the long-term outcome for systemic AV valve and ventricular function.

Freedom from TR and RV dysfunction was significantly higher in the anatomical repair than in the physiological repair (74.5% at 18 year vs 7.4% at 22 year for freedom from TR and 86.3% at 18 years vs 19% at 23 years for freedom from RV dysfunction, respectively). The reoperation-free ratio was 10.1% at 22 years after the physiological repair and 46.2% at 15 years after the anatomical repair. Meta-analysis of individual patient data reported by Alghamdi et al. [44] including 11 studies revealed superiority of the anatomical repair for in-hospital mortality.

11.4.3.4 Long-Term Outcome and Fontan Operation for ccTGA

The Fontan operation has been shown to have a better late survival over the physiological repair and comparable with anatomical repair in terms of freedom from reoperation and the late survival other than in the presence of preoperative significant TR [33, 36, 45–47].

In 2005, Hraska et al. [33] demonstrated that among 123 cases there was a much better 5-year survival in the Fontan patient group than the physiological repair, despite the Fontan patients having lower cardiac output. In a recently published retrospective review of 56 ccTGA patients by Hsu et al. [48], early and late mortality were lower after the Fontan operation compared with the anatomical and conventional repair after 6 and 25 years of follow-up. The 30-day in-hospital mortality rate was 13.3% after the physiological repair (group I), 22.2% after the anatomical repair (group II), and 0% after the Fontan (group III). The overall survival rate was 80% at 16 years in group I, 53% at 13 years in group II, and 100% at 13 years in group III. Freedom from reintervention was 74% in group I, 53% in group II, and 84% in group III. Despite these excellent clinical outcomes of Fontan for ccTGA, however, the advantages of the Fontan must be weighed against its potential disadvantages and long-term complications related to progressive cyanosis, liver cirrhosis, protein-losing enteropathy, and the development of plastic bronchitis.

11.5 Practice of Therapeutic Intervention and Indication

11.5.1 Medical Management

Medical treatment involves management of the failing systemic RV [25, 26] with diuretics, inhibitors of angiotensin-converting enzyme, and digoxin. Afterload reduction with ACE inhibitors or angiotensin II receptor blockers may be less successful for systemic morphological right ventricle than when those used for a

morphological left ventricle [49]. Data are lacking to support the use of beta-blockers to improve ventricular function in ccTGA. For medical therapy of arrhythmias, it is prudent to start antiarrhythmic therapy relatively slowly because of the potential for complete AV block and the possible need for pacemaker implantation.

11.5.2 Intervention for Arrhythmia

Spontaneous complete heart block may be present from birth in approximately 4% of cases. In addition, progressive deterioration in AV conduction can occur throughout life, with an estimated risk of spontaneous heart block of 2% per year [31]. If there are conduction abnormalities, the patient might require implantation of a pacemaker. The status of AV conduction must be monitored regularly with ECG and periodic Holter monitor in adults with ccTGA. Catheter ablation may be indicated to reentrant supraventricular tachycardia due to the casual presence of the accessory pathways or the dual AV node in a variety type of ccTGA, particularly when there is Ebstein malformation of the left-sided tricuspid valve or a straddling AV valve [50].

11.5.3 Cardiac Resynchronization Therapy (CRT)

A substantial number of ccTGA patients will eventually require permanent pacing for complete heart block, with the ventricular lead being placed in the morphologic LV. This may negatively impact on the systemic RV due to the resulting interventricular dyssynchrony. Resynchronization approaches to the systemic RV appear to be an attractive option for ccTGA patients, showing ventricular dyssynchrony. Although numbers are small, this approach appears to have produced a symptomatic improvement in some patients with class III and IV symptoms [51]. A coronary sinus lead is used to pace the RV in ccTGA, since the CS is situated adjacent to the systemic RV and drains into the systemic right atrium in ccTGA patients, which makes transvenous CRT feasible in this group of patients. Because of the heterogeneous anatomy of coronary sinus, visualization of the CS anatomy before attempting CRT implantation is strongly recommended, using different modalities such as CS venography, cardiac CT, and magnetic resonance imaging.

11.5.4 Surgical Management

The indication, procedure, pitfall, and complication of the intracardiac repair of ccTGA in adulthood.

11.5.4.1 Special Consideration for Indication in Adulthood

Initial operation for associated lesions or late consequences of ccTGA is not uncommon even in the elderly patients (i.e., in the fortieth–fiftieth decade). The indications for surgery in adult patients are usually the onset of symptoms due to associated systemic AV valve regurgitation and rarely due to pulmonary overcirculation (a large

VSD) or a significant cyanosis (a VSD with pulmonary stenosis). Nevertheless, even nowadays, the late presentation in presence of cyanosis is particularly common in developing countries due to delay in diagnosis and/or referral. Surgical intervention in the adult, therefore, often consists of systemic AV valve replacement (tricuspid valve replacement: TVR) alone or with a concomitant procedure (i.e., VSD closure) and ideally should be performed before the SV ejection fraction has deteriorated (may be below 45%) [52].

In adult ccTGA, the physiological repair is predominantly adopted, since the morphological and physiological conditions are rarely appropriate to the anatomical repair, and the anatomical repair in adults is associated with a higher mortality. Despite the limitations of significant risk for the systemic right ventricle dysfunction, the physiologic operative approach may be useful in the appropriately selected cases with good right ventricular function and tricuspid valve function.

11.5.4.2 Tricuspid Valve Replacement (TVR) for Tricuspid Regurgitation

Indication procedure and outcome: Tricuspid valve replacement (TVR) for ccTGA is often indicated in adulthood in conjunction with intracardiac repair or the other procedures in unoperated patients or after the physiological repairs. Recently Mongeon et al. [53] reported 46 patients of TVR for ccTGA, 5–72 years of age with a mean age of 40.8 + 14.8 years, with concomitant procedures in approximately 60% of the cases.

In patients with situs solitus, TVR is usually accomplished through a standard left atriotomy anterior to the right pulmonary veins and rarely through a right atriotomy and transseptal approach. In the patient with situs inversus, right-sided tricuspid valve is approached transseptally through the left-sided morphologically right atrium. The selection of prosthetic valves may depend on the patient age. The modification of chordal preservation to retain the RV function is utilized in the high-risk patients [53].

Van Son et al. [52] reported the outcome of 40 patients who underwent TVR at the Mayo Clinic between 1964 and 1993, as the early mortality was 10% and late survival was 68% at 10 years. The survival in patients with RVEF < 44% was 20% at 10 years, whereas in patients with RVEF > 44% the survival was 100%. The authors concluded that surgery for significant TR should be considered at the earliest sign of progressive RV dysfunction before EF more than 44%. Scherptong et al. [54] recently published a multicenter Dutch experience of tricuspid valve surgery in 16 patients with a systemic RV. Eight patients underwent the tricuspid repair, and eight underwent TVR. This study showed a decreased survival after valve repair compared to TVR, which supports the advantage in the approach of primary tricuspid valve replacement in ccTGA. Recent report from Mayo Clinic [53] has demonstrated the 10-year survival or freedom from cardiac transplantation after TVR in 46 patients was still 64.1%, despite the excellent surgical mortality of 0%. Therefore TVR may be only moderately successful at improving survival because it was performed too late. In this report, preoperative variables associated with late mortality were an RVEF < 40%, an RV systolic pressure ≧50 mm Hg, atrial fibrillation, and New York Heart Association functional class III to IV. And also preoperative RVEF

was the only independent predictor of postoperative systemic RV function (RVEF% at >1 year postoperatively), as the postoperative EF was preserved in 63% of patients who underwent surgery with an SVEF ≧ 40% compared with 10.5% of patients who underwent surgery with an SVEF < 40%.

Lundstrom et al. [12] proposed operation for asymptomatic or barely symptomatic patients with ccTGA and cardiac enlargement due to systemic ventricular volume overload.

11.5.4.3 Conventional Repair

In adult ccTGA, a conventional physiological repair consists of closure of the VSD, relief of LVOTO if present, and replacement of the systemic tricuspid valve (Fig. 11.4).

VSD Closure: de Leval Operation (Fig. 11.6)

The VSD is usually well visualized and closed through the mitral valve. In this circumstance, the surgical injury to the long non-branching AV bundle (NBB) should be avoided since it runs immediately adjacent to the anterosuperior edge of the perimembranous VSD on the LV side of the septum. By the DeLaval method in order to avoid damage to the NBB, the interrupted horizontal mattress sutures, reinforced with pledgets, are placed through the septal defect and anchored approximately 4 mm from the edge of the defect within the left-sided anatomical RV surface, particularly along its superior and anterior rims. The remainder of the patch is sutured to the right-sided surface of the septum [55] (Fig. 11.6).

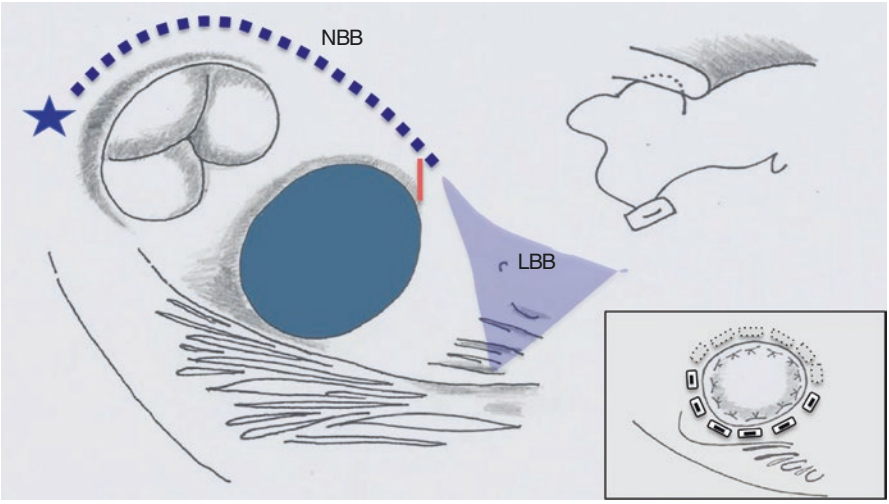

Fig. 11.6 VSD closure (The DeLaval method): in order to avoid damage to the His bundle (NBB), the interrupted horizontal mattress sutures, reinforced with pledgets, are placed through the septal defect within the left-sided anatomical RV surface, particularly along its superior and anterior rims. The remainder of the patch is sutured to the right-sided surface of the septum

In older children or in adult, the VSD may be also approached from the aorta through the aortic valve by placing a patch on left-sided RV surface without a special concern about the conduction disturbance. If the tricuspid valve is concomitantly replaced, access from the LA gives excellent exposure both to the left AVV and to the VSD. Placement of stiches on the morphological RV side of the septum is very easy.

Left Ventricle–Pulmonary Artery Conduit (LV-PA Conduit): Conventional Rastelli (Fig. 11.7)

The placement of the left ventricle–pulmonary artery conduit is needed for subpulmonary LVOTO stenosis, unless there is a resectable obstructing mass of endocardial cushion tissue. Direct relief of muscular subpulmonary stenosis is contraindicated because of the risk of causing permanent AV block and inadequate relief of the obstruction. The placement of the LV-PA conduit is at risk of compression by the sternum, heart block, or injury to the mitral anterior papillary muscle.

The left ventriculotomy is made lower in the midportion to avoid the conduction system, and therefore possibility of injury to the papillary muscles must be considered. Explore the left ventricular free wall digitally through the mitral valve to allow a direct determination of location of the papillary muscles and selection of a safe area for ventriculotomy (Fig. 11.7). Apical placement of the left ventriculotomy for the inflow conduit rather than in the midportion or base placement may avoid these complications [56], although this results in a long and winding extracardiac conduit that may be short-lived because of the proliferation of pseudointima.

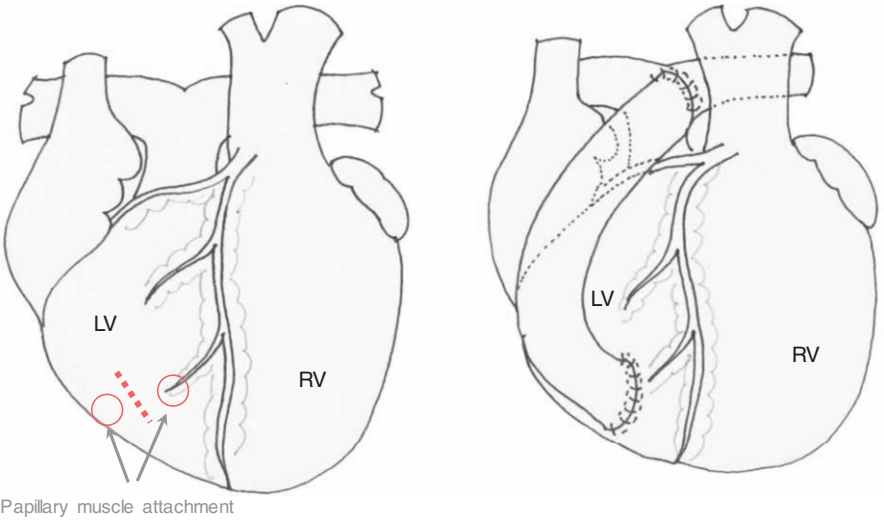

Fig. 11.7 Conventional Rastelli operation: left ventricular to pulmonary artery (LV-PA) conduit

Pitfall for Conventional Repair: Progression of TR After Relieving LVOTO

The physiological repair has been often demonstrated to worsen systemic AV valve regurgitation to significant extent [19, 57]. This may be attributed to the changes of the position of the ventricular septum after relief of pulmonary stenosis, leading to the remodeling of the tricuspid annular configuration and dilatation [12, 18].

Kollars et al. [18] demonstrated that the worsening of TR was presented in 16 patients who underwent either the conventional Rastelli-type repair involving VSD closure or the replacement of a stenotic LV to the pulmonary artery conduit, both of which procedures would decrease the LV pressure postoperatively compared to prior to operation.

Recent studies have demonstrated that the positions of the ventricular septum and septal attachments of the tricuspid valve depend on the pressure gradient between the RV and LV in patients with a ccTGA. Thereby, LV to right ventricle (RV) pressure ratio also may affect the degree of TR [18, 19]. When the LV is exposed to pulmonary pressure, the ventricular septum protrudes into the LV and the septal attachments are pulled away from their annulus, causing coaptation zone deficiency and progressive TR [18, 19]. The study by Koh et al. [19] on 15 patients with discordant atrioventricular connection and pulmonary outflow tract obstruction who underwent the physiological repair using the LV to the pulmonary artery conduit indicated that the left ventricular pressure of <60% of the systemic right ventricular pressure at the systolic phase could be among the deleterious factors in terms of TR and dilatation of the right ventricular cavity. They suggested that the surgeon can choose a smaller conduit than usually used so as to provide some pressure gradient between the LV and the pulmonary artery remained.

Erek et al. [58] experienced an acute severe TR during conduit re-replacement, in a 17-year-old male after the physiological repair, and the degree of tricuspid regurgitation successfully decreased by the pulmonary conduit banding under transesophageal echocardiography guidance, to increase the left ventricular to right ventricular pressure ratio increased from 0.33 to 0.60.

Modification: The Physiological Repair with the One and a Half Ventricular Repair Strategy

Complete relief of LVOTO by pulmonary valvotomy in ccTGA is usually difficult without the use of an extracardiac conduit, due to the outflow tract anatomy and conduction system location. In this regard, the 1.5 ventricle physiological repair in conjunction with the bidirectional Glenn appears to be an effective solution for selected cases and does avoid the need for a valved conduit.

11.5.4.4 Anatomical Repair

Poor right ventricular function or tricuspid valve function would be compelling reasons to choose the anatomic over physiological repair. In some adult ccTGA circumstances, consideration may be given to restoring the left ventricle to the SV, but careful evaluation of its function must be made. If the reroutable unrestrictive VSD

is present, then a Rastelli type of reconstruction for the LV outflow can be done by baffling the VSD to the aorta. Right ventricle-to-pulmonary artery continuity is achieved with a conduit. The DSO has not been considered in adulthood unless preceded PAB for retraining LV or as a palliation for a large VSD has been appropriately done sufficiently early in childhood. Surgical retraining of the LV is an option in children but not in adults due to unfavorable outcomes [59].

Atrial Switch Operation: Senning vs Mustard

The Senning operation utilizes the patients' own tissue to create the venous baffles, while the Mustard operation excises the interatrial septum and uses a pantaloon-shaped baffle usually of heterogeneous materials to complete the inflow switch. In the past, Senning or Mustard procedures were selected as atrial switch procedures, depending on the size of the right atrium, and a large-sized right atrium was thought to be essential for Senning procedure. However, it has been shown that Senning atrial switch can be performed without postoperative caval obstruction for all types of anatomic features including the apicocaval juxtaposition [38]. Furthermore an augmented patch in Mustard has been demonstrated to be easily calcified without growth potential and result in late caval obstruction. Currently, the Senning procedure has become the most widely used procedure as a part of anatomical repair for ccTGA, because of the lower incidence of pathway obstruction, baffle leak, and significant late arrhythmias.

The Senning Procedures: Pitfalls in ccTGA

The Senning procedure is feasible in all atrial switch procedures. When the free wall of the right atrium is relatively narrow, as in ccTGA with dextrocardia or mesocardia, a large pericardial patch to augment a new functional left atrium is a useful option.

The suture line of the free wall of the RA for creating the systemic venous pathway needs the care for the coronary sinus (CS) and conduction system. In the classical Senning, the inferior suture line would run along the tendon of Todaro, leaving the coronary sinus and the triangle of Koch anterior to the suture line, avoiding damaging the normally positioned posterior AV node. The modification of the cutback of orifice of CS to LA is useful. In contrast, in ccTGA, the suture line can be allowed to deviate anteriorly, incorporating the coronary sinus within the IVC pathway. However, the normal topology of the AV node in the triangle of Koch might be seen in the setting of situs inversus and the other varieties of the anatomical type.

Hemi-Mustard and the Bidirectional Glenn Operation

Malhotra et al. [60] propose a modified atrial switch procedure, consisting of a hemi-Mustard procedure to baffle inferior vena caval return to the tricuspid valve in conjunction with a bidirectional Glenn operation in order to avoid complications associated with the complete atrial switch and to reduce inflow volume load into RV.

The hemi-Mustard modification obviates the need for the superior caval suture lines and, as a result, might result in a reduced incidence of these late complications of traditional atrial baffle procedures. Use of the BDG operation also decreases the systemic venous return into the failing RV and reduces volume load to both a dysplastic or Ebsteinoid tricuspid valve and the RV-PA conduit.

The implicated benefits include (1) reduction of atrial baffle related- complications (i.e., sinus node dysfunction and SVC obstruction), (2) prolonged extracardiac RV-PA conduit life, and (3) promoting better coaptation of tricuspid valve and (4) technical simplicity.

The septum primum is resected completely, and, if necessary, the limbus is cut in a superior direction to further enlarge the atrial septal opening. The polytetrafluoroethylene patch is always circular in shape.

Arterial Switch Operation (ASO)

Double switch operation [Senning and arterial switch operation (ASO)] relies on successful coronary translocation. The arterial switch operation was performed using the techniques generally utilized for D-transposition of the great arteries with trapdoor flaps method for coronary implantation and the LeCompte maneuver for neopulmonary reconstruction. The LeCompte maneuver is generally performed if the vessels were in an anteroposterior relationship but not if the vessels were side by side.

In ccTGA, coronary anatomy other than the most frequently encountered 1LCx 2R (according to the Leiden classification) may be associated with incremental operative risk [61].

During DSO, the ventricular septal defect is usually closed through the morphological RV or through the aorta without concern of damaging the conduction system unlike transmitral approach.

Anatomical Rastelli Operation: Intraventricular Rerouting and RVOTR with RV-PA Conduit

Through a right ventriculotomy, a piece of 0.6-mm Gore-Tex patch is placed to direct the left ventricular flow through the ventricular septal defect into the aorta using multiple interrupted sutures inferiorly and posteriorly and continuous sutures around the aortic annulus. The right ventricle and pulmonary artery were established using a pulmonary homograft or other valved conduit (RV-PA conduit).

Previous study revealed that RV volume reduced approximately 20% after the Rastelli operation, because a part of the morphologic RV cavity is occupied by the intraventricular route. Thus, at least 120% of normal size seemed to be essential for better RV function after the anatomical repair [13, 38].

The degree of leftward rotation of the aorta and its relationship to the pulmonary artery dictate the position of the right ventriculo-pulmonary artery conduit. Placement of a conduit to the right side of the aorta results in compression of the conduit by the sternum, which may accelerate conduit dysfunction [62]. It can also result in compression of the right coronary artery by the conduit and myocardial

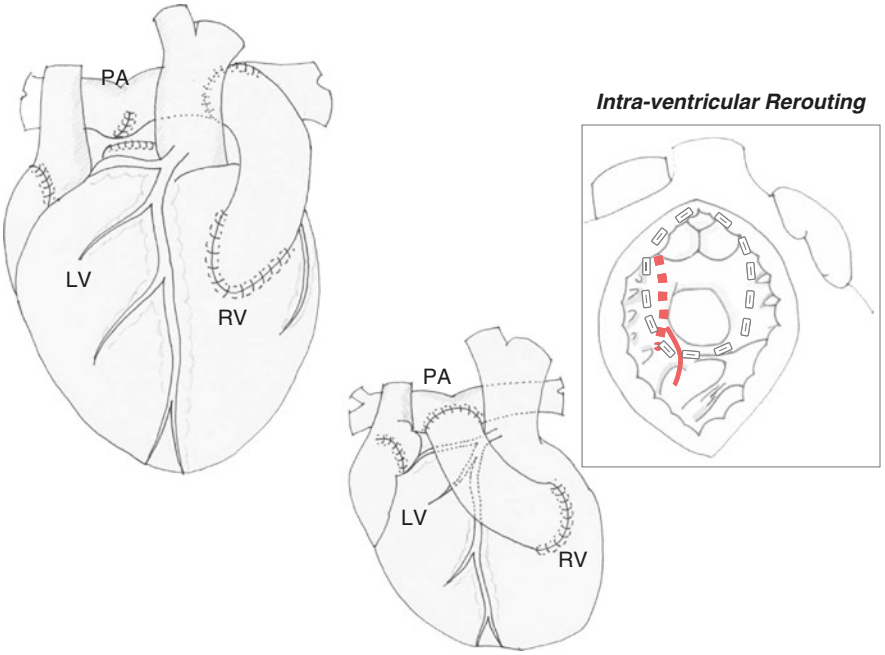

Fig. 11.8 Anatomical Rastelli operation: intraventricular rerouting and the RVOT reconstruction with the right ventricular to pulmonary artery conduit (RV-PA conduit)

ischemia. Therefore, it is ideal to place the conduit on the left side of the aorta whenever possible. Positioning of the conduit to the right of the aorta might be necessary in patients with an aorta to the extreme left (Fig. 11.8).

Additional DKS Anastomosis

Modification of Rastelli procedure for patients with pulmonary stenosis and restrictive VSD [13].

For patients with pulmonary atresia (PA), VSD size was theoretically large enough to create a nonobstructive intraventricular route. Nevertheless, for patients with pulmonary stenosis and restrictive VSD, it is required to create a nonobstructive systemic ventricular outflow tract usually by the VSD enlargement. Although the safe application of VSD enlargement needs the exact location of the conduction system, which may vary depending on the anatomical type. In this situation, additional DKS anastomosis without VSD enlargement has been demonstrated to be an effective approach to avoid postoperative systemic ventricular outflow tract obstruction and surgical heart block (Fig. 11.9).

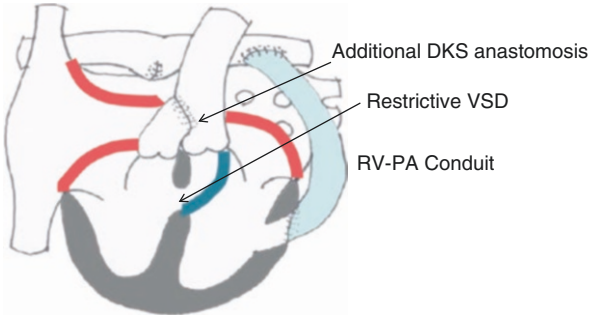

Fig. 11.9 Additional DKS anastomosis: modification of Rastelli procedure for patients with pulmonary stenosis and restrictive VSD

Aortic Root Translocation with Atrial Switch in ccTGA [63, 64]

The ccTGA with isolated pulmonary stenosis is contraindication to the anatomical repair. In some patients, the aortic root translocation (Nikaidoh operation) along with the Senning operation may be applied to achieve the anatomical repair.

The aortic root is harvested with the isolation of coronary bottom of both the right and left or left coronary artery. The harvested aortic root was turned 180, translocated posteriorly, and anastomosed to the original pulmonary root site. The detached coronary arteries were reimplanted in the aortic root. The VSD is closed using a 0.6-mm-thick expanded polytetrafluoroethylene (ePTFE) patch. The right ventricular outflow tract reconstruction was performed using extracardiac conduit.

11.5.4.5 Reparative Procedures and Indication for Late Complications for ccTGA

Indications for redo surgery in patients who have undergone the physiological repair include the initial or repeated TVR and the replacement of obstructive LV to PA conduit. As regards the anatomical repair, there is a definite incidence of late occurrence of various complications relating to each individual procedure in the anatomical repair. The indication of redo operation after the atrial switch includes the atrial baffle obstruction either systemic or pulmonary venous pathway. If the ventricular switch (Rastelli) is used, the left ventricular outflow obstruction due to the stenosis of VSD or intraventricular baffle obstruction, aortic regurgitation, or RV-PA conduit obstruction can be the reasons for reoperation. The indication of redo operation after the ASO as a part of the double switch may include coronary arterial obstruction or stenosis, aortic regurgitation, and pulmonary stenosis. Aortic valve regurgitation is seen more commonly in patients who underwent pulmonary artery banding before ASO as part of staged anatomical repair.

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Post Right Heart Bypass Operation

12

Hajime Ichikawa

Abstract

The evolutional invention in congenital heart surgery, Fontan procedure, provided the patients with single ventricle or physiological single ventricular patients to live without cyanosis. Decades after Fontan-type procedure, there are various and serious problems, which should be solved. In this chapter, the history of the right heart bypass operation and the common problems after the procedure are discussed.

Keywords

Fontan • Glenn • Bidirectional Glenn • TCPS • Total cavo-pulmonary connection • Protein-losing enteropathy • Plastic bronchitis • Heart transplantation • Left ventricular assist device • A-V malformation

12.1 Introduction

Right heart bypass operation is categorized into two types of operation, a Fontan-type operation and a Glenn-type operation. Glenn's operation is introduced firstly in 1958 by William Glenn. Following that, Fontan operation was introduced by Francis Fontan in 1971. These two right heart bypass operations could be described simply by saying that Glenn operation directs blood from SVC to the pulmonary artery and Fontan operation directs both SVC and IVC blood to the pulmonary artery without an aid of ventricle. These two right heart bypass operations play a role in improving the hypoxia in patient with various types of functional single ventricles (Table 12.1).

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Table 12.1 Various types of single ventricular physiology for the the candidate of Fontan type operation

Types of ventricle	
Mostly left ventricle	Tricuspid atresia, pulmonary atresia intact ventricular septum with hypoplastic RV, critical pulmonary stenosis with hypoplastic RV, neonatal severe form of Ebstein's anomaly, double inlet left ventricle
Mostly right ventricle	Hypoplastic left heart syndrome, mitral atresia, double outlet right ventricle with hypoplastic LV, unbalanced atrioventricular septal defect of RV type
Ambiguous	Heterotaxy syndrome

Recently, the Glenn operation plays a role as the inter-stage operation to succeed to the third and final stage, namely, Fontan operation to eliminate cyanosis. However, in some patients, because of the inadequate pulmonary vascular condition, they could not undergo Fontan-type procedure. Even with an ideal Fontan procedure, it is well known that various complications including arrhythmia, low cardiac output syndrome, liver dysfunction, and more occur several decades after Fontan-type operation. In this chapter, the various situations, the management, and the treatment strategies of the problems are described.

12.2 Right Heart Bypass Operation and the Long-Term Complication

12.2.1 Glenn and Other Similar Operation

William W.J. Glenn wrote the world's first report of a right heart bypass circulation in 1958 [1]. This original procedure is an end-to-side anastomosis of the transected right pulmonary artery to the lateral aspect of the SVC aiming to increase the effective pulmonary blood flow for the relief of cyanosis in patients with right to left shunt (Fig. 12.1). This concept was inherited by the procedure called "bidirectional Glenn procedure" or BCPS (Fig. 12.2), in which the transected SVC was anastomosed to the superior aspect of the right pulmonary artery [2, 3]. Since late 1980s, this procedure is considered to be a part of staged Fontan strategy to disperse the adverse event related to Fontan operation [4–6]. Nowadays, the word "Glenn procedure" exclusively means "bidirectional Glenn procedure" as the second stage to proceed to complete Fontan circulation. In this chapter, the explanation is solely dedicated to describe the bidirectional Glenn procedure in single ventricular physiology patients.

The amount of pulmonary flow in single ventricular patients before the Glenn operation is determined by the parallel circulation from the ventricle either through BT shunt, stenotic pulmonary trunk, or banded pulmonary artery(ies)* (trunk or bilateral banding). The pulmonary to systemic blood flow ratio (Qp/Qs) is usually more than 1.5; otherwise, it is difficult to maintain arterial blood oxygen saturation more than 70%. However, after the bidirectional Glenn procedure, Qp/Qs usually becomes anywhere between 0.5 and 0.8, if there is no additional pulmonary blood

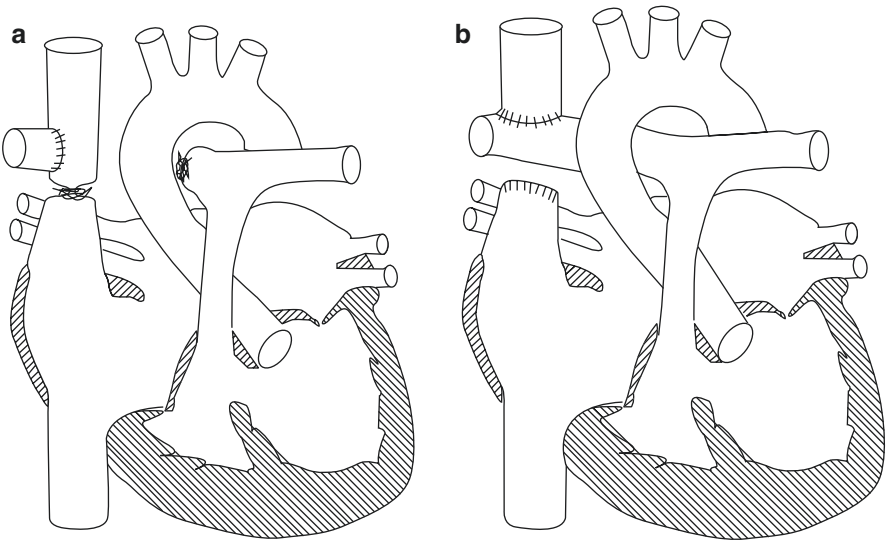

Fig. 12.1 (**a**) Original Glenn procedure described by William Glenn in 1958. (**b**) Bidirectional Glenn procedure as a second-stage palliation aiming total cavo-pulmonary connection

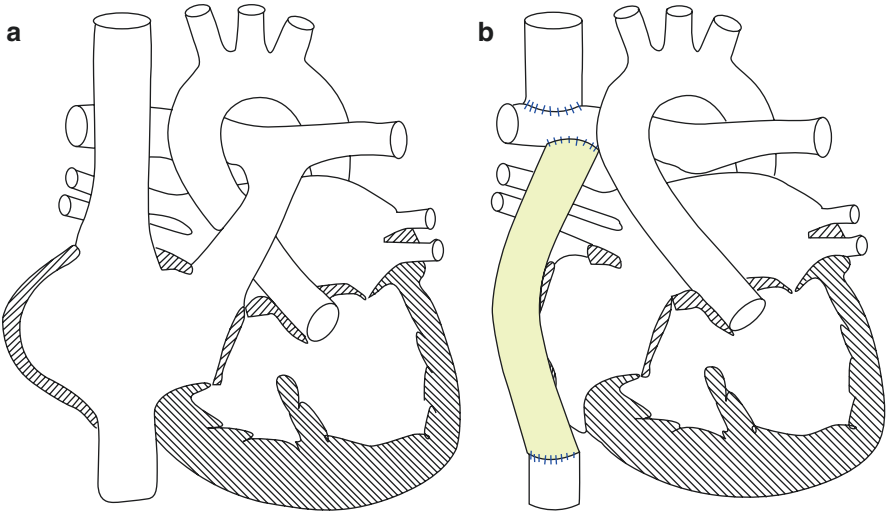

Fig. 12.2 (**a**) The figure shows classical atrio-pulmonary connection-type Fontan operation before the 1990s. The right atrium is chronically exposed to a high central venous pressure, which results in a dilated right atrium. An extremely dilated right atrium causes intra-atrial turbulent flow. (**b**) The figure shows the hemodynamic diagram of total cavo-pulmonary connection (TCPC). Atrial pressure overload is completely avoided by using ePTFE (expanded polytetrafluoroethylene) or other artificial graft for the connection between the inferior vena cava and the pulmonary artery

Table 12.2 Problems and palliative treatment for problems after Glenn procedure

Cyanosis polycythemia	Home oxygen therapy
High SVC pressure	Pulmonary vasodilator (sildenafil, tadalafil, bosentan, ambrisentan, macitentan, beraprost)
Systemic ventricular failure	Beta blocker therapy ACE inhibitor ARBs
AV valve dysfunction	Systemic atrioventricular valve repair/replacement
Development of pulmonary AV fistula	Medication/catheter ablation for atrial arrhythmia
Development of AP collaterals which leads to fatal hemoptysis is the possible complication	Coil embolization of unfavorable collaterals

flow (i.e., some surgeon prefer to leave BT shunt or tightly banded pulmonary trunk even after BDG). The sudden reduction in the preload to the single ventricle leads to a reduction in the end-diastolic ventricular volume, which usually causes a diastolic dysfunction. The patients usually tolerate this situation because the cardiac output is maintained by the stable blood supply from IVC to systemic single ventricle, whereas severe low cardiac output occurs if this is a Fontan circulation. This is the main reason why the staged strategy to Fontan circulation is preferred by most of the surgeons.

In case the patient could not undergo the completion of Fontan circulation and remains with Glenn circulation, there will be serious complications in the long-term follow-up period. Cyanosis, polycythemia, high SVC pressure, systemic ventricular failure, AV valve dysfunction, development of pulmonary AV fistula, and development of AP collaterals which leads to fatal hemoptysis are the possible complications [7, 8]. Palliative treatments for these circumstances include home oxygen therapy, pulmonary vasodilator (sildenafil, tadalafil, bosentan, ambrisentan, macitentan, beraprost), beta blocker therapy, ACE inhibitor, ARBs, systemic atrioventricular valve repair/replacement, medication/catheter ablation for atrial arrhythmia, and coil embolization of unfavorable collaterals (Table 12.2). There is a certain kind of patient group whose pulmonary blood flow is coincidentally optimal by a native pulmonary stenosis or pulmonary arterial banding who survives with acceptable quality of life [9]. However, most patients who could not reach Fontan completion, the possible solution for this situation is to have a new heart transplanted.

12.2.2 Fontan Operation

To understand the problems of adults with Fontan circulation, it is necessary to know how the modification of this procedure was developed to improve the outcome. The original Fontan operation [10] was a combination of SVC to right PA anastomosis, creation of right atrial appendage to left PA connection with pulmonary valve

homograft, and ASD closure. Shortly, the procedure was simplified as to anastomose the right atrial appendage to the pulmonary trunk and close the ASD. This type of operation is called APC (atrio-pulmonary connection) and became the standard procedure in 1970s–1980s. As the outcome being stable in patients with tricuspid atresia in which the systemic ventricle is almost normal left ventricle, the indication was extended to other single ventricular physiology patients including heterotaxia and hypoplastic left heart syndrome [11]. The classic ten commandments for Fontan procedure [12] no more exist. Fontan procedure is performed at younger age of life such as between 1 and 2 years old. In the late 1980s, de Leval et al. [13] reported the better hemodynamics with total cavo-pulmonary connection (TCPC). The main concept of this theory is that the atrial contraction between the cavae and pulmonary arteries is not necessary but is even worse. This theory was proved using flow dynamic technology and also proved recently using computer fluid dynamics (CFD) [14] method. TCPC became a standard method as a goal of the treatment of single ventricle. Aortic cross clamping was necessary to place an intra-atrial baffle with this procedure. However, after Marcelletti et al. [15] reported the less invasive method by connecting the IVC to pulmonary artery with extra-cardiac conduit, this type of procedure is the most employed in the world. As the outcome is improved, the indication for TCPC was extended to more marginal cases such as patients with poor ventricular function and high pulmonary vascular resistance, so that the incidence of late complication tends to increase. In the 1990s, the classic Fontan patients (with APC or similar procedures) were recommended to undergo "TCPC conversion" [16] because of their deteriorating hemodynamics with a dilated atrio-pulmonary connection. The dilated right atrium causes a turbulent flow in the atrium, and energy loss is prominent with the dilated Fontan pathway (Fig. 12.3a, b).

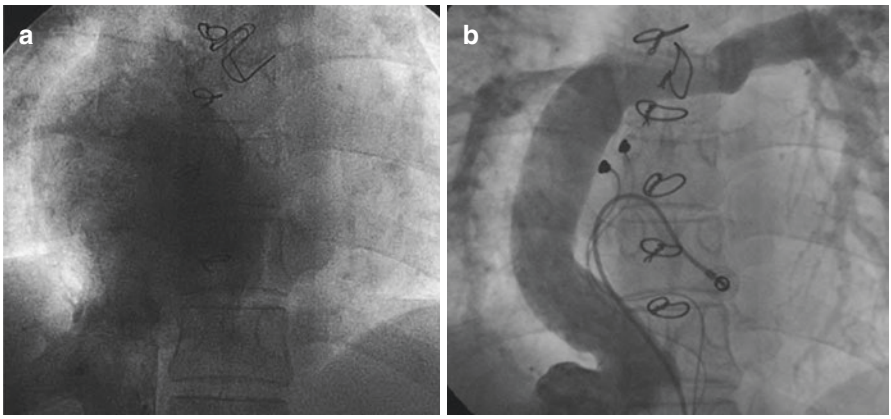

Fig. 12.3 (**a**) Extremely dilated right atrium of atrio-pulmonary connection (APC)-type Fontan operation. (**b**) After conversion from APC Fontan to TCPC

12.3 Problems Associated with Post Right Heart Bypass

Various adverse events occur after Fontan operation, either of which can lead to a life-threatening event acutely and chronically. Those are mainly caused by high central venous pressure and low cardiac output, which are the cause of arrhythmia, liver dysfunction, protein-losing enteropathy, and plastic bronchitis. They are described in the following section.

12.3.1 Arrhythmias

Arrhythmia is the most frequent adverse event both early and late after Fontan procedure. The incidence is less in patients with TCPC and extra-cardiac TCPC than in conventional Fontan with atrio-pulmonary connection, because the origin of the arrhythmia is mostly the damaged atrial wall, which is chronically dilated by the high central venous pressure of circulation.

12.3.1.1 Diagnosis

If the patient complains palpitation, it can be atrial premature beats, paroxysmal supraventricular tachycardia, or atrial fibrillation. The incidence of ventricular arrhythmia is less frequent than that of atrial origin. In any case, 24-h ECG monitoring is essential as an initial diagnosis. This should be done in the regular outpatient clinic. Further precise diagnosis to locate the origin of the arrhythmia can be done by catheter mapping [17, 18].

12.3.1.2 Treatment

If there is no hemodynamic problem in the Fontan circulation, the first choice of the treatment is pharmacological therapy with beta blocker, amiodarone, and other anti-arrhythmic agents. If the type of the Fontan circulation is a classical atrio-pulmonary connection, catheter ablation of the reentrant circuit on the damaged atrial wall is recommended for the drug-resistant atrial tachyarrhythmia. However, in patients with TCPC, especially extra-cardiac TCPC, catheter ablation is impossible because there is no transvenous access to the atrial wall. However, the incidence of atrial arrhythmia is less in extra-cardiac TCPC since the atrial wall is not exposed to high venous pressure.

12.3.2 Low Output Syndrome

12.3.2.1 Diagnosis

The cardiac output of the patients with Fontan is basically lower than that of normal circulation, although patients with “perfect Fontan” [19, 20] can perform moderate exercise. The exercise tolerance is much less than normal population. As the patients behave as they used to, it is difficult to judge their hemodynamic status from their complaint unless they show apparent signs of heart failure. Therefore, it is strongly

recommended to measure anaerobic threshold and maximum oxygen uptake regularly using proper methods [21–23]. Low cardiac output syndrome is the main cause of other associated adverse events including organ failure.

12.3.2.2 Treatment

In case of APC patients with dilated atrio-pulmonary connection pathway, TCPC conversion is recommended. If there is a residual lesion such as pulmonary arterial stenosis, pulmonary venous stenosis, atrioventricular valve regurgitation, aortic insufficiency, or other structural lesions, catheter or surgical intervention to each lesion should be considered before irreversible organ dysfunction develops. It is sometimes difficult to point out the obstructive Fontan pathway by the pressure measurement alone, when the cardiac output is very low. Multidisciplinary diagnostic approach to decide the indication for the catheter/surgical intervention is mandatory.

12.3.3 Liver Dysfunction

12.3.3.1 Diagnosis

Chronically elevated central venous pressure of Fontan circulation causes liver congestion for many years which results in liver fibrosis. Finally, irreversible and uncompensated liver dysfunction, namely, "liver cirrhosis," occurs. Rychik et al. [24] summarized the mechanism, diagnosis, and treatment of liver dysfunction late after Fontan operation. In the early stage of liver dysfunction, the elevation of serum gamma glutamyl transpeptidase is usually the first sign, followed by a slight to moderate elevation of serum direct bilirubin. In the next stage, serum hyaluronic acid level increases, which indicates the sinusoidal endothelial cell dysfunction. Thrombocytopenia gradually occurs during the course of this liver dysfunction. In the final stage of liver dysfunction, serum type IV collagen increases, which indicates the liver fibrosis. There are attempts to predict the extent of liver fibrosis by using a combination of several biomarkers [25, 26]. These biomarkers are useful to detect the early occurrence of liver dysfunction in the patients with Fontan circulation (Table 12.3). However, it is still controversial whether these biomarkers can predict the degree of the liver dysfunction [25]. The liver biopsy is still a gold standard of the diagnosis of liver cirrhosis. Many physicians are reluctant to perform liver biopsy in Fontan patients, because it only tells the exact degree of liver dysfunction but does not change the treatment strategy. Attempts are made to quantify

Table 12.3 Biomarkers to detect early liver dysfunction

Biomarkers to detect early liver dysfunction
α2-Macroglobulin, haptoglobin, apolipoprotein A1, γ-glutamyltransferase (GGT), total bilirubin (TB), hematocrit, platelet count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), creatinine (Cr), albumin (Alb), hemoglobin A1c, C-reactive protein

the degree of liver congestion and fibrosis by using noninvasive imaging modalities like echo [27], CT [28], and MRI [29].

12.3.3.2 Treatment

The only way to improve or to prevent the progression of liver failure is to improve the hemodynamics of Fontan circulation, namely, to decrease the central venous pressure and increase the cardiac output. Palliative therapies with oral medications such as glycyrrhizic acid, ursodeoxycholic acid, or Far-Eastern traditional herbal formulation (sho-sai-ko-to or xiao-chai-hu-tang) [30] show partially effective but are not a definitive solution with any evidence. Heart-only transplantation or heart-liver transplantation can theoretically be the only solution. However, heart-liver transplantation is a rare event (1% of multiple-organ transplants performed [31]). It is still controversial how to decide whether heart-only or heart-liver transplantation is indicated for failing Fontan patient with significantly impaired liver function. Each case should be discussed carefully case by case.

Greenway et al. [32] suggest that patients with evidence of cirrhosis who have normal synthetic liver function, normal hepatic venous anatomy, a liver volume of >800 ml, and evidence of only mild portal hypertension and no HCC (Hepatocellular carcinoma) are considered suitable for heart-only transplantation. Patients with further advanced liver failure should be considered as a candidate for heart-liver transplantation.

12.3.4 Protein-Losing Enteropathy

12.3.4.1 Etiology and Diagnosis

Protein-losing enteropathy is a condition where the severe loss of serum proteins into the intestine occurs. Mechanisms for this condition after Fontan operation are due to lymphatic obstruction caused by elevated CVP in Fontan circulation.

Chronic decrease in serum albumin, ascites accumulation, and edema is the sign of protein-losing enteropathy. Albumin scintigraphy [33] has been used to confirm the diagnosis by showing the existence of leaking protein into the intestine.

12.3.4.2 Treatment

There are many attempts to treat this unfavorable situation. Possible medical therapies are steroid therapy [34, 35], heparin administration [36], and various types of pulmonary vasodilators. For the purpose to decrease the CVP, catheter intervention including pulmonary arterial plasty or stent placement and a creation of fenestration [37] were reported to be effective. Of course all the identifiable abnormalities should be treated. However, PLE occurs in those who have no compromised Fontan circulation. For those patients, heart transplantation is the only solution for this fatal situation. The latest multicenter retrospective analysis showed that PLE was cured in 77.7% of hospital survivors with the 5-year survival of only 46.3%, which is far less that without PLE [38].

12.3.5 Plastic Bronchitis

12.3.5.1 Diagnosis

Plastic bronchitis is a condition in which large, bronchial casts with rubber-like consistency develop in the tracheobronchial tree and cause airway obstruction. The patient expectorates treelike cast. Even without expectoration of the cast, plastic bronchitis should be suspected in case of chronic wheezing and dyspnea in patients after Fontan procedure. The cause was thought to be a maldevelopment or malfunctioning lymphatic systems in the lung. The mortality rate with cardiac disease is reported to be 29% [39]. New survey using Facebook [40] revealed that 46 out of 671 patients after Fontan procedure reported to have plastic bronchitis. Median plastic bronchitis diagnosis was 2 years post-Fontan. Hospitalization for plastic bronchitis occurred in 91% with 61% hospitalized ≥3 times. Perioperative chylothorax occurred more frequently in the patient with plastic bronchitis than without.

12.3.5.2 Treatment

It is still controversial how to deal with plastic bronchitis. If there is any identifiable hemodynamical problem related to the Fontan circulation, it could be solved before considering heart transplantation. Trials to resolve this condition were reported, including steroid therapy [41], tissue plasmin activator [42, 43], pacemaker implantation [44], and fenestration of the atrial baffle [45]. However, there is still no consistently effective treatment for this condition. The only definitive treatment seemed to be a heart transplantation [46].

12.3.6 Autonomic Functional Disorder

Patients after Fontan operation often have indefinite complains possibly due to autonomic functional disorder. Symptoms include migraine, muscle tension headache, anxiety with palpitation even with normal sinus rhythm, orthostatic hypotension, and more. Although these problems are not fatal, they could definitely decline the patient's quality of life. There is only few evidence relating to this problem [47]. Further investigation in this field is demanding.

12.4 Catheter Intervention

If there is any obstruction or stenosis along the systemic veins to the pulmonary artery and/or branch pulmonary arteries, percutaneous balloon angioplasty with or without stent placement should be considered. Since the blood flow through the Fontan pathway is relatively slow to its diameter, one should bear it in mind that no pressure gradient does not necessarily means no obstruction. CT and MRI evaluation should be essential to evaluate the problems along the Fontan pathway.

12.4.1 Angioplasty

Angioplasty is recommended in any circumstance where there is an obstructive lesion along the Fontan circuit. Even a single-digit pressure gradient in the venous systems can cause severe energy loss in the Fontan circuit. Once liver dysfunction or PLE occurs because of the obstructive Fontan circuit, these problems often persist even after a successful angioplasty. Therefore, the catheter or surgical angioplasty should be considered in the early stage of the problems.

12.4.2 Coil Embolization

12.4.2.1 Systemic to Pulmonary Collaterals

Systemic to pulmonary collateral (SP collateral) is thought to be a risk factor [7, 8, 48] at the time of Fontan procedure. Coil embolization of SP collaterals before the Fontan operation is a standard practice in almost every institution. In spite of that, patients with Fontan circulation often develop SP collaterals many years after the Fontan procedure. When the patient has significant residual cyanosis because of the large fenestration or development of veno-venous collaterals, the development of SP collaterals is accelerated by the cyanosis-induced vascular endothelial growth factor. To eliminate the deleterious effects such as hemoptysis, ventricular volume overload, and elevation of central venous pressure, coil embolization of SP collaterals should be considered even decades after Fontan operation.

12.4.2.2 Veno-Venous Collaterals

The development of veno-venous collaterals (VV collateral) is a consequence of the chronic exposure of the venous system to a high pressure. This will cause cyanosis and followed by exercise intolerance. Favorite site of VV collateral is from the SVC or innominate vein to pulmonary veins (Fig. 12.4a, b). When the central pressure is not extremely high, catheter embolization of VV collateral improves the quality of life by resolving cyanosis. However, if the development of VV collateral is mostly due to the high venous pressure, VV collateral of other pathway will come back soon after the embolization. Further, since the embolization of VV collateral elevates the central venous pressure, it is reported that the embolization of VV collateral is associated with decreased survival [49]. There is no absolute solution for this situation.

12.4.2.3 Pulmonary AV Fistula

Pulmonary arteriovenous collateral develops with a high incidence in patients with left isomerism with interrupted IVC and azygos of hemiazygos connection. When these patients undergo bidirectional Glenn procedure, this circulation is specially called as “total cavo-pulmonary shunt (TCPS)” because all the venous blood except the hepatic venous blood flows into pulmonary circulation.

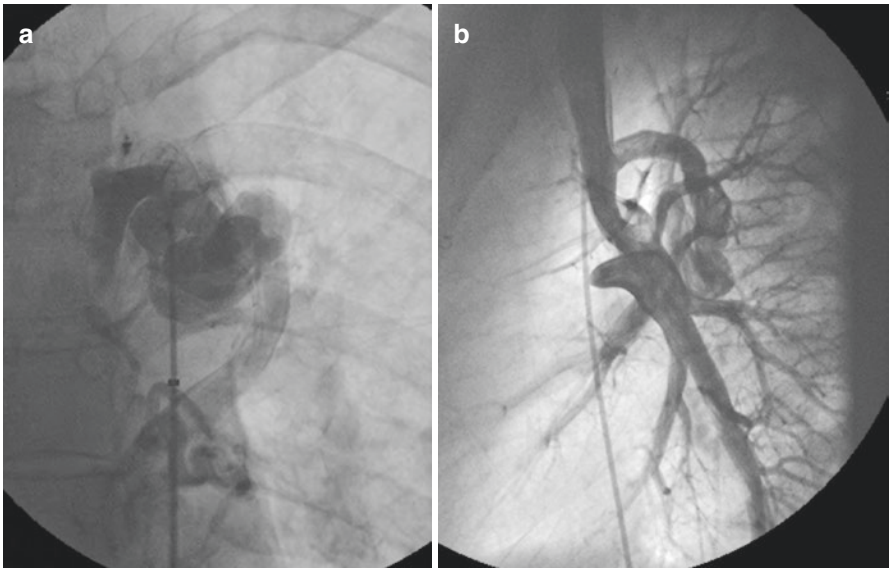

Fig. 12.4 (**a**) Veno-venous collateral (VV collateral) vessels were developed between innominate vein and pulmonary vein late after Fontan operation. (**b**) VV collaterals between superior vena cava to pulmonary vein

12.5 Surgical Intervention

12.5.1 Conversion to Total Cavo-Pulmonary Connection

There is a natural progression of pulmonary arterial pressure during the human lifetime. As the Fontan patients survive into 30s of age or more, the patients after atrio-pulmonary connection-type Fontan procedure show the dilation of the right atrial pathway by the elevated CVP. Inside the dilated atrium, blood flow from the atrium to the pulmonary arteries shows turbulence, which result in an ineffective movement of the blood. In this situation, cardiac output decreases to a critical level. Further, the dilated and impaired atrial wall is likely to cause atrial arrhythmias of various types. These two major complications lead the patients to reduced functional status and major adverse events. To rectify this situation, conversion of atrio-pulmonary connection to total cavo-pulmonary connection combined with arrhythmia surgery was started by Mavroudis et al. [16]. In their 20 years of series with TCPC conversion [50], 5 and 10 years survival were 90% and 84%, respectively.

12.5.2 Arrhythmia Surgery

Surgical treatment of post-Fontan arrhythmia is always associated with the TCPC conversion [50]. In the early phase of atrial arrhythmia, modified right-sided maze procedure is applied to eliminate right atrial macro-reentrant tachycardia, whereas left macro-reentrant tachycardia or atrial fibrillation can be treated with an additional left atrial Cox maze III [51].

12.5.3 Atrioventricular Valve Repair/Replacement

In patients with Fontan circulation, atrioventricular valve regurgitation leads to a fatal consequence because the elevated systemic atrial pressure causes the elevation in total pulmonary vascular resistance, hence elevated central venous pressure and low cardiac output. Atrioventricular valve regurgitation is known to be a significant risk factor of both Fontan completion and its long-term survival [52]. In the young generation or still growing adolescence, atrioventricular valve repair is preferable [53]. There are several techniques described particularly to repair the anatomically atypical common atrioventricular valves of Fontan patients [53–56] including bivalvation according to the Alfieri's technique [57]. However, because these unbalanced and immature valves are often difficult to repair, valve replacement with mechanical valve in adult Fontan population is not a bad option [58].

12.6 Heart Transplantation/Ventricular Assist Device

12.6.1 Heart Transplantation

12.6.1.1 Heart Transplantation for Situs Solitus

Among the pediatric heart transplantation population, a prior Fontan procedure is proved to be a major risk factor [59]. Because of the difficulty in placing the patients with Fontan circulation on left ventricular assist device, the wait-list mortality is higher than that of cardiomyopathy patients. Posttransplant outcome is also compromised, because they are usually sensitized before heart transplantation. Although the outcomes of heart transplantation for failed Fontan patients has been poorer than the patients with cardiomyopathy, the data from International Society for Heart and Lung Transplantation shows that it is getting better in the recent year. Early indication for transplantation for failed Fontan might improve their outcome.

12.6.1.2 Heart Transplantation for Visceral Situs Anomaly

Since the single ventricular patients frequently have visceral situs abnormality, orthotopic heart transplantation with normal heart is sometimes complicated by the location of the recipient's great vessels. To overcome these problems, many different methods [60] to accommodate the normal donor heart to the recipient of various anatomy were reported.

12.6.2 Ventricular Assist Device for Bridge to Transplantation

Because of the shortage of the donors, the use of left ventricular assist device (LVAD) as a bridge to transplantation is an essential strategy to wait for a heart transplantation safely in a good condition. However, a question was raised whether the LVAD is as useful in a single ventricular physiology as in a biventricular physiology. Theoretically, the use of left ventricular assist device is useful to support the patients with single ventricle either after Norwood procedure, bidirectional Glenn procedure, or total cavo-pulmonary connection [61–63]. Although multicenter registry to focus on this problem was done in 2013 [64], the number is still too small to achieve a consensus.

According to the retrospective analysis of 26 patients who had the Berlin Heart Excor implanted [65], the outcome after mechanical circulatory support with Berlin Heart Excor was better in patients after BDG than in those after TCPC.

12.7 Pregnancy in Patients with Right Heart Bypass

Patients after Fontan operation in childbearing age are increasing. Since the first successful report of successful pregnancy after Fontan operation, there are pros and cons of pregnancy in patients with Fontan circulation. As a nature of this circulation, the hemodynamic burden of pregnancy definitely deteriorates the hemodynamics, the chance of thromboembolism increases with pregnancy, and the incidence of miscarriage is reported 27–50% [66]. Although the pregnancy outcome is not ideal, it is possible to complete pregnancy with Fontan circulation by meticulous care [67] in preselected women [66].

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Aortopathy Including Hereditary Disease (Marfan Syndrome, Bicuspid Aortic Valve, etc.)

13

Kozo Matsuo and Koichiro Niwa

Abstract

Marfan syndrome, bicuspid aortic valve, and/or coarctation of the aorta are consistently associated with ascending aortic or para-coarctation medial abnormalities. Medial abnormalities in ascending aorta were prevalent in other type of patients with a variety form of congenital heart disease such as single ventricle, persistent truncus arteriosus, transposition of the great arteries, hypoplastic left heart syndrome, and tetralogy of Fallot, encompassing a wide age range, and may predispose to dilatation, aneurysm, and rapture necessitating aortic valve and root surgery. These congenital heart diseases exhibit ongoing dilatation of the aortic root and reduced aortic elasticity and increased aortic stiffness that may relate to intrinsic properties of the aortic root. These aortic dilatations and increased stiffness can induce aortic aneurysm, rapture of the aorta, and aortic regurgitation but also provoke left ventricular hypertrophy, reduced coronary artery flow, and left ventricular failure. Therefore, this association of aortic pathophysiological abnormality, aortic dilation and aorto-left ventricular interaction is called as a new clinical entity: "aortopathy".

Aortic dilation is frequently observed in congenital heart diseases (CHD). Aortic dilation predisposes to aortic annular enlargement and then severe aortic regurgitation (AR). Concomitant aortic valve replacement or plasty with replacement of the aortic root and the diseased ascending aorta will be required in those patients (aortic root replacement). The Bentall operation is an aortic root

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replacement with a composite tube graft that contains a mechanical valve in it. Valve-sparing root replacement, i.e., remodeling and reimplantation procedure, has been developed for the patients whose aortic valves are feasible to be preserved. The ascending aorta and Valsalva sinuses are replaced with a trimmed tube graft in remodeling procedure; on the other hand, the aortic root is included in the tube graft in reimplantation. In contrast, the pulmonary autograft is used to replace the aortic root and aortic valve in the Ross procedure. Enucleated RV outflow tract and the main pulmonary artery are reconstructed usually with homograft or other valved conduit. Some controversy has been provoked to indicate the Ross procedure and expanded application of valve-sparing root replacement.

Keywords
Aortic dilation • Aortic root replacement • Bentall operation • Valve-sparing operation • Ross procedure

13.1 Medical View

13.1.1 Introduction

Aortic dilation in Marfan syndrome, Turner syndrome, bicuspid aortic valve, and coarctation of the aorta is well recognized, and these disorders are consistently associated with ascending aortic and/or para-coarctation medial abnormalities [1–3]. Congenital heart disease such as single ventricle, persistent truncus arteriosus, transposition of the great arteries, hypoplastic left heart syndrome, and tetralogy of Fallot is also associated with aortic medial abnormalities, aortic dilatation, and aortic regurgitation [1]. Aortic medial abnormalities—so-called cystic medial necrosis—reach their severest form in Marfan syndrome and annuloaortic ectasia and are prevalent and qualitatively similar but seldom quantitatively as marked in a wide variety of congenital heart diseases with a wide age range [1]. This aortic medial abnormality possibly reflects a common developmental fault that weakens and attenuates the aortic wall. These congenital heart diseases with aortic dilatation are often associated with decreased elasticity and increased stiffness of the aorta [4–6]. These aortic pathophysiological changes are negatively influencing on the systemic ventricular function due to increased afterload and ventricular hypertrophy [5].

13.1.2 Historical Perspective

In 1928, Maude Abbott [7], mentioned in her textbook of congenital heart disease, the presence of a bicuspid aortic valve appears to indicate, at least in a portion of the cases in which it occurs, a tendency for spontaneous rapture." In 1972, McKusick [3] reported that the association of bicuspid aortic valve and cystic medial necrosis is more than coincidence and cystic medial necrosis was defined as follows [8]: (1) noninflammatory smooth muscle cell loss, (2) fragmentation of elastic fibers, and (3) accumulation of basophilic ground substance within cell-depleted areas of the

medial layer of the vessel wall. Edwards et al. [9] reported that among 119 necropsy specimens with aortic dissection, 11 were from bicuspid aortic valve (9%). Roberts and Roberts [2] also reported that among 186 necropsy specimens with aortic dissection, 14 were from bicuspid aortic valve (7.5%) with a mean age of 52 and severe degeneration of the elastic fiber was found in the aortic wall in 90% of them. High incidence of bicuspid aortic valve among patients with aortic dissection is suggesting a causative relationship between bicuspid aortic valve and aortic dissecting aneurysm. Hahn et al. [10] and Nistri et al. [11] reported that there is a high prevalence of aortic root enlargement in bicuspid aortic valve that occurs irrespective of altered hemodynamics, suggesting bicuspid aortic valve and aortic root dilatation may reflect a common developmental defect. It has been recognized that patients with aortic valve disease have a tendency to dilate aortic root followed by dissection and those harbor cystic medial necrosis in the aortic media. Bicuspid aortic valve was the first non-syndromic congenital heart disease in which aortic dissection and dilation were reported [12]. In 2001, Niwa et al. reported that aortic medial abnormalities—so-called cystic medial necrosis—are prevalent in a wide variety of congenital heart diseases with dilated aortic root [1]. After that, progressive aortic dilatation and regurgitation in various types of congenital heart disease regardless of intracardiac repair have been continuously reported [13–28].

13.1.3 Congenital Heart Diseases Associated with Aortic Dilatation (Table 13.1)

13.1.3.1 Bicuspid Aortic Valve and Ross Procedure

Aortic dissection is found to be nine times more prevalent in bicuspid aortic valve patients than in those with tricuspid valve [29]. Aortic dilation begins during childhood in bicuspid aortic valve patients, regardless of the presence of aortic stenosis [30]. Histologic abnormalities in the ascending aorta in bicuspid aortic valve patients are similar to those found in Marfan patients [3].

From recent report of Ross procedure [13], in 118 patients with Ross procedure with mean age of 34 years and 44 months follow-up (bicuspid aortic valve in 81%), diameter of the sinuses of Valsalva increased from 31 ± 0.4 to 33 ± 0.5 mm. In 13/118 (11%), the diameter ranged from 40 to 51 mm, and 7/118 (6%) developed

Table 13.1 Congenital heart diseases associated with aortic dilatation in adults

Marfan syndrome
Turner syndrome
Bicuspid aortic valve
Coarctation of the aorta
Tetralogy of Fallot
Single ventricle with pulmonary atresia or stenosis
Persistent truncus arteriosus
Transposition of the great arteries
Hypoplastic left heart syndrome
Fontan procedure

moderate aortic regurgitation, and 3 (3%) required aortic valve replacement. The predicted probability of no or trivial aortic regurgitation decreased from 63% in the early postoperative period to 24% after 16 years. The most common cause for the failure of Ross is pulmonary autograft dilation [15]. Dilation of the pulmonary autograft after the Ross occurs because of an intrinsic abnormality of the pulmonary root in patients with congenital aortic valve disease.

13.1.3.2 Coarctation of the Aorta

Isner et al. [16] examined by light microscopic features of coarctation segment in 33 patients with the age of 1 day to 15 years and found cystic medial necrosis, deletion and disarray of elastic tissue, was observed in all 33 specimens. Remarkable finding observed is this pathological abnormality is found as early as in neonate, and it suggests cystic medial necrosis in the aortic wall in coarctation of the aorta is possibly intrinsic.

13.1.3.3 Tetralogy of Fallot

Among the cyanotic congenital heart disease, tetralogy of Fallot was the first in which aortic dilation was recognized [17, 18]. Aortic dilatation is a well-known feature of unrepaired tetralogy of Fallot and correlates well with severity of right ventricular outflow tract stenosis and is greatest in tetralogy of Fallot and pulmonary atresia. Aortic regurgitation in unrepaired tetralogy of Fallot imposes volume overload on both ventricles [19]. A significant subset of adults late after repair of tetralogy of Fallot exhibits progressive aortic root dilatation that may lead to aortic regurgitation and predispose to dissection and rapture. The aortic dilatation relates medial abnormalities coupled with previous long-standing volume overload of the ascending aorta (right to left shunting through malalignment-type ventricular septal defect). This dilatation and histological abnormalities have been found from as early as infants [20]. Fifteen percent of repaired tetralogy of Fallot in adults had a dilated aortic root [21]. Different from the Marfan syndrome, aortic aneurysm and dissection/rapture were, rarely as low as six cases, reported in tetralogy of Fallot [21]. This is possibly because histological abnormality in the aorta in tetralogy of Fallot is less severe than those of Marfan syndrome [1].

13.1.3.4 Complete Transposition of the Great Artery with Arterial Switch Operation

Aortic dilation and aortic regurgitation are well-known complications after arterial switch operation in complete transposition of the great artery [20, 21]. Freedom from aortic regurgitation and aortic valve replacement was 69% and 97% at 15 years, respectively [22]. Neo-aortic valve regurgitation was severe in 3.7% and trivial to mild in 81% at midterm follow-up [23]. Cystic medial necrosis is observed in both neo-aorta and pulmonary artery in neonate; therefore, histological aortic abnormality in transposition of the great arteries is one of the causes of this aortic dilatation [24]. Progressive dilation of the neo-aortic root becomes out of proportion to somatic growth, and the incidence of aortic regurgitation increases with age.

Previous pulmonary artery banding, older age at repair, and presence of ventricular septal defect are the risk factors for aortic regurgitation [25].

13.1.3.5 Hypoplastic Left Heart Syndrome

Neo-aortic root dilation and aortic regurgitation after staged reconstruction for hypoplastic left heart syndrome are known complications, and these complications progress over time. Cohen et al. [26] followed 53 patients with hypoplastic left heart syndrome after Fontan procedure for 9 years and found neo-aortic root progressively dilated out of proportion to body size, with 98% having a Z-score > 2 at most recent follow-up. Neo-aortic regurgitation was present in 61%. Therefore, difference of arterial histology may be one of the causes of this regurgitation.

13.1.3.6 Other Congenital Heart Diseases

Dilated aortic root is found in the majority of operated truncus arteriosus patients; however, none has dissection or rapture [27]. In this disorder, anatomical truncal valve abnormality and truncal valve regurgitation are common; therefore, the role of dilatation of the aorta on truncal valve regurgitation is unclear. Aortic dissection after congenital heart disease is found in patients with Fontan [28], but the incidence of aortic dissection in congenital heart disease other than bicuspid aortic valve and coarctation of the aorta is extremely rare that are very much different from Marfan and related genetic disorders.

13.1.4 Pathophysiology and Cause of Aortic Dilatation

13.1.4.1 Histopathological Abnormalities in Various Congenital Heart Diseases

Niwa et al. [1] reported that in 88 congenital heart disease patients with dilated aorta with age of 3 weeks to 81 years (32 ± 6 years) (48 males, 40 females), surgical biopsy aortic specimens were obtained, and cystic medial necrosis in the aortic media was observed in all of these patients.

13.1.4.2 Cause of Aortic Dilatation in Congenital Heart Disease (Table 13.1) and Histology of the Aortic Media

Independent variables that alter the structure of ascending aortic media include Marfan syndrome, annuloaortic ectasia or Turner syndrome, systemic hypertension [31], aging [32], pregnancy [33], and others (Table 13.2). Marfan syndrome is characterized by a defect in the chromosome 15 gene that codes for fibrillin-1 [34], in the absence of which elastin is more readily degraded by metalloproteinase [35]. Deletion of TGF-β receptor has a relation with aortic dilatation [36]. The genetic fault in Marfan syndrome apparently impairs aortic medial elastic fibers more extensively than impairment in congenital heart disease, and the incidence of ascending aortic dilatation, dissection, or rapture is higher, and the degree of aortic root medial lesions is greater in former than the latter.

Table 13.2 Variables alter structure of ascending aortic media

1. Systemic hypertension
2. Aging
3. Pregnancy
4. Chromosome abnormality: Marfan syndrome, Turner syndrome, Noonan syndrome
5. Gene abnormality: fibrillin-1 defect (15q21.1)
6. Deletion of TGF-β receptor, ALK5 signaling in neural crest cell
7. Metalloproteinase and elastin
8. Hemodynamic abnormality (increased aortic flow)
9. Intrinsic abnormality of aortic wall in congenital heart diseases

13.1.4.3 Cause of Aortic Dilatation in Tetralogy of Fallot

Higher histologic grading scores in tetralogy of Fallot patients are found even in infants, which suggests the intrinsic abnormality has crucial role for this dilatation [20]. Evidence for the role of aortic overflow over time in tetralogy of Fallot includes the associations of higher age at operation, pulmonary atresia versus pulmonary stenosis, and longer presence of surgical aortopulmonary shunting with aortic dilation [37, 38]. There is a 12% increase in mean aortic diameter after surgical aortopulmonary shunting [38].

13.1.4.4 Genetics in Aortic Dilatation in Congenital Heart Disease

Comparing patients with A-P phenotype (R-L cusp fusion) bicuspid aortic valve with R-L phenotype (R-N cusp fusion), the former is more common in male and is larger and stiffer at the sinus of Valsalva and smaller at ascending aorta and aortic arch than the latter [39, 40]. This aortic shape difference is possibly due to inborn errors of aortic wall than due to hemodynamic effect [41]. Therefore, bicuspid aortic valve phenotype can predict elastic properties of ascending aorta and have potential impact on clinical outcomes.

50.9% prevalence of fibrillin-1 gene polymorphisms or mutations is found in tetralogy of Fallot patients with dilated aorta, and there is >8 times risk of aortic dilation in patients with these variants [42]. In patients with chromosome 22q11.2 partial deletion without conotruncal abnormality, aortic dilation is found in 10/93 (10.8%) [43], and chromosome 22q11.2 partial deletion is one of the risk factors of aortic dilatation [37].

13.1.5 Aortic Root Dilation and Aortic Elastic Properties

Chong et al. [6] found that in 67 children with 8.3 years after tetralogy of Fallot repair, aortic dilation (Z-score > 2) was observed in 61–88% of them, and significantly increased stiffness, reduced strain, and distensibility of the aorta are observed in aortic dilators. Senzaki et al. [5] reported that in 38 repaired tetralogy of Fallot patients comparing with 55 controls, the former had higher characteristic of

impedance and pulse wave velocity, lower total peripheral arterial compliance, and higher arterial wave reflection and also observed that the increase in aortic wall stiffness was closely associated with the increase in aortic root diameter. Therefore, central and peripheral arterial wall stiffness is characteristically increased after tetralogy of Fallot repair. Abnormal arterial elastic properties have negative impact on left ventricle and provoke aortic dilatation, and it may induce left ventricular hypertrophy and systolic and diastolic dysfunction of left ventricle. Also in repaired tetralogy of Fallot patients, increased augmentation index is found [44].

In patients after arterial switch operation, decreased aortic elasticity and distensibility are confirmed by increased pulse wave velocity [45] and increased stiffness index [46].

These aortic pathophysiological abnormalities are observed in the other types of congenital heart disease with aortic dilatation. These characteristics induce aortic dilation and aortic regurgitation [5, 46], and increased pulsatile load on left ventricle followed by decreased cardiac output [1], and also provoke decreased coronary blood flow that may have negative influence on left ventricular function [40, 42]. Aortic regurgitation may also develop and progress due to stiffness of aortic root.

We can recognize these pathophysiological abnormalities of aorta and abnormal aorto-ventricular interaction as a clinical entity "aortopathy."

13.1.6 Medication and Prevention of Aortic Dilatation

Beta-blockers are recommended for the prevention of aortic dilation in the Marfan syndrome when the diameters have not reached the surgical thresholds [47]. They might exert their action through negative inotropic and chronotropic actions, decreasing ascending aorta shear stress. Angiotensin receptor blockers showed promising results in a mouse model of Marfan syndrome [48]. They antagonize transforming growth factor beta whose excessive signaling may cause aortic root dilation in the Marfan syndrome. Recent large clinical trial showed there was no difference between these two medications for prevention of aortic dilatation in Marfan young adults [49]. Due to the histopathological resemblance of CHD aortopathy to the Marfan syndrome, it may be logical to administer these drugs to the CHD patients with aortopathy until the availability of more specific data.

13.2 Surgical View

13.2.1 Introduction

Aortic dilation might eventually cause aortic annular enlargement that will in turn predispose to severe aortic regurgitation (AR). Marfan syndrome is the most frequently associated not only with aortic dilation but aortic dissection because of hereditary disease. In such patients, concomitant aortic valve surgery together with an aortic root replacement will be required. The Bentall operation [50] was

originally developed to repair the complex lesions of an annuloaortic ectasia (AAE) associated with severe AR with a composite graft that contained a mechanical valve. For the patients of whom aortic valve might be preserved, Yacoub et al. developed the remodeling procedure [51], and David et al. made progress the reimplantation method [52]. Both procedures are well known as valve-sparing operations.

In the Ross operation [53], the intact pulmonary autograft is harvested in order to replace the aortic valve (inclusion technic) or to replace the aortic root. Enucleated RV outflow tract and the pulmonary artery are usually reconstructed with a homograft, hard to obtain in Japan, or other prosthetic valve conduits. However superiority of freedom from anticoagulation longevity of pulmonary autograft has been substantiated in many reports; application of the Ross operation for the adult patients is controversial because of complexity of the procedure.

13.2.2 Composite Valve Graft Procedure: Bentall Operation

In 1968, Bentall and de Bono described the first successful aortic root replacement with a composite Teflon tube graft and a ball valve prosthesis (Starr valve) in a male associated with ascending aortic dilation, aortic annular enlargement, and severe AR.

The Bentall operation consists of replacement of the ascending aorta and the aortic valve including the aortic root with a composite tube graft. Coronary ostia are reimplanted to the tube graft. In order to replace the ascending aorta as far distally as possible, cardiopulmonary bypass is usually established by retrograde arterial perfusion through the femoral artery. After cross-clamp of the ascending aorta, the aneurysmal ascending aorta is resected (Fig. 13.1a). The aortic valve is also excised (Fig. 13.1b), and then a composite tube graft prosthesis of appropriate size, including a prosthetic valve, is sutured to the aortic annulus. Usually a mechanical valve is used in this graft because of its longevity (Fig. 13.1c).

Circular holes are made in the tube graft at the positions of the coronary ostia. Originally, coronary ostia were approximated to the graft and directly sutured to the holes of the graft. This method might cause significant tension to the suture lines and bleeding, so that many modifications have been developed. Recently, coronary ostia are detached as large buttons of the aortic wall and dissected free along their courses to allow their mobility. The coronary buttons are directly sutured to the holes of the aortic graft (Carrel patch method) or interposing a small caliber graft (Piehler method) (Fig. 13.1d).

The Bentall operation was most indicated for AAE. The proximal arch and neck vessels are usually not involved in AAE, and then only replacement of the ascending aorta would be required. Marfan syndrome is frequently associated with aortic dilation and aortic dissection because of hereditary degenerative disease. However, in most cases of Marfan syndrome, the ascending aorta is first affected by aneurysmal lesion [54]. When the aortic valve is not damaged, a valve-sparing operation can be applicable [55].

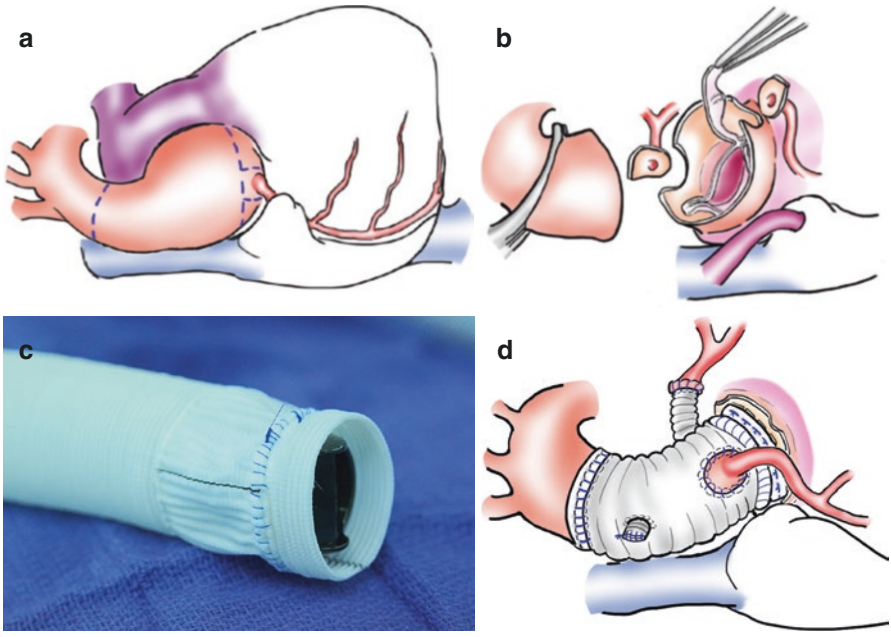

Fig. 13.1 (**a**) The aneurysmal ascending aorta is removed from just above sinotubular junction to the normal distal ascending aorta. (**b**) Coronary buttons are detached as large buttons with the aortic wall. Aortic valve is resected. (**c**) A composite tube graft for the Bentall operation. A mechanical valve is seated in the graft beforehand. (**d**) Ascending aorta is replaced with a composite graft. Coronary ostium is reattached to the graft directly (Carrel patch method) or interposing a small caliber graft (Piehler method)

A large ascending aorta is frequently observed in TOF patients, especially in the case with pulmonary atresia. Fifteen percent of adult patients with repaired TOF have a dilated aortic root [21] (Fig. 13.2a–c). Since only a small number of these patients are reported to advance to an aortic dissection, the indication for aortic replacement in TOF would be decided at a later stage compared to patients who developed an aortic aneurysm in other anomalies. However, careful follow-up will be required when the diameter of the aortic root excesses 55 mm [53, 56]. If significant aortic regurgitation appears due to annular dilation, AVR with ascending aortic replacement or Bentall operation would be considered (Table 13.3).

13.2.3 Valve-Sparing Procedures

Aortic dilation is prone to aortic annular dilation. Severe AR frequently occurs only due to the annular dilation. When the aortic valve is not affected with apparent structural lesions, it can be preserved by reducing the diameter of the aortic annulus and suspension of cusps. Based on this concept, two types of valve-sparing root replacement had been described by Yacoub in 1979 (remodeling method [51]) and

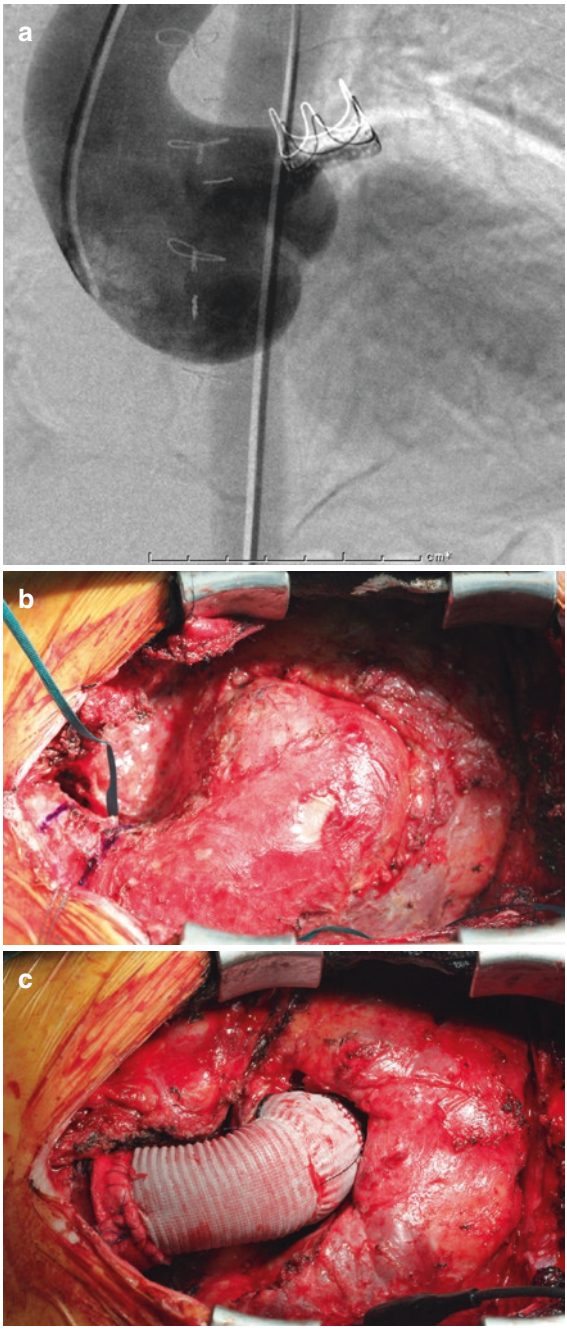

Fig. 13.2 (**a**) Aortogram of a 46-year-old male who had undergone TOF repair at 5 years old. He underwent pulmonary valve replacement at 43 years of age; however, aortic dilation and aortic valve regurgitation were rapidly developed in 2 years. (**b**) Marked aortic root dilation of the patient. Left is the cranial side. (**c**) Aneurysmal aortic root was replaced with a composite graft. Carrel patch method was applied to coronary reattachment

Table 13.3 Guidelines for ascending aortic replacement

	Marfan syndrome	BAV	Tricuspid non-Marfan
Aortic root diameter	45 mm	50 mm	55 mm
	Loyes-Dietz syndrome 40 mm	*Unless family history of aortic dissection is present*	

by David in 1992 (reimplantation method [52]). In the remodeling method, sinuses of Valsalva are replaced by the trimmed tube graft, whereas the entire aortic root after resection of sinuses is reconstructed in the tube graft in the reimplantation method. Valve-sparing procedures have been developed as alternative methods to the Bentall operation in the patients whose aortic valve is suitable for preservation. Good results have been reported in patients with Marfan syndrome or Loyes-Dietz syndrome, who have undergone elective valve-sparing procedures [55–57]. Boodhwani et al. [58] reported their excellent systematic approach to repair regurgitant BAV using valve-sparing procedures. However, not a few authors advocated superiority of the Bentall operation to valve-sparing operation because of uncertainty of long-term durability [59, 60]. The criteria for the aortic root replacement have been recommended in many reports and guidelines (Table 13.3): the aortic root diameter of more than 55 mm in non-Marfan adult patient, 50 mm in BAV, and 45 mm and 40 mm in Marfan syndrome and Loyes-Dietz syndrome, respectively [54, 55, 61, 62].

13.2.3.1 Remodeling Method

Cardiopulmonary bypass is established in the same manner as in the Bentall operation. The aneurysmal ascending aorta is removed from the distal portion to the sinus of Valsalva. The coronary ostia are detached from the aortic wall as a large button. The non-coronary sinus of Valsalva is also resected, whereas the aortic valve is preserved. A proper size tube graft, usually determined according to the diameter of the sinotubular junction, is trimmed in three portions and sutured to the wall of the sinuses of Valsalva (Fig. 13.3a). Two holes are made in the tube graft at the corresponding positions of the coronary ostia. The coronary buttons are sutured to the tube graft in the same way as in the Bentall operation (Fig. 13.3b).

13.2.3.2 Reimplantation Method

Preservation of the aortic valve and enucleation of coronary buttons are performed in the similar manner as in the remodeling method, although the reimplantation method requires two suture lines (first row and second row). Stay sutures are put on each commissure. Then, the first row of sutures is placed from inside of the left ventricular outflow tract to the outside just below the aortic cusps to seat the end of tube graft. A number of first row sutures are dependent on surgeon's preference and ranged between 6 and 15 sutures (Fig. 13.4a). Usually a tube graft of 4–5 mm larger than a diameter of inner aortic annulus is selected. Recently, a tube graft with pseudosinus is a trend because natural vortex bloodstream in the Valsalva sinus is considered to protect the aortic valve leaflets from diastolic stress (David V procedure). Then, the entire aortic root is pulled into a tube graft, and first row sutures are put in

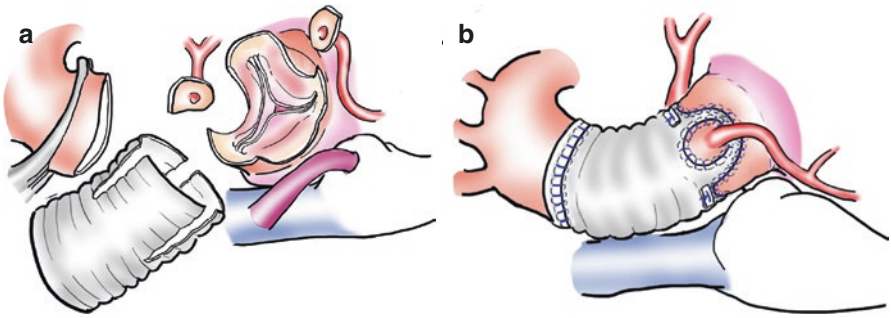

Fig. 13.3 (**a**) Aneurysmal ascending aorta is transected above sinotubular junction. Coronary ostia are detached as large buttons and the non-coronary sinus is also resected. (**b**) A proper size tube graft is trimmed in three portions, and the individual tongues of a hand-scalloped graft are sutured to fit the commissures and the Valsalva sinuses. Coronary ostia are reimplanted to the tube graft

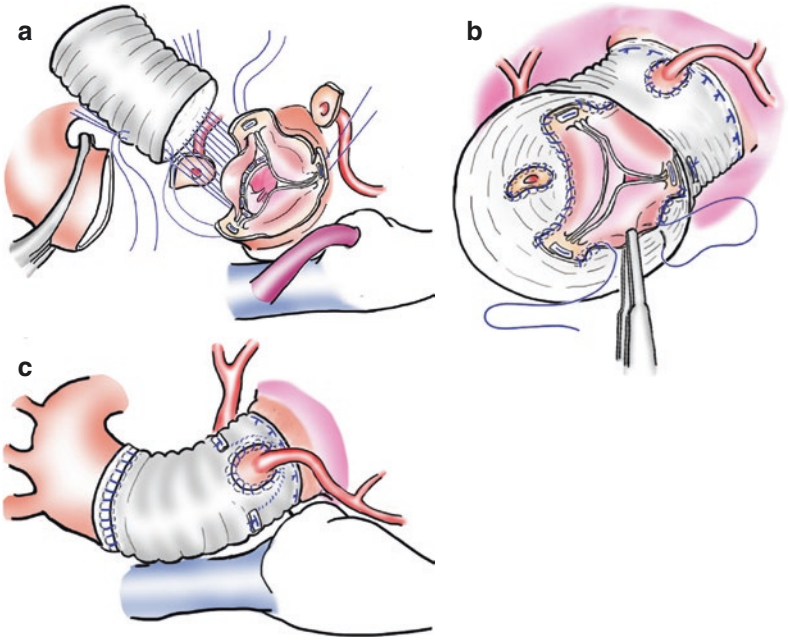

Fig. 13.4 (**a**) The aneurysmal aortic root is removed as in the remodeling procedure. The first row of sutures is placed from inside to outside just below the aortic cusps to seat the tube graft. Stay sutures are put on each commissural wall. The entire aortic root is pulled into a tube graft. (**b**) Commissures are suspended to the tube graft arranging good coaptation of the aortic valve. The free edge of the Valsalva sinuses is continuously sutured to the inside of the tube graft (second row sutures). The coronary buttons are reattached to the tube graft in the same fashion as in other forms of root replacement. Commissures and free edge of Valsalva sinuses are sutured inside of the tube graft. (**c**) The aortic root is replaced with the tube graft

the edge of the graft and tied down (Fig. 13.4b). Commissural walls are suspended to the tube graft arranging good coaptation of the aortic valve. The free remnant of the Valsalva sinuses is continuously sutured to the inside of the tube graft (second row sutures) (Fig. 13.4b). Two holes are made in the tube graft at the positions of the corresponding coronary ostia. The coronary buttons are sutured to the tube graft in the same fashion as in other forms of root replacement (Fig. 13.4c).

13.2.3.3 Difference of Valve-Sparing Operations

As the aortic annulus and aorto-ventricular junction are left untouched in the remodeling method, the risk of recurring root dilation remains in the long term. Some authors add subcommissural annuloplasty to stabilize the aortic annulus [14, 60]. Leyh et al. [63] reported that aortic root elasticity and aortic valve motion are superior in the remodeling method compared to the reimplantation method. Although unequivocal difference between two valve-sparing methods has not been indicated [64], the reimplantation method tends to be widely accepted in recent years. Many authors reported excellent long-term results in Marfan syndrome and BAV with the reimplantation method [57, 58, 61, 65, 66].

13.2.4 Autologous Tissue Procedure: Ross Operation

In 1967, Donald Ross [53] developed the idea of using an autologous pulmonary valve to replace the aortic valve. At first the pulmonary valve tissue was trimmed in scallop and reimplanted at subcoronary position. Inclusion cylinder method had also been performed to simplify the procedure. Full root replacement with pulmonary autograft is most prevailed in recent years.

After establishment of the cardiopulmonary bypass, the main pulmonary artery is transected just below the bifurcation. The pulmonary valve is carefully inspected if not diseased. The RV free wall is incised a few millimeters below the pulmonary valve with or without aortic cross-clamp. The RV incision is extended transversally and posteriorly. Great care is necessary not to injure the first septal branch of the left anterior descending coronary artery. The pulmonary root tissue is harvested (Fig. 13.5a). The ascending aorta is transected above the sinotubular junction. Both coronary ostia are detached with a large button of aortic wall, and then the aortic valve is excised. The pulmonary autograft is sutured to the aortic annulus with many simple interrupted sutures or a mixture of continuous running and interrupted sutures. Large enough holes are made on the pulmonary autograft, and coronary buttons are sutured to the corresponding hole. The distal end of the pulmonary autograft is sutured to the distal ascending aorta. The enucleated RV outflow and the main pulmonary artery are reconstructed, usually with a homograft or other valved conduits (Figs. 13.5c and 13.6). When the aortic annulus is too small for the pulmonary autograft, Ross-Konno operation [67] can be performed (Fig. 13.5a–c).

de Sa et al. examined the histologic features of the ascending aorta and the main pulmonary artery obtained from the patients with BAV and the patients with tricuspid aortic disease. The authors found that degenerative changes in the media of the ascending aorta and the main pulmonary artery were severer in the patients with

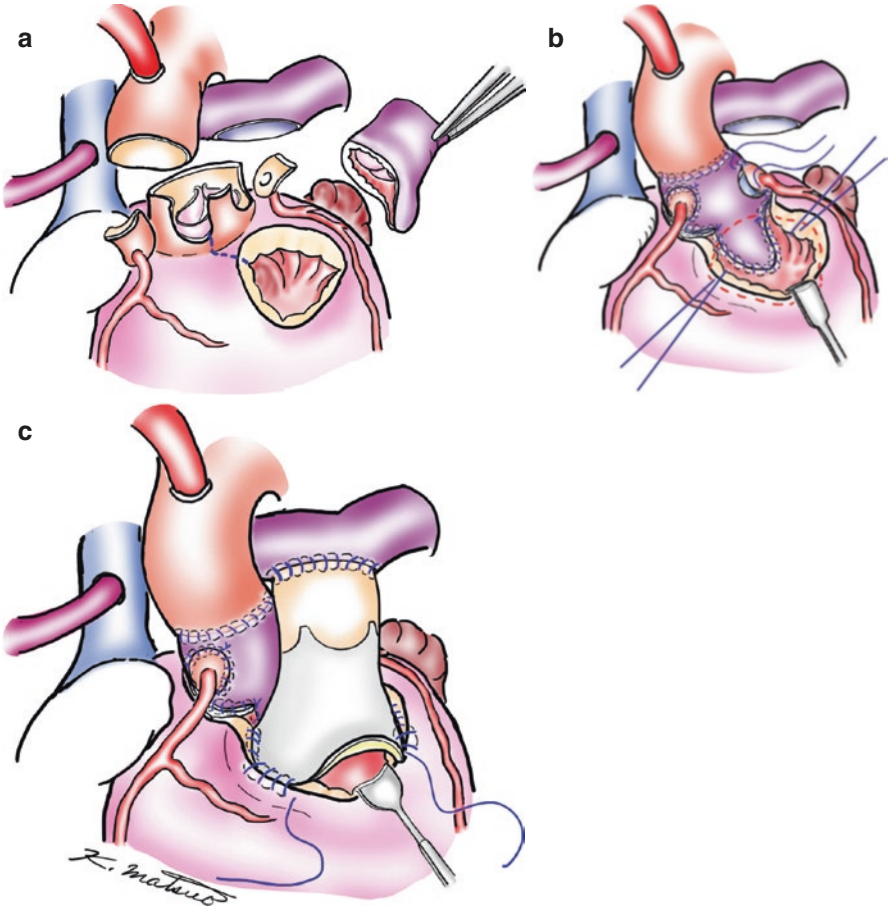

Fig. 13.5 (**a**) The pulmonary autograft is harvested. The ascending aorta is transected just above sinotubular junction. Coronary ostia are removed as large buttons. The aortic valve is resected. (**b**) The pulmonary autograft is sutured to the aortic annulus. When the aortic annulus is too small for the autograft, a vertical incision is extended to the ventricular septum. (**c**) Enucleated RV outflow and the pulmonary artery are reconstructed with a homograft or other valved conduit

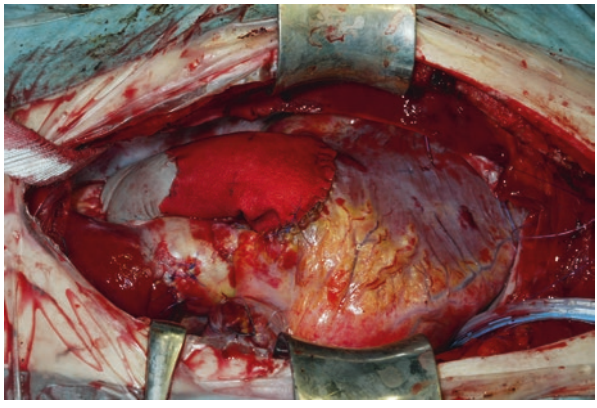

Fig. 13.6 A 15-year-old male with BAV and severe AS is repaired with Ross operation. RV-PA route is reconstructed with a handmade valved conduit

BAV than the patients with tricuspid aortic valve disease [68]. David et al. studied their 118 adult patients with the age of 34 ± 9 years who underwent Ross procedure. BAV or other congenital aortic valve disease was present in 81% of their patients, and the diameter of the sinuses of Valsalva exceeded the normal limit in 13 patients with BAV. They concluded that dilation of pulmonary autograft after Ross operation may occur because of intrinsic abnormality of pulmonary root in certain patients [69]. On the other hand, some authors realized the increase in size of the pulmonary autograft correlated with the patients' expected somatic growth in children and the young patients [70, 71]. Growth potential or balanced dilation of the pulmonary autograft with somatic growth is expected among young patients.

Elkins et al. [72] reviewed 487 consecutive patients who underwent Ross procedure between 1986 and 2002. Patient age was from 2 days to 62 years (median 24 years). Actuarial survival was 82% ± 6% at 16 years; freedom from autograft failure was 74 ± 5%. Kieverik et al. reported their 146 patients of Ross procedure, aged 4 months to 52 years (mean 22 years). Although the survival at 13 years was excellent as much as 94 ± 2%, freedom from autograft reoperation was 69.7 ± 7% at 13 years. The authors concluded that adult patients tended to be associated with higher risk of autograft reoperation, so that the Ross operation is performed only in infants and children in their center [73]. In contrast, Sievers et al. reviewed 1779 adult patients with the Ross procedure in eight centers in Germany, and they concluded the Ross procedure should be considered in young and active patients based on the excellent results in their study [74]. Since the Ross procedure requires fair degree of expertise to obtain acceptable results, introduction of the Ross procedure to the adult patients is still controversial.

Conclusions

A subset of adult patients with congenital heart disease exhibits ongoing dilatation of the aortic root and reduced aortic elasticity that may relate to intrinsic properties of the aortic root. This new concept of aortic dilatation is shifting a paradigm of aortic dilatation from so-called post stenotic dilatation to primary intrinsic aortopathy. These aortic dilatation and increased stiffness can induce aortic aneurysm, rapture, and aortic regurgitation but also provoke left ventricular hypertrophy, reduced coronary artery flow, and left ventricular failure. We can recognize this association of aortic pathophysiological abnormality, aortic dilation, and aorto-ventricular interaction as a new clinical entity "aortopathy." For prevention of aortic dilatation in Marfan syndrome, beta-blockers and angiotensin receptor blockers are now applied, but definitive medication is not yet established.

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Ebstein's Anomaly in the Adult: Timing for Surgical Intervention in Adult Population

14

Shingo Kasahara

Abstract

Ebstein's anomaly (EA) is a rare congenital cardiac malformation, and this anomaly is a disorder of a tricuspid valve (TV) development in which the valve leaflets fail to delaminate properly from the ventricular wall. Clinical symptoms are age dependent and include cyanosis (size of interatrial communication), right-sided heart failure, arrhythmias, and general fatigue on exercise. Optimal timing of surgical intervention is often difficult and must be individualized. Patients have good long-term survival and functional outcomes after undergoing surgery for Ebstein anomaly in adult population. Operation includes tricuspid valve repair or replacement, closure of any interatrial communications, and appropriate antiarrhythmia procedures.

Keywords

Ebstein's anomaly • Surgical intervention • Adult congenital heart disease

14.1 Introduction

Ebstein's anomaly (EA) is a rare congenital cardiac malformation as initially described by Wilhelm Ebstein in 1866 [1]. This anomaly is a disorder of a tricuspid valve (TV) development in which the valve leaflets fail to delaminate properly from the ventricular wall [2]. Therefore the EA of the tricuspid valve represents a spectrum of abnormalities affecting the development of the right heart, which can be

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associated with valuable pathophysiology, presentation, and management depending on the age. Patients with the most severe form of EA present in the neonatal period with severe heart failure, often with hypoxemia and consequent high morbidity and mortality [3, 4]. Management of symptomatic neonates with EA constitutes one of the most significant challenges congenital surgeon are confronted with these days [5–7]. On the other hand many patients with EA survive and require surgical repair in adulthood. Age at clinical presentation varies considerably by anatomic severity and by other associated heart disease. Clinical symptoms are age dependent and include cyanosis (size of interatrial communication), right-sided heart failure, arrhythmias, and general fatigue on exercise. Optimal timing of surgical intervention is often difficult and must be individualized.

14.2 Anatomy

14.2.1 Tricuspid Valve

Malformation of tricuspid valve is related to delamination of the valve from the underlying myocardium. If this delamination is incomplete, the malformation is expressed to a variable degree along the tricuspid annulus, varying from complete delamination in the normal heart to spectrum of lack of delamination in EA. With these increasing degrees of anatomic severity of abnormality, the fibrous transformation of leaflets from their muscular precursors remains incomplete, with the septal leaflet being most severely involved, the posterior leaflet less severely involved, and anterior leaflet least severely involved. These changes result in a downward displacement of the hinge point of the posterior and septal leaflets in a spiral fashion below the true annulus. The tricuspid leaflets are quite unusual and dysplastic and are tethered by short chordae and papillary muscles or attached to the underlying myocardium directly or by muscular bands. Also fenestrations of leaflets are usually seen in this situation. In the most anatomically severe case, the septal leaflet is only a ridge of fibrous tissue that originates below the membrane septum and is directed toward the apex. In less severe case, the anterior leaflet may form a large sail-like curtain. The anterior leaflet forms most of the true orifice that directs to the pulmonary valve, and it is likely to contain accessory fenestrations.

14.2.2 Atrialized Right Ventricle

As described above, there are varying degrees of downward displacement of the annulus, especially posterolaterally from the true annulus in EA. The gap between functional and true annulus is usually dilated and this dilated portion is called “atrialized right ventricle.” Its free wall is more dilated and thinner than the normal right ventricular wall. Morphometric histopathologic studies have demonstrated that right ventricular dilatation is associated not only with thinning of the wall but also with an absolute decrease in the number of myocardial fibers counted through the thickness of the wall from endocardium to epicardium [8].

14.2.3 Right Ventricle in EA

Because of lack of delamination followed by tricuspid regurgitation, dysplasia of the myocardium refers to abnormal muscularity of the right ventricle (RV). So the ventricular response to the regurgitant volume load is often different from that observed in acquired tricuspid regurgitation. The dilated right ventricle compressed the left ventricle (LV), displaced posteriorly and toward the supine. It is important to surgical intervention to understand the function and the functional size of right ventricle.

14.2.4 Left Ventricle in EA

Usually left ventricle in EA has normal function and normal structure in an adult. Marked dilatation of the right ventricle significantly affects the structure and function of the ventricular septum and left ventricle. In the more severe cases, the septum is D-shaped or has leftward bowing associated with paradoxical septal motion. Most of those patients have depressed left ventricular function with asynergy of wall motion.

14.3 Classification

Because of the wide spectrum of pathology and the nearly infinite variety of combinations of severity of the involved structures, a comprehensive classification or grading system would be too complex and not clinically practical. Regarding of these approaches, many classification were published in describing the severity of the anatomical deformity of hearts with EA. Many of those are based on the echocardiographic appearance in which the pathology is described anatomically formed by summation of the amount of displacement of the leaflets, the degree of tethering of the anterior leaflet, and the degree of right ventricular dilatation.

Carpentier classification was widely used in EA [9] (Fig. 14.1).

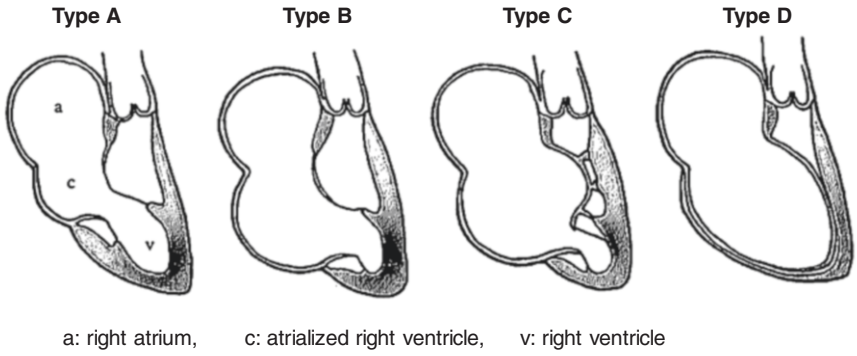

Fig. 14.1 Carpentier classification. Carpentier et al. proposed a classification system based on size of functional RV and adequacy of the anterior leaflet for repair [9]

14.4 Indication and Timing for Operation

Observation alone is usually advised for asymptomatic patients with no right-to-left shunting and only mild cardiomegaly. Regarding indications for surgery in older children and adults, ACC and AHA guideline showed the precise orientation [10]. As long as this guideline, the timing of operation indicates symptoms (dyspnea or palpitation), deteriorating exercise capacity, progression of atrial or ventricular arrhythmia, and cyanosis. The degree of tricuspid regurgitation does not correlate with symptoms, but as time passes, left ventricular dysfunction often appears as symptoms develop.

14.5 Catheter Intervention

The importance of an associated atrial septal defect is reflected in the natural history of EA. Progressive tricuspid valve dysfunction and reduced right ventricular compliance lead to elevated right atrial pressure, which in turn promotes right-to-left shunting at the arterial level with concomitant systemic hypoxia [11]. This clearly has implications in terms of paradoxical embolization in those patients with interatrial defects. The use of percutaneous closure device to ameliorate systemic hypoxia complicating right-to-left shunting through an interatrial defect has been safely performed in a number of clinical settings. Such examples include hypoxia-complicating atrial shunting in right ventricular infarction, prior to and following pneumonectomy, with use of high positive-pressure ventilation, following left ventricular assist device insertion, and in the platypnoea-orthodoexia syndrome [12]. Percutaneous device closure of both atrial septal defects, up to 40 mm in diameter, and patent foramen ovale has been demonstrated to be a safe, with excellent, outcome [13]. One of the major concerns regarding percutaneous device closure of interatrial defects in those patients with a hypoplastic right ventricle, characteristic of EA, is the precipitation of right heart failure. This reflects the possibility that the right ventricle may not be able to tolerate the additional volume loading that inevitability complicates interatrial defect closure in the setting of right-to-left shunting.

14.6 Surgical Intervention

The recommended indications for surgical intervention in EA in the adult are based on recommendations from the Canadian and European guidelines [14, 15]. Also it is important in situations as below:

- Deteriorating functional class or exercise capacity, NYHA classes III and IV
- Paradoxical embolism
- Increasing heart size as manifested by increase in cardiothoracic ratio to >0.65
- Progressive right ventricular dilatation or reduction of systolic function
- Sustained atrial flatter or fibrillation or arrhythmia secondary to an accessory pathway
- Important cyanosis (oxygen saturation < 90%)

In borderline situations, the ability to reconstruct the tricuspid valve, as determined by echocardiography, makes the decision to proceed with operation easier. A biventricular repair is usually possible, but in some circumstances when significant left ventricular dysfunction has occurred, cardiac transplantation may be the best option; however, it is a very limited selection in Japan. The vast majority of patients with EA can undergo successful biventricular repair, especially for adult patients. However, the one and a half repair or univentricular repair (Fontan procedure) can be an effective strategy if the patient has severe RV dysfunction after the agressive annuloplasty of tricuspid valve.

14.6.1 Tricuspid Valve Repair and Replacement

Tricuspid valve repair is based predominantly on a satisfactory anterior leaflet; thus significant abnormalities of the leaflet may compromise the result. Numerous valvuloplasty techniques have been described since the first report on Hunter and Lillehei [16]. Most repair techniques address the abnormal TV in a manner that focuses on the concept of monocusp repair. Monocusp repair depends on an adequate anterior leaflet with a freely mobile leading edge that allows coaptation with the ventricular septum. Significant degree of RV or annular dilatation or significant tethering of the anterior leaflet can preclude successful repair. In the early report of Danielson and colleagues, the plication of the free wall of the atrialized right ventricle, posterior tricuspid annuloplasty, and excised redundant right atrial wall combined with monocusp repair were described [17] (Fig. 14.2). Carpentier and

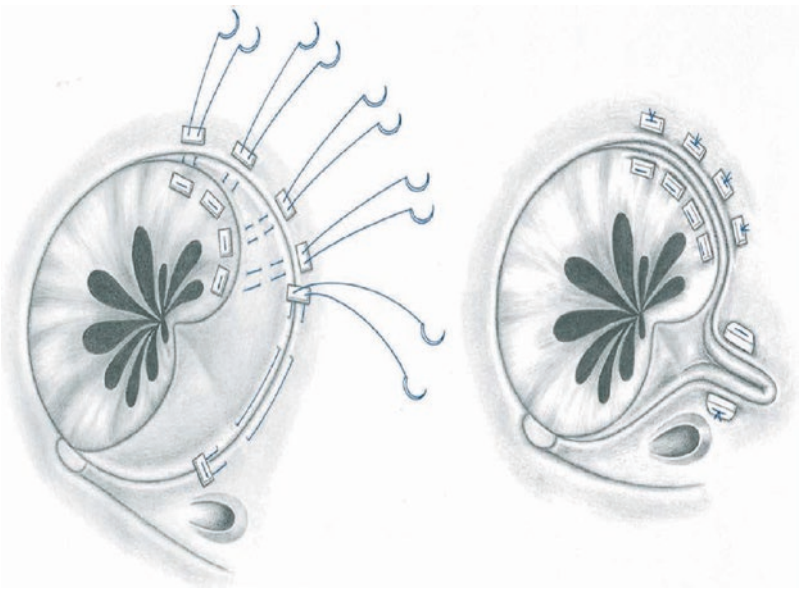

Fig. 14.2 Danielson repair. Mattress sutures passed through pledgets of Teflon felt and used to pull tricuspid annulus and tricuspid valve together (*left*). Suture is placed in atrialized portion of right ventricle and tied down sequentially to plicate aneurysmal cavity (*right*) [20]

colleagues focused on mobilization (surgical delamination) of the anterior leaflet with annular reattachment, resulting in an anterior leaflet monocusp repair [18] (Fig. 14.3). Hetzer and colleagues reported their operative technique for EA that they individualized depending on the specific anatomy in a series of 68 patients

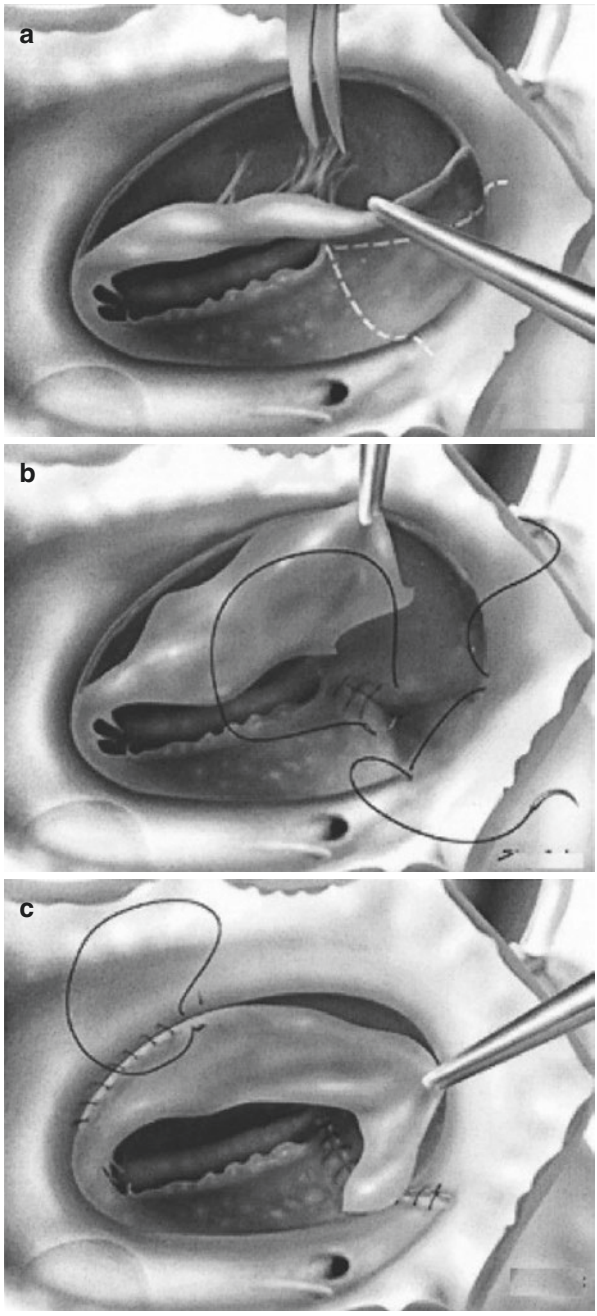

Fig. 14.3 Carpentier repair. (**a**) Detachment of the anterior leaflet and section of the muscular bands in order to individualize the lateral papillary muscle. *Dashed lines* indicate the limits of the atrialized chamber. (**b**) Longitudinal plication of the atrialized chamber from the apex of the right ventricle to the tricuspid annulus. Subsequently, the tricuspid annulus is reduced. (**c**) Reattachment of the anterior leaflet on the true annulus with a clockwise rotation [21]

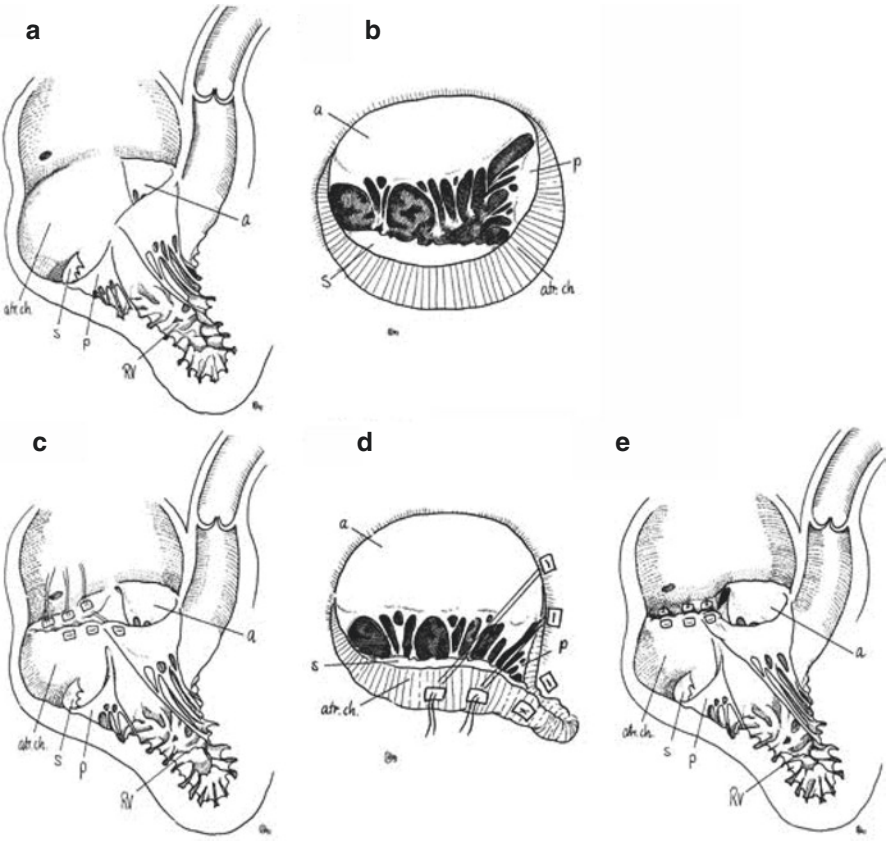

Fig. 14.4 Hetzer repair. Schematic presentation of a cross-sectional (**a**, **c**, **e**) and surgeon's views (**b**, **d**) of the intraoperative findings and the surgical technique applied. The pathologic finding corresponds to Ebstein's anomaly of Carpentier type B [12], with the displaced septal (*s*) and posterior (*p*) leaflets toward the apex of the right ventricle (*RV*). Leaflet displacement creates an atrialized chamber (*atr. ch.*) below the anatomic tricuspid annulus. There is a large, mobile anterior leaflet (*a*). (**c**, **d**, **e**) The anterior part of the anterior leaflet was chosen for the valve-closing structure. A mattress suture of 3-0 polypropylene pledgeted with autologous pericardium is passed from the anterior leaflet annulus to the atrialized septum just below the natural tricuspid annulus. A row of these sutures is added toward the posterior annulus [22]

(Fig. 14.4). They conclude that all morphologic types of EA are amenable to repair (no tricuspid replacements at initial operation) and that satisfactory long-term ventricular function and functional outcome can be obtained, even in the most severe cases [19].

14.6.1.1 Cone Reconstruction (Figs.14.5 and 14.6)

However the numerous valvuloplasty techniques have been described, tricuspid valve repair in dysplastic anterior tricuspid valve is very difficult. A further extension of the Carpentier repair has been proposed by da Silva and colleagues and termed the cone reconstruction (CR) [24]. The anterior and posterior leaflets are detached from the annulus as a single unit, mobilized from their anomalous attachments in the RV,

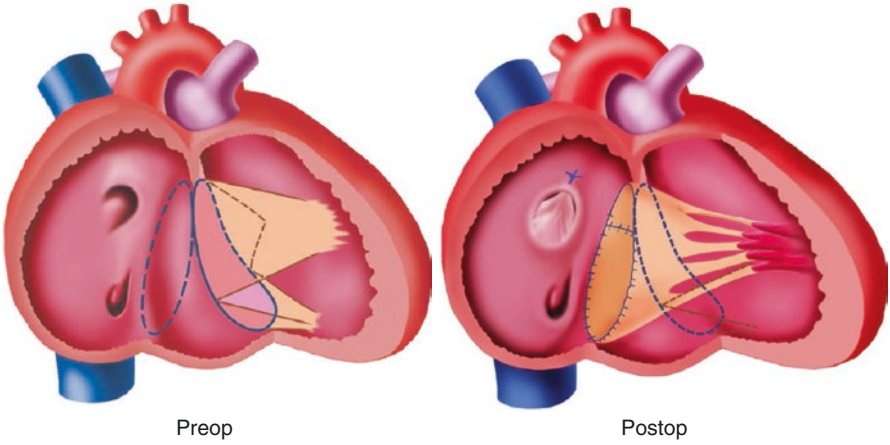

Fig. 14.5 Ebstein's malformation—the cone procedure [23]. The anterior and posterior leaflets are detached from the annulus as a single unit, mobilized from their anomalous attachments in the RV, and rotated in a clockwise fashion to be sutured to the septal border of the anterior leaflet. The principle of CR is complete surgical delamination including septal leaflet as possible and recruitment of all undelaminated leaflet tissue

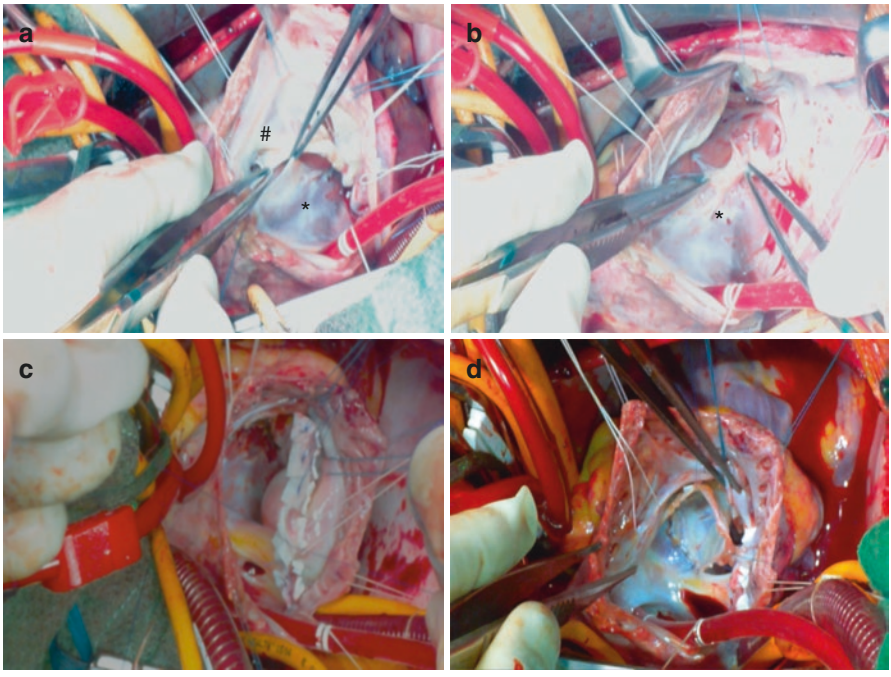

Fig. 14.6 (**a**) Appearance of valve of Ebstein anomaly. There is no coaptation zone between leaflets. #: anterior leaflet, *: septal leaflet. (**b**) Plastering of the septal leaflet. *: septal leaflet. (**c**) Plication of atrialized ventricle. (**d**) Construction of cone using three leaflets. Cone will attach to the annulus for completion of the cone procedure

and rotated in a clockwise fashion to be sutured to the septal border of the anterior leaflet. The principle of CR is complete surgical delamination including septal leaflet and recruitment of all undelaminated leaflet tissue, which is reattached at the true right atrioventricular junction, creating a 360-degree "leaflet cone." Leaflet-to-leaflet approximation is done with interrupted monofilament sutures to avoid a purse-string effect, which can decrease the height of the reconstructed leaflet. The atrialized RV is plicated internally from the apex to annulus. The plication typically crosses the true annulus to partially reduce the size of the dilated annulus. During this procedure, care is taken to avoid distortion or compromise of the right coronary artery. Reattachment of the neo-TV to the true annulus is done with interrupted or continuous suture; continuous suture does purse string the annulus, causing further reduction in annular size, which may be desired in some situation. Original corn reconstruction is no indicated ring annuloplasty. The learning curve for CR is steep, and the following steps are the most important. First, the most challenging aspect of CR is surgical delamination. Surgical delamination is complete when all muscular or fibrous attachments between the body of the leaflets and the RV free wall and ventricular septum have been completely taken down. When this is done properly, the only attachments remaining are chordae or direct papillary muscle insertion to the leading edge of mobilized leaflets. Iatrogenic fenestration of the thin RV free wall is easy to do during this process. Sometimes, there are areas of leaflet muscularization. In general, these leaflet segments should be preserved, debulked, and not excised. Heavy muscularization of the anterior leaflet is problematic because of reduced pliability. Second, recruitment of a very diminutive septal leaflet is critical. There must be some septal leaflet present that can be approximated to the other mobilized leaflets to obtain 360 degree of leaflet tissue around the atrioventricular junction. The more diminutive the septal leaflet, the more important it is to have sufficient "other valve tissue" to compensate for this deficiency. Right ventricular plication and annular reduction should be done liberally. Right ventricular plication helps reduce the size of the right ventricle and the annulus in a gradual manner and distributes tension so that it does not all reside at the annulus. The inferior annulus plication is the site of greatest tension and the most vulnerable to right coronary compromise. Also several reports have shown abnormalities of the LV [25]. These abnormalities include abnormal motion of the interventricular septum (IVS) and compression of the LV, which are induced by the enlarged right heart. The enlarged heart also occupies so much space in the thoracic cavity that the lungs are rendered hypoplasia. After free wall resection of the right ventricle, the small right heart helps the IVS motion and the LV function to improve and also provides the lungs with more space to expand immediately after the operation (Fig. 14.7).

14.6.1.2 Tricuspid Valve Replacement

When the tricuspid valve cannot be reconstructed, anterior leaflet tissue in the right ventricular outflow tract is excised and prosthetic valve (bioprosthetic valve more often than mechanical valve) is inserted. The suture line is deviated to the atrial side of the atrioventricular node and membrane septum to avoid injury to the conduction system. To avoid injury to the right coronary artery, the suture line may be deviated superiorly to the tricuspid valve annulus posterolaterally where the tissues are frequently very thin. The coronary sinus can be left to drain into the right atrium if

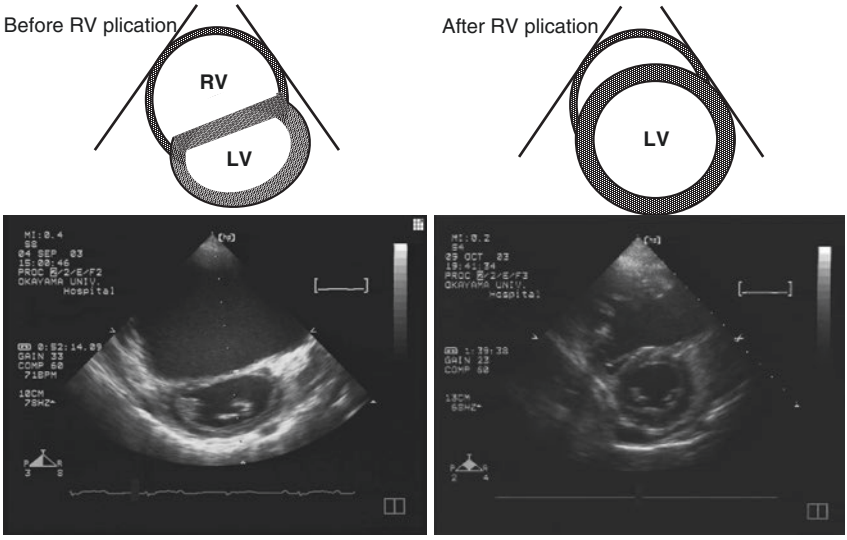

Fig. 14.7 Echocardiogram: Short axis view at endodiastolic phase. The enlarged heart also occupies so more space in the thoracic cavity that it causes hypoplasia of the lungs. After free wall resection of the right ventricle, the small right heart helps the IVS motion and the LV function to improve and also provides the lungs with more space to expand immediately after the operation

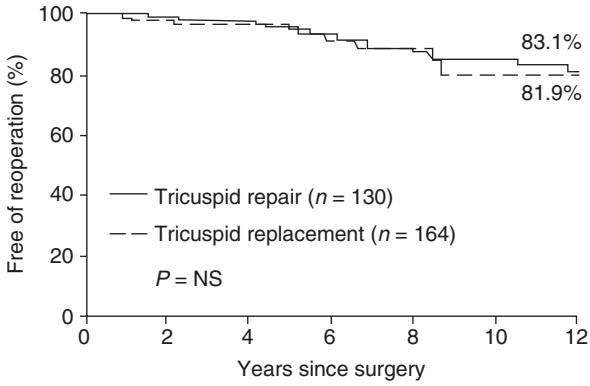

Fig. 14.8 Freedom from reoperation after tricuspid valve replacement (both bioprosthetic and mechanical) compared with freedom from reoperation after tricuspid valve repair [26]

there is sufficient space between it and atrioventricular node; if the distance is short, the coronary sinus can be left to drain into the right ventricle. The struts of the bioprosthesis are oriented so that they straddle the area of the membranous septum and conduction tissue. In the experience of Mayo Clinic, interestingly, freedom from reoperation at 12 years after tricuspid valve replacement was not significantly different from that of tricuspid valve repair (Fig. 14.8).

14.6.2 One and a Half Repair

When the right ventricle is severely enlarged or dysfunctional or low cardiac output syndrome is a concern, one and a half repair (1.5 ventricle repair) combined with

bidirectional cavo-pulmonary anastomosis (BDG) is indicated for this situation. The technique of 1.5 ventricle repair is applied selectively and is considered when there is (1) severe RV dilatation dysfunction, (2) leftward shift of the interventricular septum (IVS), and (3) postoperative right-to-left atrial pressure ratio greater than 1.5:1. These findings suggest poor RV function with the potential for low cardiac output syndrome postoperatively. Other indication of 1.5 ventricular repair is at the time of aggressive tricuspid annuloplasty. We consider that repair, if post-repair TV annulus is less than 70% of normal in diameter or transannular pressure gradient is greater than 8 mmHg. Many centers have found the 1.5 ventricle repair to decrease operative mortality and to facilitate postoperative management when severe RV enlargement or dysfunction is present [27–29].

14.6.3 Total Cavo-Pulmonary Connection (Fontan Procedure)

The potential advantages of RV exclusion for severely ill neonates with EA are discussed under survival in results after repair. For the adult patients having EA, it is not much occasion of taking the Fontan truck. We have applied this strategy successfully in the patients with severe RV dysfunction and severe tricuspid regurgitation including the patients with EA [30]. This procedure provides effective decompression of

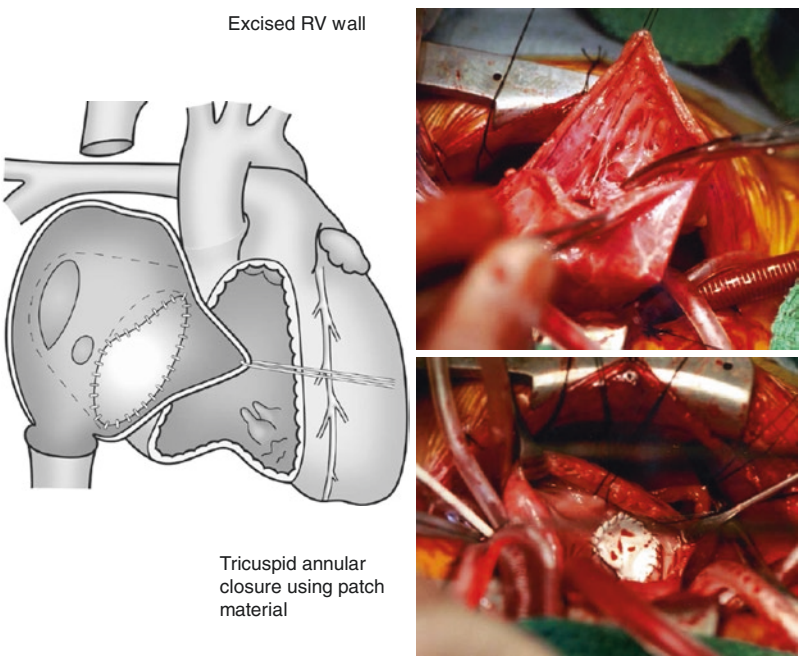

Fig. 14.9 Right atrium (RA)/right ventricle (RV) exclusion procedure. The potential advantages of RV exclusion for severely ill neonates with EA are discussed under survival in results after repair. We have applied this strategy successfully in the patients with severe RV dysfunction and severe tricuspid regurgitation including the patients with EA

the lung, as well as the left ventricle, and may result in more effective volume loading of a surgically created single ventricle with increased systemic output (Fig. 14.9).

14.7 Our Experiences in Okayama University Hospital and Case Presentation in Oldest Patient

Between December 1992 and December 2014, 55 cases with EA have undergone operation in Okayama University Hospital. Neonatal EA was 19 cases and older child or adult cases were 36 cases. Ages at operation ranged from 3 months to 70 years in older child or adult cases. Only ten cases were more than 20 years of age at the time of operation, because of mainly congenital heart service in our hospital. The patients were indicated TCPC in 6 cases, one and a half repair in 7 cases (including conversion of this procedure from biventricular repair in one case), and biventricular repair using several tricuspid valvuloplasties in 23 cases. We have only one case for valve replacement. Mortality was only one case (of 36 patients) after Fontan procedure due to protein-losing enteropathy.

14.7.1 Case Presentation

We present a case of EA in a 70-year-old woman. She was diagnosed with EA in her 50s without any symptoms. So she did not wish to undergo surgical intervention and required only just medical checkup regularly. Recently, she complained shortness of breath. Then she was referred to our hospital for surgical intervention. On her chest X-ray, severe cardiomegaly was shown with 83% of cardiothoracic ratio. Her ECG showed atrial fibrillation. Also her cardiac echogram was showed severe tricuspid regurgitation with severe downward displacement of septal and posterior tricuspid leaflets. Also her right ventricle was quite dilated with RV end-diastolic volume index = 438 ml/m^2 on cardiac MRI. Operation was performed through median sternotomy using cardiopulmonary bypass, aortic and bicaval cannulation with cross-clamping, and cold cardioplegia. The posterior leaflet and a portion of the anterior leaflet were detached from the annulus, completely mobilized from their anomalous adherence to the RV, and then rotated clockwise so that the free edge could be sutured to the septal border of the anterior leaflet. The septal leaflet was complete surgical delamination, also detached and mobilized for valve repair. The RV was longitudinally plicated, while the annulus was horizontally plicated to shrink the ring size as much as possible. The leaflets were reattached to the true tricuspid annulus and longitudinally sutured, forming a cone-shaped inlet valve. In addition, rigged ring annuloplasty was used for the reinforcement of the tricuspid annulus in this case, because the tricuspid annulus was quite dilated. Transesophageal echocardiography was performed immediately after re-beat to evaluate valve competency and systolic function. A concomitant left- and right-sided maze procedure with pulmonary vein isolation procedure was performed for chronic atrial fibrillation. She was then transferred to intensive care unit with stable condition.

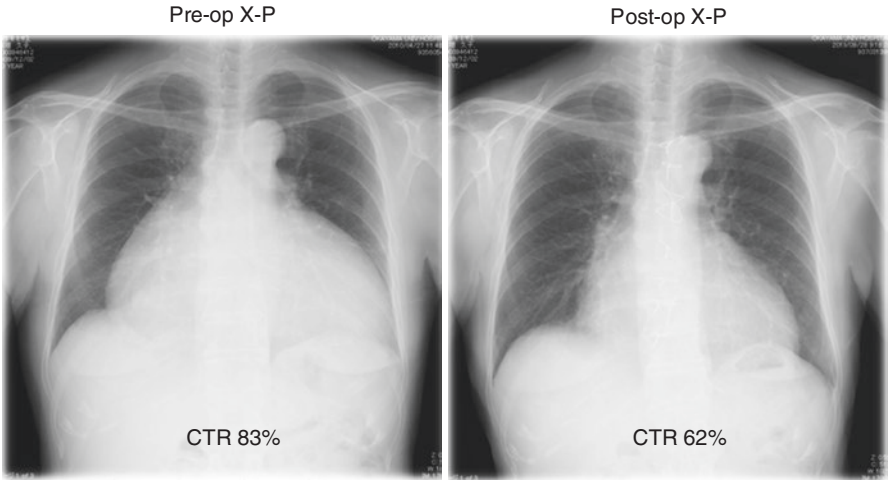

Fig. 14.10 The patients' postoperative CTR was down to 62% and trivial tricuspid regurgitation on echocardiogram comparing with 83% in preoperative CTR

Her postoperative CTR was down to 62% and trivial tricuspid regurgitation on her echocardiogram comparing with 83% in preoperative CTR (Fig. 14.10). But surprisingly, a few days after the surgery, more than moderate mitral regurgitation was developed, and she was diagnosed with congestive heart failure. The mechanism of this abnormality was thought that the mitral annular dimension was changed because of shifting of the interventricular septum to the right. After staying in intensive care unit for 2 weeks, she was then back to ward with minimal mitral regurgitation.

Conclusions

Patients have good long-term survival and functional outcomes after undergoing surgery for Ebstein anomaly in adult population. Operation includes tricuspid valve repair or replacement, closure of any interatrial communications, and appropriate antiarrhythmia procedures. Repair of Ebstein's anomaly eliminates right-to-left intracardiac shunting, improves exercise tolerance and functional class, and reduces supraventricular arrhythmias. In addition, quality of life and longevity are improved.

Acknowledgment I am grateful to Dr. Munetaka Masuda for providing Fig. 14.6.

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Erratum to: Post-RV-PA Conduit Repair

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Fig. 2b of this chapter was initially published with an error in insertion of VSD patch. The superior margin of the patch was sutured to the right side of the subaortic region, but it is sutured to the left side of the aortic valve. The chapter has been updated.

The updated original online version of this chapter can be found at
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