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Ciclo XIX

SURGERY FOR CONGENITAL HEART DISEASE IN THE ADULT AGE.

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Riassunto

Nonostante la maggior parte delle cardiopatie congenite siano attualmente corrette chirurgicamente in età neonatale o nella primissima infanzia, un numero crescente di pazienti con cardiopatia congenita giunge all'attenzione del chirurgo in età adulta.

Per tale motivo, è stato iniziato uno studio multicentrico a livello italiano, che ha coinvolto 7 tra i maggiori centri di cardiochirurgia pediatrica in Italia (Bergamo, Bologna, Massa, Milano S.Donato, Milano Niguarda, Padova, Napoli), in modo da valutare l'importanza clinica dell'intervento cardiochirurgico nel paziente adulto con cardiopatia congenita nel nostro paese, e valutarne le variabili pre-operatorie e operatorie che condizionano la sopravvivenza e la morbilità nel breve e lungo termine.

Materiali e metodi

Sono stati raccolti i dati clinici di 856 pazienti sottoposti ad un totale di 1179 procedure chirurgiche dal 1 Gennaio 2000 fino a 31 Dicembre 2004. I pazienti sono stati divisi arbitrariamente in 3 gruppi. Nel gruppo I- Palliazione (3.1%)- si includono i pazienti in cui la procedura chirurgica viene effettuata per migliorare le condizioni cliniche, senza ripristinare la normale anatomia o fisiologia. La anastomosi cavopolmonare bidirezionale ed il bendaggio dell'arteria polmonare sono risultati essere le procedure più frequenti. Nel Gruppo II- Correzione- (69.7%), si includono tutti quei pazienti in cui sia stata eseguita una correzione chirurgica, ovvero un intervento che permetta il ripristino della normalità anatomica o fisiologica con la separazione delle due circolazioni polmonare e sistemica. In tali pazienti si includono anche l'intervento di Fontan e la cosiddetta correzione ad un ventricolo e mezzo. Le procedure più frequentemente eseguite sono state: la chiusura chirurgica del difetto interatriale (35.8%), correzione del drenaggio venoso anomalo polmonare parziale (7.2%), chiusura del difetto interventricolare (5.3%).

Infine nel Gruppo III- Reintervento- (27.4%), sono incluse tutte le procedure maggiori effettuate dopo chirurgia correttiva o palliativa; i reinterventi più frequenti sono stati la

sostituzione di condotto (9.8%), e la sostituzione valvolare aortica (8.6%) o polmonare (7.7%).

Risultati

Alla valutazione preoperatoria, il 34.6% dei pazienti si presentava in classe NYHA I, il 48.4% in classe II, il 14.2% in classe III e 2.8% in classe IV. All'elettrocardiogramma, il ritmo sinusale era presente nell' 83%.

Sono state eseguite 1179 procedure chirurgiche in 856 pazienti (1.37 procedure/paziente), con una mortalità intraoperatoria globale del 3.1%. Il tempo di permanenza in terapia intensiva è risultato essere 2.3 giorni (range:1-102 giorni). Complicazioni maggiori sono avvenute in 247 pazienti (28.8%), e le aritmie postoperatorie sono risultate le più frequenti complicanze (26%).

Ad un follow-up medio di 22 mesi (range 1 mese- 5.5 anni, completo all'86%), si sono verificati 5 decessi tardivi (0.5%). I pazienti si trovavano in classe NYHA I nel 79.3 % , in classe II nel 17.6%, III in 2.9%, e solamente 1 paziente era in class IV (0.11%). L'*Ability index* è risultato essere di grado I nell'82% dei pazienti, grado II in 13.7% e grado III in 2.3%. La sopravvivenza globale a 5 anni era stimata dell'82.6% , 99% e 91.8% per i gruppi I, II, III rispettivamente. La libertà da eventi avversi a 5 anni dall'intervento veniva stimata del 91% per pazienti non cianotici, mentre era stimata pari al 63.9 % per i pazienti con cianosi preoperatoria ($p < 0.0001$). L'analisi statistica multivariata secondo Cox identifica tra i più potenti fattori incrementali di rischio per la sopravvivenza la classe NYHA preoperatoria IV nei pazienti cianotici (Hazard Ratio-HR- 8.6, p value 0.001), la classe NYHA preoperatoria III (HR 2.7, p value 0.023), ed il reintervento (HR 2.3, p value 0.029). Inoltre, la elaborazione statistica per la valutazione della morbilità postoperatoria a distanza espressa come classe NYHA superiore a 1, identifica tra i più potenti fattori incrementali di rischio il tempo di degenza in Terapia intensiva (HR 1.037, CI=1.002-1.072, p=0.036), il numero di interventi (HR 1,445 CI=1,1213-1,721, p<0.001), la presenza di cianosi preoperatoria (HR 1,555, CI1,035-2,335, p=0,034), la presenza di aritmie prima dell'intervento chirurgico (HR

1,124, CI=1,040-1,215, p=0,03), la classe preoperatoria NYHA superiore a 1 (Hazard Ratio 1,573, CI=0,954-2,593, p=0.076), e l'età maggiore di 40 anni (HR 1,466, CI1,014-2,119, p=0.042).

Conclusioni

La chirurgia per le cardiopatie congenite nell'età adulta è una terapia possibile e gravata da basso rischio operatorio. Tuttavia, i pazienti che presentino cianosi preoperatoria mostrano un maggiore rischio chirurgico e una maggiore incidenza di complicazioni e morbilità tardivamente. Inoltre, condizioni cliniche preoperatorie migliori sono statisticamente correlate con un migliore risultato clinico, sia nell'immediato in termini di sopravvivenza, che a distanza, in termini di morbilità. Pertanto, nei pazienti adulti con cardiopatia congenita operabile, la terapia chirurgica tempestiva (cioè prima che avvenga scompenso cardiaco e multiorganico) viene considerata di scelta.

Summary

Despite congenital heart malformations are currently treated in infancy and childhood, a great number of patients still need surgical treatment in adult age. For this reason, we have embarked on a multicentric study involving 7 major italian centers (Padova, Milano S.Donato, Milano Niguarda, Bergamo, Bologna, Massa, Napoli), so as to evaluate the impact of cardiac surgery in adults with congenital heart disease in our country and survival determinants. In addition, clinical late morbidity was analyzed in order to to evaluate correlated pre-operative and operative risk factors.

Methods

We collected data of 856 patients who underwent 1179 procedures from January,1st 2000 to December 31st 2004. Patients were divided into three groups: Group I- Palliation (3.1%): any operation performed to improve patient's clinical status without restoring normal anatomy or physiology. Bidirectional cavopulmonary anastomosis and pulmonary artery banding were the most frequent procedures.

Group II- Repair (69.7%): first operation performed in the patient, to achieve an anatomic or physiologic repair by separation of the pulmonary from systemic circulation (including also Fontan-types, and 1 and ½ ventricle repairs). Most frequent procedures were: atrial septal defect closure (35.8%), partial anomalous pulmonary venous connection repair (7.2%), ventricular septal defect closure (5.3%).

Group III- Reoperation (27.4%): all procedures performed after repair either anatomic or physiologic. The most frequent procedures were conduit replacement (9.8%), aortic (8.6%) or pulmonary valve replacement (7.7%) .

Results

Preoperatively 34.6% of patients were in NYHA class I, 48.4% in class II, 14.2% in class III and 2.8% in class IV. Sinus rhythm was present in 83%.

There were 1179 procedure performed in 856 patients (1.37 procedure/patient), with a hospital mortality of 3.1%. Overall mean intensive care unit stay was 2.3 days (range:1-102 days). Major complications were reported in 247 pts (28.8%), with postoperative arrhythmias being the most frequent (26%).

At mean follow-up of 22 months (range 1 month- 5.5 years), 86% of data were available. Late death occurred in 5 patients (0.5%). Patients were in NYHA class I in 79.3 % , II in 17.6%, III in 2.9%, and only one patient in class IV (0.11%). Ability index was class I in 82%, class II in 13.7% and class III in 2.3%. Overall survival estimates is 82.6% , 99% and 91.8% at 5 years for groups I, II, III respectively. Freedom from adverse events at 5 years is 91% for acyanotic vs 63.9 % for preoperative cyanotic patients ($p < 0.0001$). Multivariate Cox analysis identifies among the most powerful incremental risk factors for survival preoperative NYHA class IV in cyanotic patients (Hazard Ratio-HR- 8.6, p value 0.001), preoperative NYHA class III (HR 2.7, p value 0.023), and reoperation (HR 2.3, p value 0.029). In addition, multivariate Cox analysis for postoperative morbidity expressed as NYHA class greater than 1, identifies among the most powerful incremental risk factors the length of ICU stay (HR 1.037, CI=1.002-1.072, p=0.036), number of operations (HR 1,445 CI=1,1213-1,721, p<0.001), cyanosis (HR 1,555, CI1,035-2,335, p=0,034), alteration of cardiac rhythm before surgery (HR 1,124, CI=1,040-1,215, p=0,03), pre-operative NYHA class>1 (Hazard Ratio 1,573, CI=0,954-2,593, p=0.076), age > 40y (HR 1,466, CI1,014-2,119, p=0.042).

Conclusions

Surgery for congenital heart disease in adult age is a safe and a low risk treatment. However patients with preoperative cyanosis show a higher incidence of late non-fatal complications. In addition, better preoperative clinical conditions are correlated with better late clinical outcomes, thus early repair (before cardiac and non cardiac organ deterioration occurs) is advocated.

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SECTION I

General Overview

Introduction

Congenital heart disease (CHD) is one of the most common inborn defects, with an extimated incidence of 8/1000 live newborns. Cardiac malformations are currently treated in the pediatric age, with an overall early surgical mortality inferior to 5%.[1]Prior to advent of surgery, less than 20% of children with congenital heart malformations survived to adult life.[2] Since the late '60s, the extraordinary advances in cardiac surgery, intensive care and non-invasive diagnosis have drastically modified the natural history of almost all CHD. Currently, most deaths for CHD occur in adults, who may have had or not repair or any kind of surgery. In fact, approximately 85% of babies born with cardiovascular anomalies can expect to reach adulthood, and with continued improvement in surgical technique, this could increase further in the next future. [3] This improvement has selected a growing number of newborns and infants who have survived through adolescence, until adulthood. [4]

This growing population of adults may require lifelong cardiac and non cardiac specific services. These adults constitute a new medical community which is commonly called GUCH (or "Grown Up Congenital Heart" disease),[5] or adults with CHD (ACHD).[6] In the year 2000, the number of adult patients with CHD was calculated to be equal to pediatric patients, and it is expected that in 20 years from now, the number of ACHD will exceed those in pediatric care by a considerable margin.[4,7]

Wren and associates [8] reviewed all births in one health region (Newcastle, United Kingdom) between 1985 and 1994, and noted 1.942 cases of CHD in a population of 377.310 live births (incidence of 5.2 per 1.000). Of these newborns, 1.514 were predicted to survive > 16 years. Because additional diagnoses are sometimes made later in childhood, at least 2.192 children were expected to grow older than 16 years. In addition, an estimated 784 patients would require follow up in adult life. These figures are important because they can predict the need for follow up of adults with CHD, for > 200 cases per 100.000 live births, or >1.600 cases every year in the United Kingdom (assuming a population of 50 million).

Based on this study model, it is expected that in Italy there are currently 60.000 to 100.000 adult patients with congenital heart disease, requiring follow up.[9]

Warnes and associates have clearly identified the entity of this population of adults with CHD in United States, which currently reaches about 800,000 people affected by simple, moderate or complex CHD.[6]

According to these figures, the impact of such a huge population on international medical community is expected to be relevant. In addition, we have to consider the fact that these figures may not represent the real situation, since at least 10% of adults with CHD (such as secundum type atrial septal defects, Ebstein's anomaly or congenitally corrected transposition), due to mild symptoms, may be not diagnosed until they reach adulthood.[6] Moreover, collection of real numbers is extremely difficult since many patients, even those with complex heart defects, often attend non-specialized clinics or are totally lost to follow up.[10]

Adult patients with CHD referred to regional Adult Congenital Heart Disease (ACHD) Centers are commonly in their second or third decade of life, as it is demonstrated by the age range of patients seen in two mayor tertiary care centers (Mayo Clinic, Rochester Minnesota, United States, and Toronto Clinic, Toronto, Canada), in which 48% and 57% of patients were ranging between 21 and 40 years of age, respectively.[6]

Nowadays, it is well documented that most patients with CHD, who were submitted to surgical intervention in infancy, had a reparative but not corrective surgery.[11] Many of them face the prospect of further operations, arrhythmias, complications and increased risk of heart failure and premature death if managed inappropriately. The impact of such a peculiar group of patients on medical community is relevant. This population of adults has special needs and peculiar problems.[4,5,9,12] As outlined by Warnes,[11] despite great advances in diagnosis and therapy occurred in the last decades, many intracardiac repairs and circulations may still not function "normally". Residual problems are common, and they may need a lifelong follow up, with appropriate treatment and care, either medical, or surgical.

Basing on these data, these adults with CHD may be *"classified"* depending on their heart malformation in *Complex* CHD, *Moderate severity* CHD and *Simple* CHD. These groups are presented in detail in Tables 1,2,3.

Mayor concern is obviously expressed for patients with a complex CHD (Table 1). According to Wren et al, [8] among adults with CHD, 25-50% have a complex one, that is doomed to increase year by year. These more complex patients are obviously vulnerable to additional acquired co-morbidities that impact both their cardiac and medical care, including hypertension, pulmonary, renal, and myocardial disease, and coronary artery disease. It is estimated that about 55% of the adult patient population is at medium to high risk (defined as significant risk for premature death, re-operation and complications) and thus need to be seen regularly in an regional ACHD center and followed for life. These patients include those with tricuspid atresia, single ventricle physiology anomalies, transposition variants, complex Ebstein's anomaly, tetralogy of Fallot, pulmonary vascular disease, and complex septal defects.[6] Periodic review at a regional ACHD center continue to offer advantage over a general cardiac evaluation, specially in regards to the timing and type of intervention, follow up strategy, and general recommendations.[13]

On the other hand, approximately 45% of patients with mild CHD, such as a small ventricular septal defect, or mild pulmonary stenosis, will not require regular follow up in a regional ACHD center, but might benefit from at least one review at such center at the discretion of the patient's physician (see Table 3).[6]

In between, moderate complexity patients (as described in Table 2) account for a portion of patients who should be seen periodically at a regional ACHD center.

The profile of this peculiar population of adults will change over the years, not only because of advancing age, but also for improved survival of patients with complex anomalies. In addition, since complete repair of most CHD is currently performed in infancy, and operative procedures are on continuous evolution, there will be changes in the anticipated disease patterns. Many adult survivors will have different hemodynamic and cardiac problems from those currently seen. For example, an infant with transposition of the great arteries will no longer have a Mustard or Senning

procedure (with its late problems of systemic ventricular dysfunction and arrhythmias), but might be anticipated to have an arterial switch procedure and encounter quite different cardiac sequelae in adult life, such as aortic valve incompetence, which needs thorough evaluation.

It is self evident that this population represents an extraordinary challenge for the international medical community, who is still un-prepared to face the specific requirements of ACHD patients. This "new population" no longer fits within the traditional divisions of training and practice, which have separated adult and pediatric cardiology. Adult cardiologists are not equipped to deal with the range and complexity of grown up patients with CHD, whereas pediatric cardiologists cannot be expected to manage the several acquired adult diseases in a pediatric medical environment. Currently, care has been delivered by a number of enthusiastic and devoted centers and physicians, who have managed the complex medical, surgical and phsychosocial issues of these patients, basing on their growing experience and perseverance. In most countries, an organized system is still lacking. This is needed for continued provision of excellence in clinical care, accumulation of knowledge about late outcome of management strategies in childhood (with feedback to pediatric practice) as well as for training.

The need to reintegrate pediatric and adult cardiac services and, most important, to provide a smooth transition for adolescents is clear.

All these reasons have stimulated debate in the international community and different task forces from various medical associations have proposed clinical guidelines. Aim of these guidelines is to present all relevant evidences on a particular issue in order to help physicians in everyday clinical decision making.

In 1994, the European Society of Cardiology recognized the need for specialized care of this group of patients by establishing a working group for adults with CHD, also known as GUCH patients. Since then, size and complexity of these patients have been increasing. The first set of guidelines for the management of adults with CHD was commissioned by the Canadian Cardiovascular Society in 1998 [14], and recently revised by an international panel of experts.[15] A great number of guidelines have been subsequently issued in the recent years by different

organizations, such as European Society of Cardiology (ESC),[16] American Heart Association (AHA), American College of Cardiology (ACC). [17]

All these guidelines are easily available by means of link to websites, so as to facilitate physician to update their knowledge in some difficult tasks. Both physicians and patients who are interested in accessing such information may connect to it on www.achd-library.com or access to www.escardio.org for the most updated reccomendations by ESC. These guidelines provide point to point summaries of the major conditions including management recommendations and supporting references.

A new organization of care for adult patients with a congenital heart disease

The arrangement of transition of treatment of an adult with a complex or moderately severe CHD from the pediatric cardiology clinic to the adult service is a particular challenge.[18] A special transition clinic would be highly desirable to minimize anxiety for the patients and their families as well as disruption in care provision.[18] This process aims to realize that the patient and his/her family can adapt to abandon the firm bond with the pediatric cardiologist, and learn smoothly to rely on the expertise of the new figure of the adult congenital cardiologist. This process is begun by pediatric cardiologists that inform the patients regarding transition from around the age of 12-14 years, with final transition to the age of 18, and actively take part to the transition to an adult congenital cardiologist.[19] The patient and family should be given a detailed written therapeutical plan that include informations about treatment in childhood (such as previous investigations and operations), should be educated about their physical condition and the necessity of a regular follow up at a specialized clinic, about their medications and possible side effects and interactions, about need of endocarditis prophilaxis. They also require guidance concerning exercise, contraception, pregnancy, career planning, travel. They must be informed of possible future complications of their condition and likely associated symptoms. They must know how to operate within the adult healthcare system so as to obtain appropriate medical advice. [19]

This process has to be gradual, and children with CHD must be sensitized to their condition, so as to reach adolescence and adulthood with complete understanding of the implications of their CHD. Primary care physicians have to be involved in this process so as to facilitate the graduality of it for patient and family.[19]

Currently, healthcare needs of most adults with CHD are not being met in most western countries because of shortage of either fully trained and experienced physicians, or centres of excellence that may lead the regional and national efforts to provide high quality care. In particular,

it is fundamental the establishment of major full equipped centers, that contrast with the excess of partial service centers currently caring for this population. To be effective, the major centers must have sufficient volumes of patients and procedures so as to develope and maintain high levels of performance.[20] There is an urgent need of leadership from government and professional organizations to work towards such a cohordinated system aimed at optimizing patient care.

Improvement must start developing and employing the skilled personnel needed to lead and help to coordinate this work in specialist centers.This would serve to optimize care for all these patients and reduce care mismanaging, to consolidate specialized resources for the care of these patients, to provide sufficient number of patients to facilitate specialist training for medical and non medical personnel, and to maintain staff and faculty competence and special skills in the treatment of adults with CHD.[21]

The specialist unit (also named ACHD center) should be located in an adult medical environment with multidisciplinary speciality provision and be associated with strong pediatric cardiology groups. All specialized centers for pediatric cardiology should have defined care pathways for the appropriate transfer of care of patients to a grown up or adult congenital heart disease service. One regional ACHD center is supposed to serve 5-10 million people.[16,17,21] The ACHD cardiologist should be familiar with echocardiography and diagnostic cardiac catheterization and at least one per center should have experience with interventional cardiology. Access to an electrophysiologist with expertise in arrhythmia management in CHD, pacemaker insertion, ablation and defibrillator implantation is essential. Specilist imaging including magnetic resonance imaging and chest tomography is required. There should be close links with other specialist departments and in particular the provision of a joint service with obstetrics to manage high risk pregnancies. Access to cardiac pathology with an interest in congenital cardiac malformations is highly desirable. A minimum of two congenital cardiac surgeons is needed, together with the appropriate anesthesiologists and intensive care and surgical team. An association with a transplant service should be established.

As a rule, patient attendance at a regional care center is required for:

- the initial assessment of suspected or known CHD;
- follow up and continuing care of patients with moderate and complex lesions;
- further surgical and non surgical intervention;
- risk assessment and support for non cardiac surgery and pregnancy.

However, the majority of adults with CHD will still require local follow up for geographic, social and/or health economic reasons. Primary care physicians and general adult cardiologists must, therefore, have some understanding of the health needs and special issues in the general medical management of this relatively new adult patient population. Cardiologists and primary care phisicians have to be encouraged to establish a referral relationship with the specialist centers, and this should include provision of timely telephone advice, informal consultation, rapid consultant referals as well as collaboration in patient follow up. It is highly important that these community and hospital physicians recognize promptly when to refer these patients to an experienced center. For this reason, published management guidelines may assist in this process.

As part of this new concept of treatment of adult patients with CHD and organization of care, published guidelines stress the importance of an adequate training of specialists that work with patients with CHD.[16,22] Appropriate specialist cardiologists may come from trainees in either pediatric or adult cardiology, and specific training programs have been proposed for both kind of trainees.[16,22] The essential thing is that they have the following knowledge and skills: 1. expertise of CHD and management in infancy and childhood; 2. expertise in adult cardiology including coronary artery disease management; 3. expertise in general medicine and non-cardiac diagnosis in adults; 4. skills in echocardiography (included transesophageal echocardiography), cardiac catheterization, pacing and electrophisiology, postoperative care; 4. understanding of physiological changes of pregnancy; 5. understanding of psychosocial aspects of adolescence; 6. experience of life style counselling for adolescents and adults with CHD; 7. expertise in clinical research methodology.[6,16]

The training requirements for surgeon working in the specialist ACHD centers also need careful consideration and are currently being considered by a separate committee. A skilled and versatile cardiovascular surgeon is a key-point in the tertiary care center.[22] The surgeon must have

extensive experience in congenital and acquired cardiovascular disorders, before acquiring expertise in the surgery of adults with CHD.[16,22]

In order to ensure a minimum level of medical and surgical activity required to develop medical surgical skills and optimize results, reorganization and centralization of care for pediatric cardiology and cardiac surgery is in progress in most countries.

In 2006, in Italy, nine major tertiary level centers (Bergamo, Bologna, Genua, Massa, Milano San Donato, Padua, Palermo, Rome, Turin), with expertise in medical and surgical management of CHD, have joined together in the "Baby Heart Project",[23] whose aim is to define national guidelines and minimum structural requirements for management of CHD in infancy and child-hood, but also in the adult age, that characterize "excellence" of a tertiary care center. This effort by all these professionals have produced the *Baby Heart Handbook for excellence*, that is going to be finalized in 2008 and presented to the Italian Ministry of Health. This achievement represents a unique attempt in Europe that aims to optimize resources and organization of care in order to achieve excellence in treatment of CHD not only in infancy and childhood, but also in the grown up and adult patients.

Medical Issues

Ventricular function

The most important part of preoperative assessement, perioperative management and later follow up of any patient with CHD is the accurate measurement of ventricular performance. There is still non consensus as to the ideal technique, modality or index to apply to the analysis of left ventricular function in the biventricular circulation of adults with acquired heart disease. The issues are amplified in those with CHD. Abnormal ventricular geometry, the effects of previous surgery, extraordinary loading conditions, chronic hypoxaemia, all conspire to make meaningful analysis difficult. Furthermore, right ventricular dysfunction may be equally or more important in these patients, and similarly may be affected by the supplementary circulatory abnormality. Nonetheless, assessment of functional performance, timing of intervention, and analysis of response is central to the care of patients. It is advisable that any unit dealing with adult with CHD will require expertise in quantitative transthoracic and transesophageal echocardiography and Doppler evaluation, magnetic resonance imaging, radionuclide perfusion analysis, graded exercise function and hemodinamic assessment.

Echo Doppler evaluation

Transthoracic echo windows for parasternal left ventricular short axis function and four chamber interrogation for ventricular long axis function and Doppler studies are rarely difficult to obtain.[16] However, most of measures applied to the assessment of systolic and diastolic dysfunction in acquired heart disease are applicable to the corrected biventricular circulation, despite many caveats must be considered, such as reliability of calculated left ventricular ejection fraction when a significant regional incohordination or a residual left to right shunt is present.

In addition, in abnormally connected hearts, a reduced shortening of a systemic right ventricle may be considered a physiologic adaptation to increased afterload, and the presence of an intraatrial baffle (such as Mustard or Senning procedure) may render the Doppler inflow

measurement difficult to interpret. Regional incohordination is usual in the systemic single ventricle anomalies, and thus diastolic Doppler characteristics must be interpreted with an understanding of the inherently reduced resting preload. The potential of tissue Doppler imaging which demonstrates regional ventricular wall incohordination, is large and appropriate to the quantitative study of these patients.[24] However, in adults with CHD, the demonstration of a modification in heart function is maybe more important than the grossly abnormal single measurement.

Magnetic resonance imaging

Ventricular volume measurements are no less immune to the caveats regarding load than contractility indices obtained by echocardiography. Similarly, these measures remain crucial in clinical decision making. Magnetic resonance imaging is one of the most reliable imaging technique in its ability to measure ventricular volumes, ventricular outflow tracts and proximal pulmonary arterial tree, and assess volumetrically the degree of pulmonary regurgitation in status post Fallot repair.[25] In addition, it is able to analize ventricular mass and its hypertrophy, thickening, vector change and contractile geometry. Finally, it is able to visualize areas of fibrosis in the myocardium using the late Gadolinium enhancement in either ischemic or non ischemic cardiomiopaties.[26-28]

Radionuclide investigations

Regional abnormalities of myocardial perfusion at a microvascular level may be recongnized and may help in cardiac evaluation. On the other side, pulmonary scintigraphy is a mildly invasvie technique that can evaluate pulmonary ventilation and perfusion mismatch after multiple procedures on the pulmonary vasculature.[29]

Cardiac catheterization

Despite simple angiographic dimension based indices of ventricular performance add little to similar indices measurable by magnetic resonance imaging or echocardiography, cardiac catheterization may remain an optimal investigation tool when other techniques are contraindicated, or not reproducible.

Arrhythmias and pacemakers

Arrhyhmias are the main reason for hospitalization in adults with CHD.[5] Factors that predispose to arrhythmias include the underlying cardiac defect itself (such as atrial isomerism, or Ebstein's anomaly with intrinsic anomaly of conduction tissues pathways), hemodinamic changes as part of the natural history (such as myocardial fibrosis, ventricular hypertrophy, atrial and ventricular enlargement), surgical repair and scarring and residual postoperative hemodynamic abnormalities. This strong electrical and mechanical connection emphasizes the need for electrophysiological assessment and management to be closely integrated with care of the underlying CHD. Tachyarrhythmias associated with CHD are frequently amenable of catheter ablation, although the procedure may pose technical difficulties that require prolonged fluoroscopy times or more than one ablation procedure.[30] Surgical repair of residual hemodynamic abnormalities may be the most important tool in the treatment of arrhythmia. In fact, these patients may benefit from an approach integrating the principles of catheter ablation into the surgical repair of congenital heart disease. This rational integrated approach justifies limitation of catheter ablation procedure to a single procedure; if the procedure results unsuccessful or arrhythmia recurs, associated surgical anti-arrhythmia procedures may be performed simultaneously to surgical correction of the cardiac anomaly. Recognition of the limitations of the catheter ablation technique together with integration of the knowledge gained from this technique into the surgical repair of congenital heart disease, opens new possibilities for single stage therapy of structural and rhythm abnormalities, especially in adults with congenital heart disease.[31]

Supraventricular arrhythmias are the more common than ventricular ones. Sinus node dysfunction is common after atrial surgery (such as Fontan or Mustard /Senning procedures), and supraventricular tachycardia is becoming more frequent with longer follow up.[32-33] On the other side, the propensity for late onset ventricular tachy-arrhythmias is well documented in patients with tetralogy of Fallot, and sudden cardiac death represents the most common mode of demise in infant survivors,[34,35] with an actuarial incidence of sustained ventricular tachycardia and sudden death

estimated as high as 11.9% and 8.3%, respectively, 35 years after surgical repair.[34] Prolungation of QRS has been observed with right ventricular dilatation and pulmonary regurgitation in tetralogy of Fallot follow up, and this is used as an effective marker for risk stratification.[36]

Pharmacological therapy of arrhythmias may be limited by the hemodinamic side effects, concomitant sinus node dysfunction and by desire for pregnancy. Amiodarone therapy is demonstrated to be the most effective, despite its side effects are particularly significant in adults with CHD.[37]

Catheter ablation and sugical approaches have been increasingly applied.[38] However, despite sophisticated current mapping techniques, success rates remain lower than those in structurally normal hearts, mostly because arrhythmia circuits are complicated and often multiple, and intracardiac geometry is often abnormal.[39] As above mentioned, surgery associated to antiarrhythmia treatment is a rational strategy to optimize results.[31]

Pacing in adult with CHD is often difficult due to limited, abnormal access to the heart as well as the abnormal cardiac anatomy itself. For example, the right atrial appendage may be distorted or absent, and active fixation electrodes are required.[40] In addition, intracardiac shunts and thromboembolic risk may preclude an endocardial approach. A rate responsive system is often required, and dual chamber pacing is highly desirable, especially in univentricular hearts.

Implantable cardioverter defibrillator trials in patients with ischemic heart disease or dilated cardiomiopathy have shown survival benefit in selected subgroups, and these devices are being used with increasing frequency in adults with CHD, such as in patients with tetralogy of Fallot, which currently represent the largest subgroup of implantable cardioverter defibrillator recipients with congenital heart disease.[41-42] However, despite high effectiveness, late lead related complications are reported to be common.[43]

The need for risk stratification, understanding of anatomy and function, choice of drug, catheter/implantable defibrillator or surgical intervention emphasizes the importance of very close integration of the electro-physiologist with the ACHD cardiologists and surgeons.

Cyanosis

Cyanosis is the term to indicate the bluish skin color caused by presence of more than 5 gr/dl of reduced hemoglobin in blood capillary circuit (normal value is 2-2.5 gr/dl). This corresponds to an oxigen arterial saturation of about 70% when hemoglobin blood level are within normal range.

Right to left shunt associated to several CHD, and the resulting hypoxemia and cyanosis, have profound hematological consequences which may affect multiple organs.

Erithrocitosis and hemostatic dysfunction

The increase in red cell mass accompanies chronic cyanosis as a compensatory response to improve oxygen transport, and it may rise up to 3 times normal, and the total blood volume may reach 100ml/kg.[44] The consequent hyperviscosity increases the risk of thrombosis and stroke. Cyanotic patients can fall into one of the following category: 1. most patients have a stable hemoglobin and compensated erythropoiesis, and symptoms of hyperviscosity are rare; 2. others have decompensated erythropoiesis, with uncontrolled production od red cells and symptoms of hyperviscosity are frequent.[45] Therapeutical interventions such as phlebotomy are required when hemoglobin level is greater than 20g/dl, or hematocrit is greater than 65%. In fact, at these levels, patient may experienced the so called *hyperviscosity syndrome*, which mainly consists of headache, faintness, visual disturbances, myalgias, muscle weakness, paresthesias and poor concentration.[45-46] These symptoms are related to hypoxia, hyperviscosity itself and iron deficiency. They are usually relieved by removal of one unit of blood, always replaced by an equal volume of saline or destrose. Since this procedure may further stimulate erythropoietin production and consequently bone marrow red cells production, it is advisable to limit therapeutical phlebotomies to 1-3 per year. Repeated phlebotomies deplete iron storages. In addition, iron deficiencies in adults with CHD may occur from red blood cell lysis due to increased turbulence through stenotic or incompetent valves, stenotic conduits, or shear injuries from previously placed patches. These phenomena may result in production of iron deficient microcytic red cells which are less deformable and compliant, and increase the risk of hyperviscosity. Treatment of iron deficiency in a patient with destabilized

erithropoiesis is difficult since oral iron intake frequently results in rapid increase in red blood cells.[44,46]

Furthermore, it is typical of cyanotic patients that platelet count is reduced and platelet function abnormal, together with clotting factor deficiencies.[46] The etiology is not well known yet, but it includes the combination of hypofibrinogenemia, accelerated fibrinolysis and clotting pathways disorders.[44,46] These abnormalities result in a bleeding tendency, either spontaneous or perioperatively. Bleeding risks may be mild such as easy bruising, gingival bleeding, epistaxis, menorrhagia, gastric bleeding, but also more severe such as hemoptysis from pulmonary hemorrhage, that sometimes may be fatal. For these reasons, anticoagulation and use of antiplatelets agents should be well meditated and confined to well defined indications, with a careful monitoring of the degree of anticoagulation.

Renal function

Chronic cyanosis in patients with CHD is associated with decreased glomerular filtration rate and proteinuria. This is caused by hypercellular congested glomeruli with segmental sclerosis and basement membrane thickening.[47] Nonsteroidal anti-inflammatory drugs and amino-glicosides may worsen glomerular function, therefore careful prescription is advisable. Since cardiac catheterization and contrast agents may pose an increased risk for renal failure, those patient who required this procedure should be well hydrated before and after the procedure, and a minimal amount of contrast agent should be used for imaging.

Abnormal urate clearence frequently occurrs and this, in addition to increased turnover of red cells, leads to hyperuricemia, which is usually well tolerated, with occurrence of acute gouts in 2% only of adults with cyanotic CHD, and it usually does not require therapy.[48]

Gallstones

Bilirubin may be produced by the breakdown of Haeme in chronic cyanosis, and calcium bilirubinate gallstones are common in adults with CHD.[49]

Orthopedic complications

Hypertrophic osteoarthropathy with thickened irregular periosteoum occurs in adult age. This is sometimes accompanied by aching and tenderness in the long bones of the legs. Scoliosis is another important complication which may be sufficiently severe to compromise pulmonary function.[16]

Skin

Acne on the face and trunk often accompanies cyanosis. This is not only a cosmetic concern, but also a potential source of sepsis and endocarditis.[16]

Pulmonary vascular disease and Eisenmenger's syndrome

In 1897, Victor Eisenmenger described for the first time a 32 year old man with a non restrictive ventricular septal defect, cyanosis and dyspnea, who died following fatal hemoptysis.[50] Sixty years later, Paul Wood described the clinical and pathological features of 127 patients with "Eisenmenger Syndrome",[51] an entity that he coined and that consisted in the association of *pulmonary hypertension at systemic level, due to high pulmonary vascular resistances, with reversed or bidirectional intracardiac shunt at any level.*

In the last decades, early diagnosis and improved surgical results of repair of congenital heart disease in infancy have drastically reduced the number of adolescents and adults with pulmonary vascular disease and Eisenmenger's syndrome. However, a considerable number of such patients still need medical attention. Despite this condition is irreversible and progressive, a careful management of these patients can improve considerably mortality and morbidity.[52]

Many patients with Eisenmenger's syndrome maintain a good quality of life in early adulthood but subsequently the reduction of effort tolerance and increased cyanosis is usually progressive. As in other cyanotic patients, Eisenmenger's ones are prone to spontaneous bleeding and have abnormal hemostasis and platelet function. Thus, anticoagulation therapy, which is effective in primary pulmonary hypertension, is a difficult and controversial decision in such patients.

The most relevant events are pulmonary and cerebral complications. Hemoptysis may be due to both pulmonary infarction or to ruptured blood vessels, and it may be precipitated by stress/excitement or a chest infection and can be copious and fatal. However, it is difficult to identify patients with high risk of thromboembolic complications, either at pulmonary or at cerebral level. Mean age of death of patients with Eisenmenger's syndrome and simple CHD was 32.5 years compared to 25.8 years in thosed with complex CHD.[52] Eisenmenger's patients are at particular risk from pregnancy, with about 50% maternal fatality after delivery, even in those with moderate pulmonary hypertension,[53]and have an increased surgical risk for non cardiac procedures, despite

appearingly innocuous.[53] A general policy of "non intervention" unless absolutely indicated is recommended to avoid destabilizing the *balanced physiology* of the delicate Eisenmenger's patient.

Various treatments such as systemic vasodilators, prostacycline, endothelin antagonists and Sildenafil have shown some effect, but none is absolutely convincing yet.[53] Long term oxigen therapy at home for a minimum of 12-15 hours per day may improve symptoms, but does not modify survival.[16] Recently heart and lung transplantation is considered for some patients,[54] despite a high risk of early mortality.

Infective endocarditis

Infective endocarditis is a condition characterized by a microbiological inflammation of the lining-endocardium of the heart chambers, valves and vessels, as described by Osler in 1885. Predisposing factors for infective endocarditis are a susceptible cardiac or vascular substrate (lesions associated with high velocity flow, jet impact and focal increases in the rate of shear), and a source of bacteremia.

While at the beginning of the twentieth century a large proportion of patients with infective endocarditis had previous rheumatic heart disease, nowadays it is more observed in patients with complex CHD who have survived to adulthood. Most adults with CHD have a life long risk of infective endocarditis. Thus, education of patients and families, but also of primary care physicians about the risks and importance of early diagnosis needs constant reinforcement. There may be a wide variety of portals of entry of infection, in addition to dental and surgical procedures, such as body piercing, acne, tattoing and intrauterine contraceptive devices.[55]

Delay in diagnosis and referral is common, and antibiotics are often prescribed before diagnosis of endocarditis is considered or blood cultures taken. Since transthoracic echocardiography may miss vegetations, use of transesophageal echocardiography is advisable.

Prompt referral to a ACHD unit is indicated as hemodynamic deterioration may be rapid and surgical management be required soon.

However, not all patients with CHD are at risk of endocarditis, such as secundum type atrial septal defects, totally anomalous pulmonary venous connection and is rare after closure of ventricular septal defect, in pulmonary valve stenosis and small patent ductus arteriosus. Specific antibiotic regimes have been published and are currently those followed by international community.[56,57]

Pregnancy in adults with congenital heart disease

Most adult patients with CHD can tolerate pregnancy if they received proper care.[58,59] Pregnancy counselling and evaluation is mandatory, and should include physical examination, assessment of hemodynamic status (usually including echocardiography) and functional capacity. A review of medications is necessary to avoid any drug which may be deleterious to the fetal development. A complete family history is to be taken so as to offer a complete informed genetic counselling.

Patient are stratified into high, medium and low risk. The highest maternal risk is associated with Eisenmenger's syndrome, with a maternal mortality greater than 50%, often after delivery.[53] The number of mothers with complex postoperative circulations (such as Fontan or Mustard/Senning) is small and risk stratification is difficult.[60,61] High risk patients include those with significant aortic stenosis (mean gradient greater than 40 mm Hg, valve area < 0.7 cm^2), significant coarctation, significant mitral stenosis, impaired ventricular function, mechanical prosthetic valve, pulmonary hypertension, Marfan's syndrome, cyanotic heart disease. These patients require: iron and prenatal vitamin supplementation to reduce anemia; constant monitoring of maternal and fetal well-being; fetal cardiac echocardiography, to evaluate potential fetal CHD; bed rest in very high risk patients; vaginal delivery is preferable to cesarean section unless there are obstetric indications; cardiac monitoring during delivery in patients with fragile hemodynamic status.

On the other side, pregnancy in women with CHD not complicated by Eisenmenger's syndrome is associated with low mortality.[62]

The managing of patients with CHD and mechanical valve prosthesis is challenging. Warfarin treatment is the safer one for the mother, but is associated with fetal embriopathy. However this risk is small if warfarin dose is inferior to 5 mg/day.[63] Heparin treatment is usually employed as a bridge therapy during pregnancy and delivery, but may be associated with thromboembolic complications.[64] Role of low molecular weight heparin is not clarified yet.

Cyanotic heart disease also poses a significant risk to fetus and this is proportional to the degree of maternal hypoxia. Low birth weight for gestational age and prematurity are common with maternal cyanosis, and if arterial oxigen saturation is lower than 85%, only 12% of pregnancies are successful.[65]

Patients who should be counselled against pregnancy include those with Eisenmenger syndrome, Marfan syndrome with dilated aortic root, severe aortic stenosis or coarctation, systemic ventricular ejection fraction lower than 35%.[16] Pregnancy of these high risk women with CHD has to be managed by a specialized unit that includes an obstetrician, an ACHD cardiologist, an anesthesiologist and a pediatrician-neonatologist. This team should be involved from early pregnancy and plan monitoring of pregnancy, mode of delivery and postdelivery care.[16]

Finally, medical or surgical termination of pregnancy in high and medium risk patients requires a careful monitoring and should be done in regional ACHD centers.[16]

Contraception

The risks of pregnancy vary greatly in adults with CHD, and must be weighed against the risks of contraception. Systematic studies, however, on contraception in women with congenital heart disease are lacking.[66] Patient compliance and sexual behaviour must be considered, as they will affect contraceptive efficacy and the incidence of complications.

Usually, the patient chooses her own preferred method, but the physician should provide informed advice. Often, there is no ideal method and the least hazardous one is indicated. Barrier methods are safe from a cardiovascular standpoint and have a high degree of contraceptive efficacy in compliant couples and women >35 years. Low dose estrogen combined oral contraceptive pills

are very efficacious, but their thrombogenic properties may make them hazardous in certain situations, such as after the Fontan operation or in patients with atrial fibrillation/flutter. Combined oral contraceptives are contraindicated in patients at risk of paradoxical embolism, unless they are also receiving anticoagulants. The estrogen containing contraceptive pill should not be used in patients with pulmonary or systemic hypertension. Medroxyprogesterone injection (Depo-Provera®), subcutaneous deposition of levonorgestrel (Norplant®) or progesterone only pills are effective, but may cause fluid retention and should not be used in patients with heart failure.[67] Depression and breakthrough bleeding may prevent the use of progesterone pills and there is a higher failure rate than with the combined oral contraceptives.[67]

Intrauterine devices have been associated with an increased incidence of pelvic inflammatory disease and increased risk of endocarditis, especially in cyanotic women, those with artificial valves/shunts/conduits and those with previous endocarditis. However, the reported number of women with intrauterine devices complicated by endocarditis is very low and concerns mainly old-fashioned intrauterine devices.[68] However, in women who have not experienced pregnancy, intrauterine devices are not a first choice.[68]

Surgical sterilization may be considered in a woman at high risk from pregnancy, but should not be undertaken without discussion of potential medical advances, which might later allow pregnancy at an acceptable risk.[19]

Genetic counseling

Genetic counseling regarding etiology, inheritance, recurrence risk, and prenatal diagnosis options is advisable in all patients with CHD. It is important to obtain the patient's prenatal and postnatal history, including maternal exposure to teratogens, detailed family history, and to perform a thorough examination looking for congenital abnormalities.[68]

In all women contemplating pregnancy, exposure to teratogens should be investigated; in some cases, finding an alternative medication will be necessary. Angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists should not be used during pregnancy. Warfarin and amiodarone should be substituted. No medications, including over-the-counter preparations, should be taken during pregnancy without physician approval. Preconception consumption of multivitamins including folic acid decreases the incidence of CHD.[69]

Knowledge of the genetic basis of CHD is expanding rapidly. The role of genetic testing is evolving, and genetic counseling should be made available. The recurrence rate of CHD in offspring is variable, ranging from 3% to 50%.[70] A higher recurrence risk when the mother rather than the father is affected has raised the possibility of mitochondrial inheritance in some patients.[70]

Diseases with a single gene disorder and/or chromosomal abnormalities are associated with a high recurrence rate. In Marfan, Noonan, and Holt-Oram syndromes, there is a 50% risk of recurrence. Fetal echocardiography at 16 to 18 weeks gestation should be available to all patients with CHD. Chorionic villus sampling or amniocentesis may be useful after discussion of the potential risks and benefits.[19]

Co-morbidities and syndromes

Congenital and acquired co-morbidity is common in adults with CHD, and has an important effect on outcome and treatment. Cognitive and intellectual impairment may be a feature of co-existing heritable or chromosomal syndromes, which are present in 15–20% of congenital heart disease (Table 4). In fact, such patients are surviving into adult life with increasing frequency due to a more active approach to their treatment in childhood. Alternatively, late problems may result from neurological complications occurred in the perinatal and perioperative period and are likely to pose a serious burden on the families and to produce an important demand on medical and social institutions. Knowledge of the individual characteristics of such syndromes assists cardiac diagnosis and provides a clue to the presence of extra cardiac problems.

As above mentioned, chronic cyanosis is associated with pulmonary, metabolic and haematological problems, and sequelae from previous operations or catheterization may include arterial or venous peripheral occlusions and scars on the chest. Skeletal deformities are common in cyanotic states, especially when a lateral thoracotomy incision was performed in early life. There may also be visible chest or breast deformities, which have psychosocial impact.

Acquired heart disease will occur with increasing frequency as the population with congenital heart disease ages. Coronary artery disease and/or systemic hypertension can affect the haemodynamics of the congenital heart disease, requiring treatment of both the congenital and acquired disorders. This emphasizes the importance of the close collaboration and interaction between the specialist of an ACHD center and members of the general adult cardiology and internal medicine.[16]

Emergencies

Acute cardiac and non-cardiac emergencies occur in grown-ups with congenital heart disease and their optimal management may be above the ability of emergency room, general medical or adult cardiology staff. [71] The most frequent causes of admission are arrhythmia, infections, heart failure, cerebral ischaemia or aortic root problems. It may be possible to provide appropriate initial treatment in the local hospital. However, patients with more severe complications or more complex CHD will usually require transfer to the specialist centre.

Surgical issues

Cardiac surgery

Adolescents and adults with CHD who require surgery fall into three categories:[72]

(1)those who have not previously undergone operation;

(2)those who have had palliative surgery;

(3)those who have had reparative surgery.

In each category, there are several considerations, which make surgery, in this population, different from other types of cardiac surgery (either adult surgery for acquired heart disease or paediatric surgery for congenital defects).

There are strong arguments for concentrating surgical management of grown-up patients with CHD into specialist units for both care provision and training.[20] Surgery can be performed safely only by teams who have extensive experience in the management of congenital heart defects in infants and children as well as knowledge of the principles of conventional adult cardiac surgery.[16,22]

General planning of the operation

A first operation may be required in patients with simple defects (such as an atrial septal defect), but more often is needed in patients with complex malformations (i.e., pulmonary atresia with ventricular septal defect).

In patients who have previously undergone palliative or reparative surgery, the consequences of previous operations may add to the complexity of the management of the primary defect.

Thorough cardiac evaluation is mandatory in all cases. Surgical planning requires knowledge of the basic congenital malformation, of the previous surgical procedures and of the potential residual or recurrent lesions after these operations. The surgical team needs to be

intimately involved in the review of the diagnostic information, the decision-making and planning of the patients overall management. It is mandatory that the previous surgical reports be available.

In adult cardiac surgery for acquired heart disease, the risk and benefits of most surgical procedures are well established. In contrast, every adult with CHD poses specific problems, and the risk/benefit ratio of any proposed surgical procedure is often difficult to assess. It may therefore be difficult to communicate the necessary information about risks and benefits to the patient.

Specific surgical challenges

Preservation of myocardial function

In most patients, preoperative ventricular function is abnormal as a result of ventricular morphology, ventricular hypertrophy and long-standing pressure or volume overload. Myocardial fibrosis and ischemia as well as the sequelae of previous operations may also influence ventricular function and require meticulous preoperative assessment. To achieve optimal intraoperative preservation of myocardial function, aortic cross clamping should be avoided where possible. Most operations involving the right heart (e.g. replacement of right ventricle to pulmonary artery valved conduit or extracardiac Fontan procedure) can be carried out under normothermic cardiopulmonary bypass with mono or bicaval cannulation and a beating heart. When aortic cross clamping is necessary, cross-clamp time should be kept as short as possible and particular attention should be paid to cardioplegic myocardial preservation.

Strategies for myocardial protection and cardioplegia should include:

- use of the appropriate cardioplegic solution;
- induction of myocardial hypothermia using a cold blood cardioplegic solution;
- maintenance of diastolic arrest and hypothermia using multi-dose blood cardioplegia. This is particularly important in cyanotic adults, in whom non-coronary collateral vessels to the heart may result in wash out of cardioplegia and myocardial re-warming;
- enhanced warm blood reperfusion administered prior to aortic unclamping under careful pressure monitoring;

- adequate venting of the heart to avoid ventricular distention, wall tension increase and subsequent inadequate delivery of cardioplegic solution.

Blood salvage techniques

Autologous transfusion should be encouraged and be used wherever possible. In cyanotic patients, preoperative phlebotomy may be indicated to improve haemostatic status and the blood should be kept for autologous transfusion. Patients undergoing re-operation after initial reparative surgery are less likely to be cyanotic but they can usually predonate an adequate amount of blood and fresh frozen plasma. Iron repletion is indicated in most cases managed in this way. Erythropoietin administration may allow rapid and timely increases in haematocrit.

Patients with CHD are prone to intraoperative and postoperative bleeding because of relatively long suture lines, an increase in tissue vascularity, intrinsic haemostatic defects and prolonged periods of cardiopulmonary bypass. Replacement of consumed or inactivated clotting factors, particularly platelets, is an important requirement. Aprotinin has proved effective in reducing intraoperative bleeding, particularly in patients undergoing re-operation.[73,74] The routine intraoperative use of a cell saver system is important.

Ultrafiltration (either conventional during cardiopulmonary bypass or modified after cessation of bypass) has been shown to result in a significant reduction in the need for postoperative blood transfusion as well as to improve myocardial and lung function and extraction of soluble inflammatory mediators.[75-78]

Redo sternotomy

Reopening a sternal incision remains a crucial step, particularly when an enlarged right ventricle or an extracardiac conduit may be apposed or adherent to the back of the sternum, or when the aorta lies anteriorly (transposition of the great arteries). Review of prior operative notes, postero-anterior and lateral chest radiographs, and cardiac catheterization can aid in planning the resternotomy. If particular difficulty is anticipated, cannulation of the femoral vessels, institution of bypass and decompression of the heart before reopening the sternum are prudent precautions. Peripheral cardiopulmonary bypass can be converted to central atrial-aortic bypass once the heart

has been dissected from the surrounding structures. Once the sternum is opened, early identification of aorta and atrium should be achieved so that a rapid institution of cardiopulmonary bypass may be accomplished in the event of uncontrollable bleeding during dissection of the heart. Dissection plane has to remain medial to the pericardium to avoid injury to the phrenic nerve. If entry into the cardiac chambers occurs, suture closure of the defect should be performed promptly in order to avoid paradoxical air emboli occurring through residual intracardiac shunts.

Finally, attention should be paid to patient's hemodynamics during dissection, since these patients may be more prone to instability during difficult dissection or traction of cardiac structures.

When re-operation is anticipated, at previous operation, implantation of a retrosternal prosthetic membrane greatly facilitates reopening of the sternum, although this sometimes makes more difficult the subsequent identification of the mediastinal and cardiac structures.

As a rule, with careful preoperative planning and care during the conduction of resternotomy, poor outcomes can be avoided.

Pulmonary vascular bed abnormalities

While in most patients undergoing surgery for acquired heart disease the pulmonary vascular bed is normal, this is not true for many adults with CHD, and management of elevated pulmonary vascular resistance is particularly important in the early post-operative period.

Severe distortion of the pulmonary arteries may be present in previously operated patients (pulmonary artery banding, aortopulmonary shunt or previous surgery involving the pulmonary arteries). Preoperative dilatation and stent implantation is sometimes indicated. Alternatively, these lesions may be repaired adequately using pericardial patches. Pulmonary arterio-venous fistulae may develop in patients after a long-standing classic Glenn shunt. Rarely, large fistulae can be occluded with devices such as coils. More often, however, there are multiple small fistulae, which are not amenable to occlusion. Such lesions may regress after reparative surgery, but may be the source of severe, often lethal postoperative complications. In all patients, the pulmonary vascular bed (anatomy and physiology) must be evaluated very carefully, as abnormalities may preclude

further surgery or be an important cause of failure after surgery in grown-ups with congenital heart disease.

Aortopulmonary collateral circulation

In cyanotic patients, aortopulmonary collateral vessels may complicate peri-operative and post-operative management. Important collateral circulation, if not curtailed, results in excessive return to the left atrium, and it may result in myocardial distention and subsequent reduced myocardial function due to overdistention. In addition, it obscures visualization of the operative field, washes out cardioplegia, compromises systemic perfusion and causes volume overload of the left side of the heart during the critical, post-operative period. During resternotomy, care should be taken to avoid injury to these vessels. If injury occurs, large volume blood loss can occur before control of the vessel, which may be difficult due to the friable nature of these vessels. The size, location and end-parenchymal distribution of the collateral vessels must therefore be established precisely. Adequate management may include (1) pre-operative occlusion (by interventional catheterization) or surgical ligation at the beginning of operation, (2) surgical unifocalization of large collateral vessels which are the sole sources of blood flow to significant portions of the lungs, (3) deep hypothermic low flow cardiopulmonary bypass to prevent the deleterious effects of multiple small collateral vessels not amenable to surgical occlusion.

Anaesthesia and post operative care

Adults with CHD requiring cardiac and non-cardiac surgery present a spectrum of severity ranging from asymptomatic patients with minor problems to those with extreme deviations from normal cardiovascular physiology. There is however, little evidence-based information to enable choice of anaesthetic technique in these patients. Anaesthesia demands particular attention to endocarditis prophylaxis, avoidance of air emboli, appropriate placement of vascular catheters and regulation of intra-vascular volume and systemic/pulmonary flow. The most important aspect of peri-operative care is the involvement of a clinical team with detailed understanding of the patient's cardiac defect, functional status and anticipated peri-operative stresses.

Physiology

Cardiovascular impairment and increased anaesthetic risk may be due to hypoxaemia, pulmonary vascular disease, cardiac failure or arrhythmia. Polycythemia is the major adaptive response to hypoxemia. Blood viscosity increases exponentially with haematocrit and may be further increased with iron deficiency.[79] Polycythemic patients must not become dehydrated and should receive intravenous fluids from the night before surgery. In patients with decreased pulmonary blood flow, hypoxemia should be minimized by ensuring adequate hydration, maintaining systemic arterial pressure, minimizing transient elevation in pulmonary vascular resistance and avoiding increases in oxygen consumption. Elevated pulmonary blood flow, on the other hand, may increase excessively cardiac work or decrease systemic perfusion. The strategy in this situation is to maintain ventricular performance and optimise pulmonary to systemic flow ratio. In the presence of a systemic to pulmonary shunt (such as a Blalock-Taussig one) pulmonary flow will vary with the pressure gradient. Increases in pulmonary blood flow decrease pulmonary compliance and increase airway resistance and work of breathing. Significantly increased pulmonary blood flow leads to airway obstruction and non-compliant lungs. Reactive pulmonary vasculature can be treated with anaesthetic drugs, positive pressure hyperventilation, oxygen and pulmonary vasodilators. If pulmonary blood flow is reduced, it is important to prevent further

reductions. Airway dead space volume is increased with positive pressure ventilation, increased alveolar pressure or decreased left atrial or pulmonary artery pressures.

Assessment

Pre-operative assessment should define baseline problems and identify patients at increased risk. The cardiac anaesthesiologist should be involved in pre-operative conferences and overall planning of the management strategy. Access to all previous operation notes is invaluable. Clinical evaluation should be supplemented by laboratory data, ECG, chest X-ray, echocardiography and catheterization information. Lung function tests should be performed if the patient has scoliosis. Previous surgery may have resulted in recurrent laryngeal and phrenic nerve injuries or Horner's syndrome.

Anaesthetic management

Sedative pre-medication is popular. Oxygen consumption is reduced although caution must be exercised in the presence of hypoxaemia. Selection of induction agent is an individual choice. While there is a well-known influence of cardiac shunts on rapidity of inhalation induction, the clinical significance is rarely large. Vasodilatation is common during most induction techniques and will increase right to left shunting. However, the effect of this on arterial oxygen saturation will be partially offset by the reduction in total oxygen consumption and consequent increased mixed venous oxygen saturation. In general, the choice of drugs is less important than appropriate haemodynamic goals. Narcotic based anaesthesia is quite suitable in the presence of ventricular dysfunction. Ketamine may depress cardiac function if maximal sympathetic stimulation is present.

Monitoring

The use of invasive monitoring depends on the magnitude of surgery and the underlying cardiovascular pathophysiology. Placement of a pulmonary artery catheter can be technically difficult on account of anatomical abnormalities and might actually be dangerous in the presence of reactive pulmonary vasculature. Transoesophageal echocardiography is useful for following ventricular performance, valve function and blood flow. Some practical considerations for monitoring are important. End tidal CO2 will under estimate paC02 in the presence of right to left

shunting or common mixing. Previous systemic to pulmonary shunt placement requires blood pressure monitoring on the contra-lateral side. Accuracy of pulse oximeters is not guaranteed below levels of 80%. Vascular access may be problematic due to venous thrombosis or interrupted vena cava with azygos continuation. Central venous necklines pose a significant thromboembolic risk in the Fontan circulation and should be removed as soon as possible. Femoral veins can be used for central drug administration.

Post anaesthesia care

Post operative care is usually provided in a high dependency or intensive care environment and standard management principles apply to most patients. Experience in the management of pulmonary vascular resistance, shunt lesions, ventricular outflow tract obstruction and right ventricular dysfunction is particularly important. There is a trend in modern intensive care units to emphasize fluid administration and systemic oxygen delivery in high-risk surgical patients. This approach may not be well-tolerated by ACHD patients with poor ventricular function.

Cardiopulmonary interaction is important. Control of arterial blood gases (particularly paCO2) is fundamental to regulating pulmonary blood flow. While low airway pressures and weaning from ventilation are beneficial to trans-pulmonary flow, it is important to remember that the duration of the inspiratory phase during positive pressure ventilation has more influence than the absolute level of peak inspiratory pressure. Indeed shortening the inspiratory time (with consequent increase in peak inspiratory pressure) is usually the best strategy to maximise pulmonary flow. The alveolar ventilation CO2 response curve is normal. Hence, adequate analgesia is important and appropriate. This is particularly important in the presence of labile pulmonary artery pressures. The hyperbolic relationship between arterial oxygen saturation and Qp:Qs is often not understood by general intensive care staff. As a result, the significance of inappropriately high saturations in a complete mixing circulation may not be appreciated or raise concern, unless team is well trained in ACHD patients' postoperative care.

Non-cardiac surgery

The risks of non-cardiac surgery depend on the nature of the underlying cardiovascular abnormality, the extent of the surgical procedure, and whether or not it is an elective procedure or an urgent one. Preoperative planning must include consultation with a specialist ACHD centre.[61] Frequently encountered management issues include cessation of anticoagulant agents and use of antibiotics for endocarditis prophylaxis. [80] Ideally, operations in patients with complex CHD should be performed at a regional ACHD center with physicians experienced in the care of these individuals and with the consultation of cardiologists trained in this discipline.[81]

Important considerations for anesthetic management include the functional class of the patient, ventricular function, persistent shunts, valvular disease, arrhythmias, erythrocytosis, pulmonary disease, and pulmonary vascular disease.

Risk factors that help predict the possibility of perioperative risk include cyanosis ($p = 0.002$), treatment for congestive heart failure (p-value < 0.001), poor general health (p-value < 0.001), and younger age (p-value 0.03).[82] Patients with pulmonary hypertension probably have a higher complication rate (15%) than patients without pulmonary hypertension (4.7%; p-value 0.08).[82] Procedures performed on the respiratory and nervous systems seem to be associated with the most complications.

Additional coexistent problems, which frequently accompany CHD, such as renal or pulmonary dysfunction, must also be evaluated in addition to those acquired disorders to which adult patients are vulnerable (systemic hypertension, ischemic heart disease, both ventricular and supraventricular arrhythmias, peripheral varicosities).

Planning the procedure carefully is essential for optimizing outcomes. Urgent non-cardiac operations carry a higher risk, and complications may be more frequent in patients undergoing respiratory or nervous system procedures. Intraoperative monitoring may be helpful in detecting early haemodynamic changes so that appropriate treatment can be initiated promptly. Continuous intra-arterial monitoring enables sudden changes in intravascular volume and hemodynamics to be detected, and facilitates periodic arterial blood gas determinations. The decision of whether or not to

utilize a central venous line or pulmonary artery pressure recording (with or without oximetry) must be determined in each individual case and the risk-to-benefit ratio assessed. The latter may be associated with an increased risk of ventricular arrhythmia and paradoxical embolism in patients with pulmonary hypertension and right-to-left shunt.

Unoperated congenital heart disease

Patients with significant obstructive lesions (aortic stenosis, coarctation, and pulmonary stenosis) are vulnerable to intraoperative hypotension especially if ventricular function is depressed. Rapid fluid infusion may precipitate pulmonary edema. Elective non-cardiac surgery may be performed more safely after repair or replacement of the obstructive valve or arterial lesion. A patient with ventricular dysfunction from any cause is more vulnerable to perioperative complications (such as congenitally corrected transposition of the great arteries when the systemic ventricle is the morphologic right ventricle).

Operated congenital heart disease

Patients with repaired congenital heart disease are vulnerable to arrhythmia and hemodynamic deterioration, particularly when they have impaired ventricular function, which may be exacerbated by the loss of atrial transport. A multidisciplinary approach to their perioperative management will help to minimize the complications.

Cyanotic heart disease

Patients with cyanotic congenital heart disease are most at risk from noncardiac surgery, especially if they to have pulmonary hypertension.[61] The increased risk of haemorrhage secondary to the inherent haemostatic abnormalities can be temporarily reduced by preoperative phlebotomy, if the haematocrit is >65%. One unit accompanied by isovolumic fluid replacement may be performed, and the blood can be saved for potential autologous transfusion. For cyanotic patients a fall in systemic vascular resistance can increase the right-to-left shunt and increase hypoxia. This is not tolerated well and can potentiate cardiovascular collapse. Prolonged operations associated with hemodynamic instability necessitating large volume fluid replacements are also associated with

increased perioperative mortality. Spinal anesthesia, similarly, can result in a fall in systemic vascular resistance and reduced venous return, and thus is best avoided in cyanotic patients. For any patient with a right-to-left shunt, there is an increased risk of a paradoxical embolus and air filters should be placed on all intravenous lines. Bacterial endocarditis prophylaxis should be given when appropriate.[80]

Transplantation

Transplantation is the final palliation for many adult patients with CHD, and must be considered when the short-term prognosis is reduced or the quality of life unacceptable. Transplantation may involve either heart, heart-lung, single or double lung with intracardiac repair.

The most common congenital lesions that ultimately may require transplantation include failed Fontan, Mustard or Senning procedures, congenitally corrected transposition, complex pulmonary atresia and Eisenmenger complex.[83-85] In addition, an increasing number of recipients will include those requiring re-transplantation after primary transplantation for congenital lesions in childhood.

Risk stratification scores are available for terminal congestive heart failure,[86] but may not apply to adults with CHD. This makes decisions regarding timing of transplantation difficult.

In addition to standard pretransplant work up, attention needs to be directed towards specific issues in these difficult patients. Sensitization from previous transfusions may increase the early risk of rejection and graft failure. Treatment to reduce the HLA antibody level may be required before placement on the waiting list. Assessment of pulmonary vascular resistance is difficult in patients with low cardiac output, residual lesions, shunts or collaterals. Detailed planning of the surgical approach is crucial in many complex lesions and all anatomic details, including the systemic and pulmonary venous return need to be defined. Magnetic resonance imaging is particularly informative. Non-adherence to post transplant medications is a major problem in young adults and pre-existing psychosocial issues may require careful evaluation before listing. Other risk factors that

are specific to the failing 'Fontan' patient include protein losing enteropathy and pulmonary arteriovenous fistulae. An increasing number of patients with terminal cardiopulmonary lesions have underlying chromosomal anomalies, which may further complicate decision-making.

Surgical issues in previously operated patients include difficulties with cannulation, dissection, abnormal anatomy, need for an additional conduit for reconstruction, bleeding and prediction of the time needed to prepare the recipient. This often leads to longer ischemia and bypass times, which may jeopardize graft function and survival.

The current 1-, 5- and 10-year survival after cardiac transplantation in adult patients is 80, 70 and 55%.[87] For heart-lung transplantation the survival is only 65, 45 and 30%, respectively.[87] The outcome after heart transplantation is significantly lower in many ACHD patients, including Fontan patients, primarily due to a higher early attrition.[83-85] Late attrition after transplantation has not improved significantly during the last 10–20 years despite introduction of new immunosuppressants. Chronic rejection (graft coronary vasculopathy in hearts and obliterative bronchiolitis in lungs) and malignancy remain the main concerns. Immunologic progress and new drugs will hopefully improve this in the future.

The increasing donor shortage and inferior results may influence donor organ allocation to adults with congenital heart disease patients. The increasing number of patients surviving with palliated lesions and those with previous transplants will worsen the donor situation dramatically and many patients will never get to transplantation until viable alternatives such as reliable long-term mechanical support systems or xenotransplantation become available. This problem is of particular concern for adults with congenital heart disease requiring heart-lung grafts.[16]

Psychosocial issues

In addition to provision of care for complex medical and surgical problems, the specialist center for adults with CHD must provide support for the many psychosocial problems in this population.[88] In fact, only recently have patients with complex CHD survived into adult life in large numbers. Their survival creates hope that continuing advances will help them maintain both quality of life and longevity. However, patients may experience despair due to their awareness of residual morbidities and the knowledge of possible or probable early mortality, or limitations in their social lives and educational or occupational attainment. Healthy psychosocial functioning depends on their ability to balance hope and despair. Adults with CHD must also confront both CHD-specific and general developmental tasks. Psychosocial issues may be affected by lesion severity (simple vs. complex), visibility (e.g., cyanosis), and functional disability, and include a high level of anxiety about the underlying heart condition and prognosis, difficulties with social interaction as well as specific issues regarding employment, insurance and physical activity.[89] Staff with appropriate expertise should form part of the specialist team and are frequently called upon to act as advocates for the patients who may face unfair discrimination.

Further studies are required to investigate the relationship between the underlying disability, level and type of follow up care, emotional status and affect on psychosocial health and performance. These should examine well-characterized populations of patients, use validated questionnaires, grading of physiological performance and appropriate control groups for comparison. Currently, validated congenital heart disease specific measures are not available. This information will assist in the training of professionals and enable the provision of counselling services, specific to the needs of adolescents and adults with congenital heart disease.

Intellectual development/education

Intellectual development may be influenced by genotype, the presence of syndromes, as well as the disturbed hemodynamics of the cardiac defect and its treatment. Many patients with syndromes involving learning disabilities of varying degree now survive into adult life, including William's syndrome, Down's syndrome and 22q11 deletion. They have specific educational needs. Cognitive function may be affected by early neurological complications of low cardiac output, acidosis, and hypoxia as well as by the consequences of cardiac surgery, anaesthesia, hypothermia, circulatory arrest and cardiopulmonary bypass. Intellect may be further influenced by chronic cardiac failure, arrhythmia and/or cyanosis as well as absence from school.[15,16]

Studies of intellectual outcome in young adults with relatively simple congenital heart defects have been very encouraging. Indeed, level of educational attachment may be superior to that in the general population, reflecting the high level of motivation of grown-ups with congenital heart disease and the support of their families and health care providers.[90] Data in patients with complex defects are more limited. Studies from the '80s have shown below average I.Q. scores in cyanotic congenital heart disease, including Tetralogy of Fallot and transposition of the great arteries.[91] Individual factors such as duration of chronic hypoxia and elevated haematocrit may have a limited impact but, in general, combinations of adverse factors appear to have long-term detrimental effects.

Up to 10% of children with congenital heart disease will have a cerebovascular infarction, most within the first 2 days of life.[92] Early correction of congenital heart disease, as is currently undertaken, may reduce these neurological complications, but may in itself, have neurocognitive effects which will become manifest in later life.

Employment

Ability to obtain and maintain employment will depend on intellectual and physical capacity, motivation, and interaction with peers as well as potential discrimination by society. Several reports of employment status of grown-ups with congenital heart disease have shown that unemployment is more common in patients with complex lesions, and that approximately 10% are considered totally disabled.[93] The economic consequences of unemployment vary in different countries, because of the marked differences in the levels of social and welfare programmes across Europe. Nevertheless, even under the most generous systems, unemployment has major adverse effects including lowered self-esteem and social contact, especially in this potentially vulnerable population.

Appropriate employment counselling is part of the responsibility of the medical profession, assisted by other members of the specialist team, including nurse counsellors. Advice needs to be realistic and based on physical and intellectual capacity as well as on specific issues, such as arrhythmia, which may preclude certain types of job (e.g. car driving). Other services such as vocational and physical rehabilitation as well as job training may broaden the patient's range of employment options.

Discrimination against job applicants with CHD is often based on concerns about performance, absenteeism, premature retirement and medical insurance. Legislation against such behaviour by potential employers varies between countries, including affirmative action to employ disabled persons.

Insurance

Life insurance and health insurance availability vary greatly both within and between countries. Life insurance remains an important component of financial planning, not least in relation to mortgage and house purchase. Life insurance may be denied, be made available at normal rates or have a heavily loaded additional premium.[94] A study in 1993 in the UK evaluated both life and health insurance available to adults with congenital heart disease.[95] The findings revealed a

surprising discordance between insurance policy and medical outcome data. For example, patients with repaired aortic coarctation were insurable at normal rates, whilst patients were often denied insurance after successful repair of ventricular septal defect.

Health insurance was usually available, but almost always excluded benefit for the underlying cardiac condition. This can have a major impact on delivery of optimal medical care to grown-ups with congenital heart disease in an insurance-based medical system. In an earlier German survey among a cohort of ACHD patients, more than 30% were refused life insurance.[96]Further studies are in progress in the UK and France to obtain up to date information. Insurance recommendations from cardiac societies exist in Italy and Switzerland, but not in the other European countries surveyed.

Physical activity/sport

Participation in sports and regular physical exercise have well documented beneficial effects on fitness, psychological well-being, confidence and social interaction as well as on the later risk of acquired cardiac disease. Recently, it was demonstrated that young patients who have undergone the Fontan operation can safely undertake exercise training and that this results in an improvement in aerobic capacity; those findings were suggesting that aerobic training could be useful even in the long-term management of palliated single ventricle patients, so as to optimize their cardiovascular fitness for more active lives.[97]

Recommendations on exercise in adults with CHD need to be based on the ability of the patient as well as on the impact of physical training on cardiac haemodynamics (e.g. ventricular remodelling, myocardial ischaemia).[98]

Counselling should include an appreciation of the type of energy expenditure involved in different sports and teaching of a method to enable the patient to limit his or her activities. These include the Borg scale of perceived effort, a target heart rate range (60–80% of maximum heart rate achieved during testing without symptoms or hemodynamic deterioration) and a simple breathing rule (activity can be carried out safely as long as breathing still permits comfortable speech).[16]

Impact sport should be avoided in patients with Marfan's syndrome or other aortic anomalies, those on oral anticoagulants or those with pacemakers. Formal testing, assessing the impact of exercise levels relevant to the patients' expectations during normal day life, should be undertaken and protocols derived from conventional adult exercise testing programmes need to be adapted.[99]

In general, primary care physicians are conservative and often unnecessarily proscriptive in their recommendations; this may have important adverse effects on quality of life.

Exercise may have acute, chronic and potentially harmful haemodynamic effects in patients with congenital heart disease. These include fluid depletion, blood pressure rise or fall, tachycardia and/or arrhythmia as well as long-term effects on ventricular hypertrophy and function. Of most concern is the risk of sudden death during or after exercise. Most cases of sudden death during physical activity in the young are due to a previously unrecognized cardiac disorder and sudden death in patients with known congenital heart disease is very rare (1 in 10 000 patients in a recent survey in nine specialist centres for grown-ups with congenital heart disease). Potentially lethal situations may occur with arrhythmia and haemodynamically vulnerable circulations (e.g. preload jeopardized circuits such as after Mustard/Senning or Fontan operation or with heart failure). Advice to perform social exercise to a level of comfort, but not to attempt competitive sports is applicable in most situations.[100]

Quality of life

Few studies of quality of life have been performed using validated measures in large populations of adolescent or adults with congenital heart disease. [12] Most patients, when questioned, will say that they are 'asymptomatic'. Whilst many are able to enjoy the full range of normal life activities, patient symptom reporting should be interpreted with caution as they may always have been limited and thus 'do not know any better'.[101] Alternatively, they may be reluctant to admit limitations and to discuss problems. Allocation of sufficient time to obtain a good history (often by the nurse counsellor) is essential and may need to be supplemented by objective testing.

Finally, psychosocial adjustment to adult life depends, not only on the type and severity of the congenital heart defect, but also on the attitude and behaviour of family, friends and the ACHD team. Sensitive handling and education can be enormously valuable and the advocacy role of the ACHD team cannot be over emphasized. [16]

SECTION II

Specific congenital heart lesions and management strategy

Specific congenital heart lesions and management strategy

This section summarises the current management strategy for the commonest lesions seen in grown-ups with congenital heart disease, as indicated by European Society of Cardiology.[16] Many recommendations are based at clinical experiences rather than evidence trial randomized clinical trials.

Atrial septal defect

Criteria	Comments	
1. Introduction and background	• common defect which may be diagnosed first in adult life	
2. Survival—adult life	• small defects-excellent prognosis • large defects—reduced survival, depending on age at treatment	
3. Haemodynamic issues	• PHT • RV dilation/failure • potential for paradoxical embolism • reduced LV compliance	
4. Arrhythmia/pacing	• atrial arrhythmia (atrial fibrillation and flutter) • sick sinus syndrome • pacing rarely required	
5. Investigations	ECG	• baseline—if clinically indicated (arrhythmias)
	Chest X-ray	• baseline—otherwise little value
	ECHO/TOE	• baseline-location, size, RV size, PA pressure, Qp:Qs, associated lesions • TOE usually performed in older patients and at device closure
	Catheterization	• device closure • PVR assessment
	MRI	• rarely helpful
	Holter	• if symptomatic arrhythmia
	Exercise function	• baseline—little value
6. Indications for intervention	• large defects (>10mm) unless pulmonary vascular disease (PVR>8Um^2, L-R shunt <1.5, no response to pulmonary vasodilators) • paradoxical embolism	
7. Interventional options	• surgery or device closure (stretched diameter <38mm)	
8. Post treatment outcome	• low risk procedure unless PVD • late intervention less successful	
9. Endocarditis	• very rare • prophylaxis not indicated	
10. Pregnancy/contraception/ recurrence/fetal	• no contra-indications unless PVD • no restrictions for contraception • consider fetal echocardiography	
11. Recurrence/genetics	• 3% of first degree relatives • familial ASD (with long PR interval) • autosomal dominant	
12. Syndromes	• Holt Oram—upper limb deformity • autosomal dominant	
13. Sport/physical activity	• no restrictions unless moderate/severe PVD	
14. Insurance	• category 1 • generally no problem if defect closed early	
15. Follow-up interval	• early repair (<30 years)—no problems—discharge • late repair—regular f/u	
16. Follow-up care	• level 2	
17. Unresolved issues	• surgery vs device closure • when to close in PHT • concomitant Maze procedure • upper age limit for surgery • PFO closure in patients with suspected paradoxical embolism	

Ventricular septal defect—unrepaired

Criteria	Comments	
1. Introduction and background	• significant ventricular septal defects usually repaired in childhood• see ventricular septal defect and PVD (Eisenmenger) but diminishing • small ventricular septal defect or postoperative septal defect common in adults • Eisenmenger patients becoming less frequent	
2. Survival—adult life	• excellent for small ventricular septal defect • large ventricular septal defect may have pulmonary vascular disease (Eisenmenger) • may develop aortic regurgitation	
3. Haemodynamic issues	• left-right shunt • LV dilatation and impaired function • aortic regurgitation • pulmonary vascular resistance in uncorrected large ventricular septal defect	
4. Arrhythmia/pacing	• rare	
5. Investigations	Chest X-ray	• baseline-cardiomegaly
	ECG	• routine • rhythm chamber enlargement
	ECHO	• number size and location of defects • LV/RV function • aortic regurgitation
	TOE	• if TTE image inadequate
	Catheter	• pulmonary vascular resistance • associated lesions.
	MRI	• rarely helpful
	Holter	• only if symptomatic
	Exercise test	• only if symptomatic • sports counselling
6. Indications for intervention	• left—right shunt with left heart volume overload • reversible pulmonary hypertension • aortic regurgitation • associated abnormalities (RV outflow tract, subaortic stenosis) • previous endocarditis	
7. Interventional options	• surgery • catheter closure in muscular VSD(s)	
8. Post treatment outcome	• good surgical results	
9. Endocarditis	• prophylaxis in all	
10. Pregnancy/contraception	• no contra-indications in uncomplicated VSD • pregnancy condra-indicated in pulmonary vascular disease (Eisenmenger disease)	
11. Recurrence/genetics	• occasionally familial • usual recurrence risk • common cardiac anomaly in syndromes e.g. Down's	
12. Sport/physical activity	• no restriction in small ventricular septal defect	
13. Insurance	• small ventricular septal defects category 1	
14. Follow-up interval	• infrequent follow-up unless haemodynamic abnormalities (e.g. aortic regurgitation)	
15. Follow-up care	• small ventricular septal defect 3, pulmonary vascular disease (Eisenmenger) 2, aortic regurgitation/complicated haemodynamics 1	
16. Unresolved issues	• optimal management of Eisenmenger patients	

Repaired ventricular septal defect

Criteria	Comments	
1. Introduction and background	• common lesion • most patients now adults	
2. Survival—adult life	• excellent survival • occasional residual shunt • some develop RV or LV outflow tract obstruction • some develop aortic regurgitation	
3. Haemodynamic issues	• residual shunt • ventricular function • aortic regurgitation • new haemodynamic abnormalities (RV outflow obstruction)	
4. Arrhythmia/pacing	• rare AV block, ventricular arhythmia	
5. Investigations	Chest X-ray	• baseline—cardiomegaly
	ECG	• rhythm
	Echo	• residual VSD(s) • LV/RV function • aortic regurgitation
	TOE if TTE insufficient	• TOE only it TTE inadequate
	Catheter	• rarely required
	MRI	• rarely helpful
	Holter	• only if symptomatic
	Stress test	• only if symptomatic • sports counselling
6. Indications for intervention	• if residual VSD; see 'unrepaired VSD'	
7. Interventional options	• see 'unrepaired VSD'	
8. Post treatment outcome	• see 'unrepaired VSD'	
9. Endocarditis	• prophylaxis if residual VSD • questionable in closed VSD	
10. Pregnancy/contraception	• no contra-indications in uncomplicated closed VSD Pregnancy contra-indicated in PVOD (Eisenmenger)	
11. Recurrence/genetics	• see: 'unrepaired VSD'	
12. Sport/physical activity	• no restriction in closed VSD	
13. Insurance	• category 1	
14. Follow-up interval	• can discharge if closed VSD without any residual abnormalities • infrequent follow-up for minor residual lesions	
15. Follow-up care	• Eisenmenger 2, small VSD 3, aortic regurgitation/complicated haemodynamic 1	
16. Unresolved issues	—	

Postoperative complete atrio-ventricular septal defect

Criteria	Comments	
1. Introduction and background		
2. Survival—adult life	• unoperated survivors develop PVD • surgical results markedly improved • status after repair depends mostly on left AV valve function • many patients have Down's syndrome	
3. Hemodynamic issues	• left AV-valve regurgitation (±stenosis) • pulmonary vascular disease • late sub-aortic stenosis	
4. Arrhythmia/pacing	• risk of complete heart block low (<2%) • atrial arrhythmias especially with left AV-valve dysfunction	
5. Investigations	Chest X-ray	• cardiomegaly • pulmonary vascular markings • pulmonary vascular disease
	ECG	• routine (LVH, RVH, CVH) • superior QRS-axis • right bundle branch block • conductance disturbances
	ECHO/TOE	• most useful investigation for • left AV valve morphology and function • ventricular function • residual lesions (shunt, sub-aortic stenosis)
	Catheter	• rarely required unless reoperation considered
	MRI	• rarely indicated
	Holter	• only in symptomatic patients
	Exercise testing	• rarely indicated
	Additional investigations	• significant left AV valve dysfunction • significant residual shunt • subaorticstenosis
6. Indications for reintervention	• significant left AV-valve dysfunction • significant residual shunt • sub-aortic stenosis • progressive/symptomaticAV-Block	
7. Interventional options	• re-operation may require valve replacement	
8. Post treatment outcome	• excellent long-term results unless • actuarial survival after 20 years >80% • left AV valve regurgitation (+stenosis) • pulmonary vascular disease • late sub-aortic stenosis	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception	• pregnancy contra-indicated in PVD (Eisenmenger) • anticoagulation management in patients with prosthetic valves• avoid oestrogen containing pill in pulmonary hypertension	
11. Recurrence/genetics/syndromes	• above average recurrence risk Down's syndrome in >50% of complete AVSD • app. 10–14% CCD in mothers with AVSD	
12. Physical activity/sports	• no restrictions if good repair and no significant arrythmias	
13. Insurance	• category 2 if well repaired	
14. Follow-up interval	• 1–2 yearly intervals with ECG and ECHO in stable cases	
15. Follow-up care	• level 2 unless significant haemodynamic problems	
16. Unresolved issues	• only limited data regarding long term prognosis	

Postoperative partial atrio-ventricular septal defect (p-AVSD)

Criteria	Comments	
1. Introduction and background		
2. Survival—adult life	• similar to secundum atrial septal defect unless significant to left AV-valve regurgitation • unoperated p-AVSD have reduced life expectancy • PVOD may develop late • status after repair depends on left AV valve function	
3. Hemodynamic issues	• before repair • size of shunt • degree of AV valve regurgitation • after repair • residual shunt and left AV valve regurgitation • subaortic stenosis	
4. Arrhythmia/pacing	• atrial arrhythmias rare unless left AV-valve regurgitation • complete heart block very rare • pacing rarely required unless sick sinus syndrome	
5. Investigations	ECG	• superior-QRS axis • right bundle branch block • rhythm follow-up
	Chest X-ray	• routine • cardiomegaly
	ECHO/TOE	• most useful investigation both for and after operation • left AV valve function • ventricular function • residual lesion
	Catheter	• rarely required unless reoperation considered
	MRI	• rarely indicated
	Holter	• rarely indicated
	Exercise testing	• rarely indicated
	Additional investigations	—
6. Indications for intervention	• all cases to be considered for intervention unless pulmonary vascular disease • reoperation for significant left AV-valve regurgitation • residual shunt or subaortic stenosis • progressive/symptomatic arrhythmias	
7. Interventional options	• surgery with valve repair or replacement • closure of re-/residual ASD • Pacemaker (DDD) in progressive/symptomatic complete block	
8. Outcome	• excellent long term provided left AV-valve repair satisfactory	
9. Endocarditis	• prophylaxis indicated if left AV-valve regurgitation is present	
10. Pregnancy/contraception	• well tolerated in repaired cases • contraindicated in rare cases with PVOD (Eisenmenger) • anticoagulation management in patients with prosthetic valves • avoid oestrogen containing pill in pulmonary hypertension	
11. Recurrence/genetics/syndromes	• none	
12. Physical activity/sports	• no restrictions if good repair and no significant arrythmias	
13. Insurance	• category 2	
14. Follow-up interval	• 2 yearly intervals with ECG and ECHO in stable cases	
15. Follow-up care	• unoperated level 1, postoperative level 2	
16. Unresolved issues	• long term function of a non-reconstructed AV-valve is uncertain	

Pulmonary stenosis

Criteria	Comments	
1. Introduction and background		
2. Survival—adult life	• excellent if relieved effectively • poor if severe valve PS untreated	
3. Haemodynamic issues	• PS severity • PR severity • leaflet dysplasia • right ventricular function	
4. Arrhythmia/pacing	• atrial arrhythmias in RV failure and tricuspid regurgitation • pacing not indicated	
5. Investigations	Chest X-ray	• baseline otherwise little value unless RV failure
	ECG	• rhythm RV • hypertrophy
	ECHO/TOE	• investigation of choice for RVOT gradient pulmonary regurgitation RV size/function tricuspid regurgitation
	Catheter	• rarely needed except for balloon dilatation
	MRI	• rarely needed • assess RV size/function and RA dilation in sevre pulmonary regurgitation
	Holter	• not routinely indicated
	Exercise	• not routinely indicated
	Additional investigations	• none
6. Indications for intervention	• valve gradient >30mmHg at rest or for symptoms	
7. Interventional options	• balloon valvuloplasty almost always • surgery if valve calcified/dysplasty	
8. Post treatment outcome	• excellent long-term results unless early failure significant pulmonary regurgitation uncommon	
9. Endocarditis	• low risk. Prophylaxis may not be required in mild cases	
10. Pregnancy/contraception/fetal	• routine pregnancy unless moderate to severe PS or right to left shunt through ASD or PFO	
11. Recurrence/genetics	• 4% approximately	
12. Syndromes	• Noonan • congenital rubella • Williams • Alagille	
13. Sport/physical activity	• unrestricted unless severe	
14. Insurance	• category 1 after successful treatment or mild PS	
15. Follow-up interval	• can discharge if mild with ECHO. Every 1–3 years if more than mild, PR, or desaturation.	
16. Follow-up care	• mild PS: 3, Excellent early result: 2, Residual gradient or significant PR: 2	
17. Unresolved issues	• none	

Tetralogy of fallot—postoperative

Criteria	Comments	
1. Introduction and background	• common lesion. Most Fallot patients are now adults	
2. Survival—adult life	• survival rate after surgery excellent (normal in selected groups) • occasionally unoperated patients survive into adulthood.	
3. Haemodynamic issues	• pulmonary regurgitation/PS and RV function • tricuspid regurgitation • aortic regurgitation • residual lesions	
4. Arrhythmia/pacing	• late complete heart block rare • ventricular premature beats common in asymptomatic patients • sympotomatic VT rare • atrial arrhythmias common and relate to poor haemodynamics • small incidence of late sudden death	
5. Investigations	Chest X-ray	• baseline and occasionally follow-up • cardiomegaly • RV outflow
	ECG	• routine • rhythm • access/QRS width (usually complete right bundle branch block)
	ECHO/TOE	• regularly for PR/RVOTO/RV size function/tricuspid regurgitation? Aortic regurgitation/LV function
	Catheter	• preoperative for residual lesions, coronary anatomy intervention for dilatation/stent of pulmonary artries • possibly in future for implantable pulmonary valve
	MRI	• may become investigation of choice for RV size function and pulmonary regurgitation
	Holter	• for symptoms and in poor haemodynamics
	Exercise	• exercise capacity, arrhytnmias
	Additional investigations	• electrophysiological study for syncope, sustained arrhythmia (atrial or ventricular), RFA
6. Indications for intervention	• significant RVOT or PA branch stenosis • aortic regurgitation • residual VSD, significant pulmonary regurgitation (with symptoms and RV dilatation)	
7. Interventional options	• surgery, surgery with ablation, balloon dilatation/stenting, RF ablatin catheter intervention for pulmonary valve insertion	
8. Post treatment outcome	• most patients well • RV function may not normalize after pulmonary valve replacement • arrhythmia may persist • risk of sudden death	
9. Endocarditis	• prophylaxis in all	
10. Pregnancy/contraception/fetal	• no contra-indication to pregnancy in well repaired patients• monitor ventricular function and arrhythmia • no additional fetal risk	
11. Recurrence/genetics	• 1.5% for father, 2.5–4% for mother with TOF, 16% of Fallot patients have deletion of chromosome 22q11- recurrence risk 50%.	
12. Syndromes	• 22q11	
13. Sport/physical activity	• no contra-indication to sport unless documented arrhythmia • significant ventricular dysfunction	
14. Insurance	• category 2	
15. Follow-up interval	• one/two yearly with ECG, ECHO±Holter, exercise test	
16. Follow-up care	• 1 if documented residual abnormalities/arrhythmia, 2 otherwise	
17. Unresolved issues	• risk stratification for sudden death • indication for implantable defibrillator • timing of reoperation for pulmonary regurgitation	

Conduits

Criteria	Comments	
1. Introduction and background	• conduits used in repair of complex congenital heart disease • usually RV-PA (e.g. PA/VSD, Truncus, ToF, TGA/VSD/PS)	
2. Survival—→adult life	• all conduits in children deteriorate and require replacement (usually <10 years) • longevity of replacement unclear	
3. Haemodynamic issues	• stenosis of valve, subvalve or anastomosis to PA • pulmonary regurgitation with RV volume overload • LV-Aortic pathway in complex repairs	
4. Arrhythmia/pacing	• ventricular arrhythmias, surgical heart-block	
5. Investigations	Chest X-ray	• baseline and follow-up • conduit calcification • cardiomegaly
	ECG	• routine • rhythm
	ECHO	• investigation of choice for follow-up of RV • pressure gradient across conduit and PI • LV aortic pathway • ECHO may underestimate gradient
	TOE	• not routine
	Catheterization	• evaluation for surgery • balloon dilatation or stenting
	MRI	• very useful for investigation of conduit function • may become investigation of choice
	Holter	• only if arrhythmia suspected
	Exercise function	• not routine • useful for objective evaluation of exercise tolerance
6. Indications for intervention	• significant symptoms or conduit obstruction	
7. Interventional options	• usually surgical replacement of conduits • occasionally balloon dilatation or stenting	
8. Post treatment outcome	• fate of replaced conduit uncertain • need long term follow-up	
9. Endocarditis	• prophylaxis in all	
10. Pregnancy/contraception	• pregnancy tolerated if haemodynamics stable • no contraception issues	
11. Recurrence/genetics	• usual recurrence rate for congenital heart disease • higher if 22q11 deletion	
12. Syndromes	• 22q11 deletion	
13. Sport/physical activity	• avoid contact sports • otherwise no restrictions if haemodynamics good	
14. Insurance	• level 2	
15. Follow-up interval	• yearly with ECHO, ETT for ventricular function, arrhythmia surveillance (ECG, Holter if symptoms) • significant conduit dysfunction may be present in mildly symptomatic patients	
16. Follow-up care	• category 1	
17. Unresolved issues	• type of conduit (homograft versus xenograft) • role of balloon dilatation stenting	

Aortic valve stenosis (unoperated)

Criteria	Comments	
1. Introduction and background	• common especially biscupid aortic valve (1–2% of population)• may occur with other lesions	
2. Survival—→adult life	• normal if mild obstruction	
3. Hemodynamic issues	• degree of stenosis may progress • associated aortic regurgitation • LV hypertrophy and function	
4. Arrhythmia/pacing	• VT and VF may occur during exertion with severe obstruction	
5. Investigations	ECG	• LVH and repolarization changes
	Chest X-ray	• baseline • calcification
	ECHO	• investigation of choice • LV mass/function • aortic valve/size/morphology/area • LV to aortic gradiant • aortic regurgitation
	TOE	• rarely of value except in endocarditis
	MRI	• rarely of value
	Catheter	• not for diagnosis • for coronary angiography and balloon dilatation
	Exercise testing	• for repolarization changes and symptoms • surgical decision making
6. Indications for intervention	• symptoms: severe LV pressure overload • severe aortic stenosis	
7. Interventional options	• balloon valvuloplasty if valve uncalcified • rarely good option in adult • mechanical valve replacement, homograft or Ross procedure depending on patient's age, sex, preferences and local expertise	
8. Outcome	• recurrence common late after valvotomy • very good in uncomplicated cases of valve replacement.	
9. Endocarditis	Prophylaxis indicated in all	
10. Pregnancy/contraception	• low risk in asymptomatic patents even with moderate obstruction • high risk in patients with severe obstruction • transcatheter intervention may be indicated in unplanned pregnancy	
11. Recurrence/genetics/Syndromes	• bicuspid valve may be familial • association with coarctation • recurrence rate may be higher in syndromes.	
12. Physical activity/sports	• no competitive sports if obstruction is moderate or severe	
13. Insurance	• category 2	
14. Follow-up interval	• depends on severity and progression rate ECG/ECHO±exercise test	
15. Follow-up care	• mild 3-moderate/severe 1	
16. Unresolved issues	• late outcome after the Ross operation	

Postoperative valvar aortic stenosis

Criteria	Comments	
1. Introduction and background	• common lesion • most interventions in children are balloon dilation or open aortic valvotomy, aortic valve replacement, mechanical or biological prostheses or Ross procedure may have been performed	
2. Survival—adult life	• excellent	
3. Hemodynamic issues	• obstruction • regurgitation • LV function • pulmonary homograft (Ross)	
4. Arrhythmia/pacing	• arrhythmia rare • more common in LV hypertrophy • may cause sudden death	
5. Investigations	ECG	• routine LVH • conduction disturbances • repolarization changes
	Chest X-ray	• cardiomegaly
	ECHO	• see valvar aortic stenosis unoperated • prosthesis function and paravalvular leak
	TOE	• useful in assessment of paravalvular leaks and suspected endocarditis
	MRI	• rarely indicated
	Cath	• rarely indicated (see valvar aortic stenosis unoperated)
	Exercise testing	• surgical decision making for timing of reintervention
6. Indications for reintervention	• recurrent obstruction (native valve or prothesis) • regurgitation• occassionally haemolysis	
7. Interventional options	• mechanical valve, homograft or Ross operation • prosthesis may be preffered by olderly • homograft may be preferred in endocarditis	
8. Outcome	• very good but anticagulant problems with mechanical valve and late failure	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception	• anticoagulants may cause embryopathy	
11. Recurrence/genetics/syndromes	• see aortic valve stenosis unoperated	
12. Physical activity/sports	• high level activity possible in uncomplicated cases with good LV function • contact contra-indicated in patients on anticoagulants	
13. Insurance	• category 2	
14. Follow-up interval	• yearly	
15. Follow-up care	• Ross 1 otherwise 2	
16. Unresolved issues	• long-term outcome of Ross procedure • best anticoagulation protocol in pregnancy	

Subaortic stenosis unoperated

Criteria	Comments	
1. Introduction and background	• uncommon form of obstruction • may be discrete or extend to adjacent structures • often progressive.	
2. Survival—adult life	• normal if obstruction not severe	
3. Hemodynamic issues	• progression very common • may cause aortic regurgitation• associated lesions common (e.g. VSD)	
4. Arrhythmia/pacing	• See 'aortic valve stenosis'	
5. Investigations	Chest X-ray	• baseline
	ECG	• routine LVH and repolarization changes
	ECHO	• investigation of choice • visualise obstruction • gradient across LV outflow tract • LV mass/function • aortic regurgitation
	TOE	• may be useful to define anatomy
	MRI	• rarely indicated
	Cath	• rarely indicated (see 'aortic valve stenosis')
	Exercise test	• for repolarization changes and symptoms
6. Indications for intervention	• progressive obstruction • lower threshold and aortic valve stenosis • aortic regurgitation	
7. Interventional options	• surgical resection	
8. Outcome	• recurrence possible	
9. Endocarditis	• prophylaxis in all	
10. Pregnancy/contraception	• low risk if no severe obstruction	
11. Recurrence/genetics/syndromes	• may occur left heart abnormalities e.g. coarctation, Shone's syndrome • familial cases described	
12. Physical activity/sports	• no restriction if mild obstruction or after resection	
13. Insurance	• category 2	
14. Follow-up interval	• depends on severity and progression rate usually 1–2 yearly	
15. Follow-up care	• level 1	
16. Unresolved issues	• recurrence rate after resection • optimal timing of surgery	

Unoperated coarctation

Criteria	Comments	
1. Introduction and background	• may present in infancy or later in adolescence	
2. Survival—adult life	• rarely undiagnosed in childhood but long term survival ispossible	
3. Haemodynamic issues	• hypertension • premature atherosclerosis • LV hypertrophy/failure • aortic dissection • associated aortic/MV lesions	
4. Arrhythmia/pacing	• rare problems	
5. Investigations	ECG	• LVH + repolarization changes
	Chest X-ray	• cardiomegaly • ascending aorta dilation • rib notching
	ECHO	• assessment of arch anatomy/gradient • associated lesions LVH and function
	TOE	• rarely provides additional information
	MRI	• investigation of choice
	Holter	• not indicated unless for ambulatory blood pressure
	Exercise test	• hypertension on exercise • arm/leg gradient • inducible repolarization abnormalities
	Catheterization	• if MRI unavailable for arch anatomy • for coronary angiography when indicated for intervention
	Additional	• screen for intracerebral vascular anomalies
6. Indications for intervention	• resting or exercise induced hypertension • resting gradient >30mmHg	
7. Interventional options	• balloon/stenting • surgical repair	
8. Post treatment outcome	• residual hypertension common despite adequate relief of obstruction • accelerated atherosclerosis • reduced life expectancy	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception/ recurrence/fetal	• repair prior to pregnancy if possible • transcatheter intervention may be indicated in unplanned pregnancy (worsening BP, LV failure)• avoid oestrogen containing pill • growth retardation common • spontaneous fetal loss increased	
11. Recurrence/genetics	• recurrence may be familial • 22q11 deletion in complex forms	
12. Syndromes	• Turners (present in approx 30%) • Williams (present in approx 10%) • Shones (associated LV inflow/outflow abnormalities)	
13. Sport/physical activity	• should be restricted prior to repair	
14. Insurance	• category 3 for significant unoperated coarctation	
15. Follow-up interval	• most patients referred for intervention on diagnosis • 1 yearly of mild cases with BP at rest and exercise/ECHO/Doppler/MRI	
16. Follow-up care	• level 1	
17. Unresolved issues	• influence of age at operation on long-term outcome • influence of drugs on vascular phenotype in successful cases • role of intervention for mild gradients • role of stenting as adjunct to balloon	

Operated coarctation

Criteria	Comments	
1. Introduction and background		
2. Survival—adult life	• long-term survival still reduced despite adequate early repair	
3. Haemodynamic issues	• persistent and late developing hypertension at rest and exercise • aortic valve dysfunction • rare dissection	
4. Arrhythmia/pacing	• not an issue	
5. Investigations	ECG	• LVH±repolarization changes
	Chest X-ray	• cardiomegaly • ascending aorta dilation • rib notching
	ECHO	• assessment of arch anatomy/gradient • associated lesions LVH and function
	TOE	• rarely provides additional information
	MRI	• investigation of choice
	Holter	• not indicated unless for ambulatory blood pressure
	Exercise test	• hypertension on exercise • arm/leg gradient • inducible repolarization abnormalities
	Catheterization	• if MRI unavailable for arch anatomy • for coronary angiography when indicated for intervention
	Additional	• screen for intracerebral vascular anomalies advocated by some
6. Indications for intervention	• significant recoarctation (gradient > 30mmHg at rest) • aortic aneurysm	
7. Interventional options	• balloon/stenting for anatomically suitable recoarctation• surgery for complex situations±aneurysms	
8. Post treatment outcome	• excellent but late hypertension and premature atherosclerosis/CVA/MI/heart failure	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception/ recurrence/fetal	• relieve residual coarctation prior to pregnancy or during unplanned pregnancy • monitor closely for hypertension • avoid oestrogen containing pill if rest or exercise hypertension	
11. Recurrence/genetics	—	
12. Syndromes	—	
13. Sport/physical activity	• no restrictions if adequate relief of obstruction/no residual hypertension	
14. Insurance	• category 2	
15. Follow-up interval	• yearly with same investigations as for unoperated coarctation	
16. Follow-up care	• level 2	
17. Unresolved issues	• influence of age at repair, type of repair of intervention on late hypertension • late outcome of balloon/stenting • pathophysiology of late hypertension	

Patent arterial duct

Criteria	Comments	
1. Introduction and background		
2. Survival—adult life	• normal life expectancy in closed PDA • rare PVD for large PDA	
3. Haemodynamic issues	• usually none—LV dilatation/pulmonary hypertension in significant PDA	
4. Arrhythmia/pacing	• none	
5. Investigations	Chest X-ray	• baseline • cardiomegaly • ductal calcification
	ECG	• usually normal • LVH with large PDA
	ECHO/TOE	• usually diagnostic • TOE rarely indicated
	Catheter	• for closure coronary angiography in older patients
	MRI	• not indicated
	Holter	• not indicated
	Exercise	• not indicated
	Additional investigations	• none
6. Indications for intervention	• controversial for silent of very small PDA • continuous murmur • LV dilatation	
7. Interventional options	• catheter closure Intervention of choice • several device options • surgery for rare cases	
8. Post treatment outcome	• excellent • residual shunt in up to 10%	
9. Endocarditis	• not required after complete closure • prohylaxis indicated otherwise	
10. Pregnancy/contraception/fetal	• no problems unless pulmonary vascular disease	
11. Recurrence/genetics	• none	
12. Syndromes	• congenital rubella	
13. Sport/physical activity	• no restrictions unless PVD	
14. Insurance	• category 1 for small PDA or after closure	
15. Follow-up interval	• discharge 1 year after closure	
16. Follow-up care	• level 3 unless PVD (1)	
17. Unresolved issues	• indication of closure for small PDA	

Ebstein's anomaly

Criteria	Comments	
1. Introduction and background	• wide spectrum of pathologic anatomy which determines onset of severity of symptoms	
2. Survival—adult life	• extremely variable natural history • infant survivors usually reach	
3. Haemodynamic issues	• cyanosis at rest and/or exercise (right—left shunt at atrial level) reduced exercise capacity • congestive heart failure (tricuspid stenosis/regurgitation/small RV) • associated lesions • LV abnormalities	
4. Arrhythmia/pacing	• atrial arrhythmias are common • increase with age • related to pre exultation and atrial dilatation • risk of sudden death	
5. Investigations	Chest X-ray	• marked cardiomegaly • right atrial enlargement
	ECG	• baseline (characteristic pattern) • follow-up for rhythm
	ECHO/TOE	• severity of tricuspid valve displacement dysplasia and regurgitation • RV size • associated lesions • LV function
	Catheter	• rarely required unless for coronary angiography in older patients or at EPS
	MRI	• rarely required
	Holter	• useful for arrhythmia monitoring
	Exercise	• baseline and follow-up • cyanosis • exercise tolerance • arrhythmia
	Additional investigations	• EPS for arrhythmia diagnosis and RFA
6. Indications for intervention	• decrease in exercise tolerance • heart failure • increase in cyanosis • arrhythmia	
7. Interventional options	• surgery for tricuspid valve repair or replacement • RFA for arrhythmias/pre exultation	
8. Post treatment outcome	• symptomatic improvement usual • tricuspid valve replacement—reoperation, thrombotic complications • ongoing arrhythmia problems frequent • risk of sudden death remains • anticoagulants for atrial arrhythmia and prosthetic tricuspid valve	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception/fetal	• well tolerated unless cyanosis or heart failure • fetus at risk in cyanosed mother	
11. Recurrence/genetics	• 6% in affected mother. 1% in affected father. Familiar occurrence documented.	
12. Syndromes	• rare	
13. Sport/physical activity	• recreational sport in asymptomatic patient	
14. Insurance	• unoperated asymptomatic or well post operative category 2	
15. Follow-up interval	• depends on clinical status • annual follow-up with ECHO/Holter + exercise test	
16. Follow-up care	• level 1 (operated and unoperated)	
17. Unresolved issues	• recurrence of arrhythmias • long-term fate of repairs	

Fontan

Criteria	Comments	
1. Introduction and background	• palliative procedure for single ventricle physiology in which all systemic venous return directed to the lungs–multiple modifications	
2. Survival→adult life	• improved survival with strict selection criteria • late failure even in best cases	
3. Haemodynamic issues	• function of systemic ventricle (preload deproved) • pulmonary vascular resistance • obstruction in Fontan connection • atrial enlargement • pulmonary venous obstruction • AV valve regurgitation • chronic venous hypertension • desaturation/paradoxical embolus in fenestrated Fontan • pulmonary arterio venous malformations in some	
4. Arrhythmia/pacing	• atrial arrhythmias common • increase with follow-up • sinus node dysfunction • pacing–ventricular pacing requires epicardial system	
5. Investigations	Chest X-ray:	• baseline and follow-up • cardiomegaly • pulmonary vascular markings
	ECG:	• rhythm
	ECHO/TOE:	• most useful investigation for • ventricular function • AV valve regurgitation • residual shunts • obstruction of Fontan connections • thrombus in atrium • routine TOE (2 yearly may be indicated or of arrhythmia present)
	Catheter:	• for haemodynamic assessment and angiography in clinical deterioration
	MRI:	• obstruction of Fontan connection • occasionally useful for RA size and anastamieos
	Holter:	• routine and for symptomatic arrhythmia
	Exercise testing	• reaction activities only
	Additional investigations:	• blood/stool for PLE
6. Indications for intervention	• cyanosis • obstruction to Fontan connection • systemic AV valve regurgitation • ventricular failure • arrhythmia • pulmonary venous obstruction	
7. Interventional options	• consider conversion to TCPC or transplant in failing Fontan• closure of fenestration • AV malformations • RFA • Supraventricular arrhythmia • AV sequential pacing	
8. Post treatment outcome	• variable success with catheter ablation of atrial arrhythmias• PLE has <50% 5 year survival • Fontan conversion results unclearatrial arrhythmias common.	
9. Endocarditis	• prophylaxis in all	
10. Pregnancy/contraception/fetal	• pregnancy possible with perfectly selected patients and proper care • high maternal risk in 'failing Fontan' • higher miscarriage rate • fetal risk of CHD may be higher • avoid oestrogen pill if ejection fraction <40%, residual shunt, or spontaneous contrast in RA • ACE inhibitors should be withdrawn if on anticoagulants–need meticulous management	
11. Recurrence/genetics	• non	
12. Syndromes	• none	
13. Sport/physical activity	• recreational sports only	
14. Insurance	• category 3	
15. Follow-up interval	• at least yearly review with ECHO, ECG Holter, exercise testing, blood testing	
16. Follow-up care	• level 1	

17. Unresolved issues	• indications for and results of Fontan conversion • outcome of TCPC in modern era • role of anticoagulation • medical therapy for failing systemic ventricle • role of ACE inhibitors

Marfan's syndrome

Criteria	Comments	
1. Introduction and background	• abnormal fibrillin gene on chromosome 15q • autosomal dominant inheritance • cardiac defect largely determined outcome	
2. Survival—adult life	• death from cardiac problems • life expectancy reduced but improved by good cardiac follow-up and surgery	
3. Haemodynamic issues	• acute aortic dissection—risk higher if the aortic sinuses >55mm • aortic regurgitation • mitral valve prolapse/regurgitation	
4. Arrhythmia/pacing	• atrial and ventricular arrhythmia in mitral valve prolapse/regurgitation	
5. Investigations	Chest X-ray	• not helpful for follow-up of aorta
	ECG	• rarely useful
	ECHO/TOE	• most valuable investigation for serial follow-up of aortic root dimensions, valve function (aortic and mitral)
	Catheter	• rarely indicated
	MRI	• excellent investigation for aortic arch and descending aorta • compliments echocardiography
	Holter	• not routine
	Exercise testing	• not routine
	Additional investigations	• non-cardiac assessment (ophthalmic, orthopaedic etc.)
6. Indications for intervention	• beta blockers for aortic dilatation • surgery if aortic diameter >55mm or rapid increase • significant aortic regurgitation • significant mitral regurgitation	
7. Interventional options	• urgent surgery for dissection • aortic root and valve replacement • valve sparing operation may be indicated	
8. Post treatment outcome	• Surgery improves life expectancy but other dissections still possible • beta blockers delay/prevent progression	
9. Endocarditis	• prophylaxis in valve regurgitation and after aortic surgery	
10. Pregnancy/contraception/fetal	• pregnancy contraindicated if aorta is >45mm • pregnant women should be on beta blockers • caesarean section to be discussed if aorta is dilated	
11. Recurrence/genetics/syndrome	• approximately 50% (autosomal dominant)	
12. Sport/physical activity	• strenuous exercise contra-indicated high altitude and diving contra-indicated (spontaneous pneumothorax)	
13. Insurance	• category 3	
14. Follow-up interval	• annual follow up for aortic dilatation • more frequent evaluation if aortic diameter increasing	
15. Follow-up care	• level 1	
16. Unresolved issues	• role of early beta blockade • long term results of surgery including valve sparing	

Postoperative transposition (Mustard/Senning)

Criteria	Comments	
1. Introduction and background	• common lesion—most Mustard/Sennings patients now adults—operation replaced by arterial switch mid 1980's	
2. Survival—adult life	• low early mortality • significant late morbidity/mortality from arrhythmia/baffle obstruction/RV failure with risk of sudden death	
3. Haemodynamic issues	• intra-atrial baffle obstruction (systemic and pulmonary venous) more common in Mustard than Senning • tricuspid regurgitation/RV failure relatively rare but important to detect early	
4. Arrhythmia/pacing	• progressive loss of sinus rhythm on Holter with follow-up • slow junctional rhythm may rarely require pacing • tachyarrhythmias (predominantly atrial flutter) may be related to high incidence of late sudden death • pacing may be required if antiarrhythmic drugs	
5. Investigations	ECG	• RVH with basic rhythm (often junctional)
	Chest X-ray	• useful for cardiomegaly • pulmonary venous obstruction
	ECHO/TOE	• TTE for ventricular function/tricuspid regurgitation • TOE essential if questions remain regarding baffle function
	MRI	• rarely required if TOE available
	Holter	• occult arrhythmia • not predictive of SD
	Exercise test	• exercise tolerance • evaluation of arrhythmia
	Catheterization	• for intervention and assessment of new onset symptoms
	Additional	EP study/RFA for refractory atrial arrhythmias
6. Indications for intervention	• baffle obstruction • baffle leaks • tricuspid valve dysfunction • RV failure	
7. Interventional options	• balloon/stenting for pathway obstruction • transcatheter closure for baffle leaks • tricuspid valve/replacement • conversion to arterial switch (pulmonary artery banding) • transplantation	
8. Post treatment outcome	• risk of sudden death despite lack of symptoms or overt haemodynamic disturbance	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception/ recurrence/fetal	• pregnancy not contra-indicated in most cases • monitor RV function throughout • no contraceptive issues • long-term consequences on RV function not known	
11. Recurrence/genetics	• familial recurrence of TGA rare	
12. Syndromes	• none	
13. Sport/physical activity	• generally normal activities • maximal exercise tolerance likely to be diminished	
14. Insurance	• category 3	
15. Follow-up interval	• yearly	
16. Follow-up care	• level 1	
17. Unresolved issues	• risk stratification for sudden death • fate of systemic RV/tricuspid valve • indication/conversion/transplant strategies	

Congenitally corrected transposition

Criteria	Comments	
1. Introduction and background	• rare lesion • usually associated with other abnormalities • may occur with dextrocardia	
2. Survival—→adult life	• common to survive to adult life • associated lesions common (VSD, PS, left AV valve regurgitation) determine outcome	
3. Haemodynamic issues	• cyanosis with VSD and PS • PVD if VSD and no PS • systemic ventricular failure with systemic A-V valve regurgitation • referral before systemic ventricular dysfunction	
4. Arrhythmia/pacing	• spontaneous CHB (2% per year) and post surgical heart block• endocardial pacing in the morphologic LV • atrial arrhythmias common • ventricular arrhythmias with systemic ventricular dysfunction • epicardial pacing if potential for paradoxical embolus	
5. Investigations	Chest X-ray:	• baseline • follow-up for associated lesions • cardiomegaly
	ECG:	• rhythm
	ECHO/TOE:	• size and function of systemic ventricle• morphology of left A-V valve • associated lesions
	Catheter:	• for pulmonary haemodynamics and anatomy of associated lesions
	MRI:	• rarely required
	Holter:	• for occult arrhythmia detection
	Exercise function:	• helpful for timing of surgery • oximetry • exercise tolerance
	Additional investigations:	• occasionally MUGA for ventricular function
6. Indications for Intervention	• +>moderate systemic AV valve regurgitation • significant associated lesions • pacemaker for complete AV block with symptoms, profound bradycardia or chronotropic incompetence	
7. Interventional options	• valve replacement • pulmonary artery banding • 'double switch' (controversial in adults)	
8. Post treatment outcome	• good if left A-V valve replacement before systemic ventricular function deteriorates • atrial arrhythmias common	
9. Endocarditis	• prophylaxis in all cases	
10. Pregnancy/contraception/fetal	• pregnancy not contra-indicated if asymptomatic • monitor ventricular function and rhythm • long-term consequences on systemic ventricular function unknown • avoid oestrogen containing contraceptive pill if cyanosed/pulmonary hypertension	
11. Recurrence/genetics	• 4%	
12. Syndromes	• none	
13. Sport/physical activity	• no restriction on recreational activities	
14. Insurance	• Category 3 in most cases	
15. Follow-up interval	• yearly, with ECHO, exercise test±Holter	
16. Follow-up care	• level 1 (pre and postoperative)	
17. Unresolved issues	• classical repair of VSD and PS versus 'double switch.'	

SECTION III

Original Investigation.

Results of surgery for Congenital Heart Disease in the adult age.

An Italian Multi-Center Study.

Clinical Study

Comprehensive data on results of surgery for congenital heart disease in the adult age are still lacking. We have designed a multi-center study involving 7 major Italian cardiac centers, so as to evaluate the early and mid term outcome of cardiac surgery in this particular group in our country. Cardiac centers involved were the following:

a. Pediatric and Congenital Cardiac Surgery Unit, Centro Gallucci, University of Padova Medical School, Padova, Italy;

b. Department of Cardiovascular Surgery, Ospedali Riuniti di Bergamo, Bergamo, Italy;

c. Department of Pediatric Cardiology, Ospedale G. Pasquinucci CREAS-CNR, Massa, Italy;

d. Department of Pediatric Cardiac Surgery, Azienda Ospedaliera S. Orsola-Malpighi, Bologna, Italy;

e. Department of Cardiac Surgery, Istituto Policlinico San Donato, Milano, Italy;

f. Department of Cardiac Surgery, Ospedale Niguarda Cà Granda, Milano, Italy;

g. Pediatric Cardiology, Ospedale Monaldi, Seconda Università degli Studi di Napoli, Naples, Italy.

Materials and methods

All mayor congenital cardiac centers in Italy (12) were invited to be part of this study, in a 5 years time frame, under supervision of the Italian Society of Cardiology. Seven centers joined the study by sending complete data and respecting requirements as indicated in a pre-set database. All these centers are medium–high surgical volume centers, with a number of cases ranging between 200 and 450 case/year. All the participating centers are tertiary level national centers. Five of the

seven centers have a cardiac transplant program; 2 centers are authorized for heart-lung transplantation.

Database was designed basing on demographic, pathological, surgical and postoperative data as requested in the EACTS Congenital Database (www.eactscongenitaldb.org),[1] and data were collected in 4 different Microsoft Access sheets (preoperative, operative, postoperative and follow up, were variables were listed for each patient, according to the EACTS Congenital Database).[1]

Eight hundred fifty six patients were enrolled, who underwent surgery for a variety of congenital heart diseases between January, 1st 2000 and December, 31st 2004. Male/female ratio was 1.13 (455 men-53,2 %; 401 women-46,8 %). Age ranged between 18 and 80 years (mean 37.2 years, median 34.2 years). Diagnoses, procedures, extracardiac anomalies, preoperative risk factors and postoperative complications were classified according to the EACTS Congenital Database classification as described elsewhere.[72] Diagnoses were divided into "anatomic" (as the basic heart malformation) and "leading to surgery" (as the cause for operation, regardless of the basic anatomy) diagnoses (Tables 5a-5b).

Surgical procedures (intended as a surgical procedure for a single major congenital cardiac lesion; more than one surgical procedure may be associated in the same operation in the same patient with a complex congenital cardiac lesion) were arbitrarily divided into 3 groups:

- Group 1: Palliative procedures, as any operation performed to improve the patient's clinical status, without restoring normal anatomy or physiology (Table 6).
- Group 2: Repair procedures, as any operation designed to achieve an anatomical or physiological correction resulting in a separation of the pulmonary from the systemic circulation. We have included in this group also the Fontan-type repair and "one and a half ventricle repair" (Table 7).
- Group 3: Reoperation, as any cardiac surgical procedure after either physiologic or anatomic repair (Table 8).

Postoperative clinical variables such as postoperative low cardiac output (defined as a cardiac index below 2.0 l/min/m^2), onset of pneumonia, pleural effusions, pericardial effusions,

arrhythmias, length of stay in intensive care unit (ICU), surgical wounds complications were recorded and utilized for statistical analysis.

Follow up was based on clinical data derived from the "Congenital Heart Disease in Adults" Database followed by each center, which considers onset of adverse events listed as follows: late cardiac death, late non cardiac death, reoperation, interventional cardiology procedure, other. Late term clinical status was defined according to NYHA functional class and Ability Index (AI), as reported on clinical charts. We arbitrarily chose NYHA class and Ability indexes as variables that characterize cardiac status. These indexes are commonly recognized to be equally suitable for the judgement of heart failure in post surgical patients.[102] These indexes were subsequently transformed into binary variables to perform the proportional hazard regression analysis (NYHA Class I=0; NYHA Class II, III, IV = 1; Ability index class 1=0; Ability index class 2,3,4=1)

Statystical analysis

Survival estimates for all patients were analyzed with Kaplan Meyer method applied to the most represented main cardiac lesions (ASD, Right heart lesion, Left heart lesion, single ventricle) and to the main lesions stratified in the 3 different operative categories, (palliation, repair, reoperation). The effect of preoperative functional NYHA class III and IV, with or without associated cyanosis, was similarly evaluated. Statistically significant incremental (Hazard Ratio-HR > 1.0) or decremental (HR < 1.0) risk factors were identified by means of a forward stepwise (p to enter 0.05, p to remain 0.2) Cox analysis of operative categories of surgery, pathologies and preoperative risk factors.

Cox analysis was also applied to estimate the effect of the same covariates on patients' postoperative and late morbidity. Morbidity was estimated by means two dummed variables, i.e. post operative NYHA class, and post operative Ability Index, defined as 0 when the postoperative NYHA class and Ability index were = 1 (i.e. no symptoms), or 1 when NYHA class and Ability Index were other than 1, and therefore patients were symptomatic.

Results

Noninvasive preoperative diagnosis by means of 2-Dimensional and Doppler echocardiography (associated or not to other non invasive techniques) was possible in 530 patients (61.9%). Cardiac catheterization in association to non invasive techniques was used in 273 patients (31.8%); in 39 patients (4.5%) diagnosis was made by cardiac catheterization only; magnetic resonance imaging (MRI) was self sufficient in 13 patients (1.5%). No data were available for 1 patient.

According to the preoperative clinical and instrumental evaluation, 294 patients (34.6%) were classified in the New York Heart Association (NYHA) functional class I, 412 in class II (48.4%), 120 in class III (14.2 %), and 24 in class IV (2.8%). No data were available for 7 patients.

Preoperative electrocardiogram showed sinus rhythm in 83% of the patients. Major arrhythmias included atrial fibrillation in 55 patients (6.4%), supraventricular tachyarrhythmias in 13 (1.5%), complete atrioventricular block in 1.1 %, atrial flutter in 0.7%.No data were available in 8.8% of patients.

Associated extracardiac anomalies were present in 40 patients and included Marfan syndrome in 19 (2.3%), Down's syndrome in 12 (1.4%), Williams Beuren syndrome in 3 (0.3%) and Turner's syndrome in 1 patient. Other non significant chromosomal anomalies were found in 4 patients.

We collected 1196 "anatomic diagnoses" in 856 patients. Tables 5a and 5b shows diagnoses of basic heart malformation and diagnoses "leading to surgery".

There were 1179 surgical procedures performed in 856 patients in 7 centers (mean, 122.3 procedure/center; range, 34 to 334 procedures). Among these, there were 30 palliative procedures (Group 1) performed in 18 patients (2.4%, Table 6); 742 repair procedures (Group 2) in 628 patients (69.5 %, Table 7); 322 reoperations (Group 3) in 210 patients (27.4%, Table 8). Types of procedures are shown in Tables 6-8.

Twenty seven patients died within 30 days or prior to hospital discharge (early overall mortality equal to 3.1 %). Most common causes of death were: low cardiac output syndrome (13 patients, 1.5%), bleeding in 3 patients and sepsis in 2. Palliation group presented the highest early mortality (16.6%) when compared to group 2 (1.3%) and group 3 (7.6%). Main causes of early death and complications are listed in Table 9.

Mean intensive care unit stay was 2.3 days (ranged from 1 to 102 days); 5.2 days in Group 1, 1.8 days in Group 2, and 3.5 days in Group 3. Postoperative complications were reported in 247 patients (28.8%). The most common complications included: postoperative arrhythmias (64 events), low cardiac output syndrome (28 events), bleeding requiring reoperation (24 events), pleural effusion requiring drainage (19 events) postoperative mechanical ventilation for more than 7 days (17 events), pneumothorax (10 events). Postoperative arrhythmia and bleeding were the commonest complications in Group 2, while in Groups 1 and 3 low cardiac output syndrome complicated postoperative course more commonly (Table 9). Seven patients, the majority of whom were younger than 30 years, were put unsuccessfully on mechanical circulatory support device.

Cardiac rhythm at the moment of discharge from the hospital showed 90.5% of patients with sinus rhythm by electrocardiogram, while 2.5 % showed atrial fibrillation, 0.8% complete atrioventricular block (III degree, CAVB), 0.2% atrial flutter. This compares favorably with preoperative ECG data; however, these differences where not statistically significant. In addition, CAVB incidence is reduced because 3 of the patients affected died at operation. (Table 10)

Follow-Up

Follow-up period ranged from 1 month to 5.2 years (mean 21.8 months, median 18.9). Follow up completeness was 87% (744/856 patients).

Overall, there were 48 adverse events among survivors, arrhythmias and chest effusions (pleural or pericardial) being the most common. Late cardiac death occurred in 4 patients (0.46%); in one additional case, death was non cardiac related. Reoperation was necessary in 9 pts (1%), consisting mainly in valve replacement (2 pts) and pacemaker implantation (2); heart transplant was performed in 1. Interventional cardiology procedures were done in 5 patients (0.5%), and were mainly anti-arrhythmia procedures (3 pts). All data exposed in Table 11.

At latest follow up, 79.3 % of the patients are in NYHA class I, 17.6 % in NYHA class II , 2.9 in NYHA class III, and only one patient is in NYHA class IV (corrected TGA after PA banding and mitral valve plasty). Ability Index is estimated as grade I in 82.4%, II in 13.7 %, and III in 2.3 %. None was found to be in Ability Index grade IV. Data were not available in 1.6% of patients.

Statistical Analisys

Overall survival at 5 years for all procedures is 96%. Survival curves according to Kaplan-Meyer are shown in Figures 1-13. Survival is evaluated according to different variables. Survival estimate is 82.6% at 4 years for palliation procedures, 98.9% for repair and 91.8% for reoperation at 5 years, p value < 0.0001 (Figure 1). Patients presenting with preoperative NYHA class IV (associated or not to cyanosis) are characterized by a survival estimate which is significantly lower vs other patients, 70% and 92.3% respectively, vs 97.1, p value < 0.0001 (Figure 2). Survival estimate for patients in preoperative NYHA class III is significantly lower vs other patients, 97.1% vs 90.4%, p value = 0.012 (Figure 3) ; in addition it is 99.7% at 5 years for ASD and 93.5% at 5 years for all the other pathologies, p value<0.0001(Figure 4).

When estimates are analized considering the main anatomical diagnoses, interesting data are produced. Patients with single ventricle present a survival estimate equal to 75% vs 97% for non single ventricle patients, p value < 0.0001 (Figure 5); in addition, there is no significant difference for these patients when considered by surgical category, p value= 0.24 (Figure 6). Survival estimate for patients with a right heart lesion is 92.8% vs 97.2% for patients with other tha right heart lesion diagnosis , p value = 0.023, (Figure 7); in addition, survival in patients with a right heart lesion by category is 77.8% for palliation, 95.9% for repair, 91.2% in reoperation, p value = 0.0292 (Figure 8). Survival estimate for patients with left heart lesion is 98.9% vs 95.3% for patients without, p value 0.05 (Figure 9); however, there is no significant difference for these patients when considered by category (p value = 0.0884) (Figure 10).

Considering association to cyanosis, survival estimate is 97.4% at 5 years for preoperative acyanotic patients and 88.8 % at 5 years for patients who presented preoperatively with associated cyanosis, p value <0.0001 (Figure 11).

When we focus attention to late morbility, overall freedom from adverse events is 88% at 5 years, CI 95% (Figure 12). Furthermore, freedom from any kind of adverse event is 91% for non cyanotic vs 63.9% at 5 years, p value < 0.0001 (Figure 13).

Multivariate Cox analysis identifies among the most powerful incremental risk factors for survival preoperative NYHA class IV in cyanotic patients (Hazard Ratio 8.6, p value =0.001), and NYHA class III (Hazard Ratio 2.7, p value =0.023); single ventricle as preoperative diagnosis (Hazard Ratio 2.6, p value= 0.032) and reoperation surgical category (Hazard Ratio 2.3, p value= 0.029). On the contrary, the most powerful decremental risk factors for survival result to be ASD (Hazard Ratio 0.08, p value =0.0018) and left heart lesion (Hazard Ratio 0.16, p value =0.014) diagnoses. All these data are reported in detail in Table 12.

We subsequently focused our attention on late morbidity as characterized by NYHA class and Ability Index evaluation. Multivariate Cox analysis identifies as the most powerful incremental risk factors for postoperative NYHA class greater than 1 the length of ICU stay (Hazard Ratio 1.037, CI 95%=1.002-1.072, p=0.036), the number of previous operations (Hazard Ratio 1,445 CI 95%= 1,1213-1,721, p<0.001), associated preoperative cyanosis (Hazard Ratio 1,555, CI 95%= 1,035-2,335, p=0,034), alteration of cardiac rhythm before surgery (Hazard Ratio 1,124, CI 95%=1,040-1,215, p=0,03), a pre-operative NYHA class>1 (Hazard Ratio 1,573, CI 95%=0,954-2,593, p=0.076), and age > 40 years (Hazard Ratio 1,466, CI 95%= 1,014-2,119, p=0.042). These data are reported in Table 13.

Similarly, as far as the Ability Index evaluation at follow up, Cox analysis identifies among the most powerful incremental risk factors for having an Ability Index worse than grade 1, the following parameters: number of operations (Hazard Ratio 1,197 CI=1,030-1,391, p<0.019); preoperative cyanosis (Hazard Ratio 1,649 CI 95%=1,178-2,307, p=0,004; alteration of cardiac rhythm before surgery (Hazard Ratio 1,096, CI 95%=1,021-1,117, p=0,011); pre-operative NYHA class>1 (Hazard Ratio 2,454, CI 95%=1,565-3,847, p<0.001). These final data are listed in Table 14.

Discussion

As above mentioned, since the late '60s, the success of cardiac medical and surgical therapy has drastically modified the natural history of almost all congenital heart diseases. This improvement has selected a growing number of newborns and infants who have survived through adolescence, until adulthood. These adults constitute the new challenge for the third millenium not only for cardiologists and cardiac surgeons, but also for the entire medical community. Jane Somerville has named these patients as GUCH (or Grown Up Congenital Heart disease),[5] while in United States these adults are commonly referred as adults with CHD or ACHD.[6]

This population specifically includes: 1. patients with a recognized CHD who have survived into adult age without any kind of surgical treatment and without chronic deleterious effects on heart and lungs; 2. patients who need repair, or additional palliative procedures, or even heart transplantation after a previous palliative procedure; 3. patients who require reoperation because of late complications or residual defects after complete repair; 4. patients with late diagnosis of CHD in adult age.

As reported elsewhere, the number of adult patients with CHD was calculated to be equal to pediatric patients in the year 2000, and it is expected that it will exceed those in pediatric care by a considerable margin soon.[4,7] Chessa and associates reported that it is expected that in Italy there are currently 60,000 to 100,000 adult patients with congenital heart disease, requiring follow up.[9]

The impact of such a peculiar group of patients on medical community is relevant. This population of adults has special needs and peculiar problems.[4-6,9,12] As outlined by Warnes,[11] despite great advances in diagnosis and therapy occurred in the last decades, many intracardiac repairs and circulations may still not function "normally", and most ACHD patients should not be considered as "cured". In fact, residual problems are common, and they may need a lifelong follow up, with appropriate treatment and care, either medical, or surgical.

Somerville and associates estimates that almost 20% of admissions to a so called ”GUCH unit” is for surgical indication.[5] Adult patients are usually referred for surgery because of increasing of symptoms when not controllable by medical therapy.[5] In our experience, prior to operation, the majority of patients have been on NYHA class I and II, and surgery was dictated more by the existing diagnosis than symptoms, with the aim of restoring the normal circulation and modifying the natural history of CHD.

The analysis of data collected in our multi-center study shows that cardiac surgery in ACHD has been characterized by a relatively low overall operative mortality (3.1%). This is comparable to a previous reported European experience of 2.4%,[72] and considerably lower than 6.3%, as reported by Srinathan et al.[103] It is of note, however, that in our study, we have analized patients who, frequently, were preoperatively in good clinical conditions (NYHA class I or II in the majority), and ASD was undoubtly a very common “leading to surgery” diagnosis. This has certainly influenced our good early outcome. For this reason, in our analysis we have extrapolated the survival for patients with a diagnosis-other-than-ASD, and we have found that in this selected group, mortality is still inferior to 6% (see Figure 4). This may support the common feeling that precocious diagnosis and surgical treatment before irreversible cardiac decompensation and onset of severe symptoms is a rational strategy to improve results.

In addition, our statistical analysis shows an estimated cumulative survival of 96% at 5 years; when considered by category, it is higher for complete repair (98.9%) as compared with reoperations (91.8 %) and palliation (82.6%). Thus, despite repair of congenital heart defects is performed later than the ”proper time” (which is currently early infancy for most CHD), this can still be carried out with a relatively low mortality risk.

In our experience, the most represented group is the repair one (Group 2), which shows excellent operative results in the early and mid term. This is generally true also for patients with single ventricle anatomy, who have undergone a physiological correction by means of a Fontan repair and one and half ventricle repair. However, our analysis demonstrates that single ventricle diagnosis is still a considerable risk factor for mortality in the mid term (HR: 2.6, p value 0.032).

As reported by Srinathan and associates,[103] it is expectable that the rate of first repair in adults will decrease as the time goes by, while redo operations will represent the major portion of these procedures in the next future. About 30% of lesions undergoing repair in our series consisted of ASDs. It's surprising that such a large population of patients in our country are still undergoing surgical rather than transcatheter device closure. We could not identify specific reason in this matter. However, despite reported advantages of percutaneous closure in adults,[104] our experience shows excellent early and mid term results, either in terms of mortality or clinical improvement, with no operative risk. In light of these results, we believe that especially in those patients with history of transitory ischemic attack or neurological deficit due to patency of foramen ovale, or atrial septal aneurysm, or coagulation disorders, ASD surgical closure still plays an important role so as to avoid persistence of artificial conditions linked to the device implantation. Longer follow up is certainly needed also in these patients in order to outline occurrence of arrhythmic events that are often causes of important morbidity in the long term. [105]

Group 1 (Palliation) is the least represented group, but presents with the worse results. It is predictable that palliative procedures will soon decrease in number since patients with cyanotic CHD are currently repaired in early infancy, with the aim of correct or avoid long term cyanosis. A palliative procedure in the adult age is still undertaken in order to improve temporarily the clinical status in patients with no chance for correction, or other substitutive type of surgery. A considerable rate of non fatal complications has doomed the palliation group either in the postoperative course or in the follow up time. This is predictable as we know that preoperative cyanosis is an important risk factor for early and mid term outcome of ACHD patients.[72,105,106] The reason for this common finding is the existence of complex pathology, additional collateral pulmonary and mediastinal vascularization, bleeding disorders and impaired cardiac function.[45-48,107] Our statistical analysis confirms these data and underlines that when cyanosis is associated to NYHA IV functional class, the patient has an extremely high risk, accounting for an Hazard Ratio of 8.6 (Figure 2).

As the number of patients who are treated for CHD in pediatric age is increasing around the world, a new emerging class is that of adult patients who are now facing the long term effects of a

residual congenital defect and /or the sequele of the treatment. Many of them do need a reoperation after primary repair. Limited knowledge exists on optimal timing for reoperations, perioperative risk factors and long term benefits. Surgical mortality in this subset of patients varies between 5.6 and 8.6%.[103,106,108,109] In our multicenter experience, early mortality of 7.6% is higher than for repair, and reoperation is associated to Hazard Ratio equal to 2.3. In this group of patients, the intrinsic risk of intra and/or postoperative hemorrhage by redo-sternotomy, and managing of adherences has to be taken into account. However, redo sternotomy has not been a cause on death in our experience. These patients are often in a more compromised preoperative clinical status, and, as expected, they present a high frequency of postoperative complications (42.4% in Berdat' series, [106] 36.4% in ours). As also outlined by others,[103,108,109] in our experience postoperative low cardiac output syndrome has been the main complication and cause of death in this subgroup This finding confirms the current opinion that condition which may have a negative impact on cardiac function such as heart failure as indication for reoperation, or cyanosis, are identified as additional risk factors for postoperative death.[103] In addition, we are inclined to think that some of these patients may have benefited from earlier intervention before irreversible myocardial deterioration was established, as proposed by some authors.[110]

If assessment of survival is certainly necessary to evaluate operative risks of surgery in adults with CHD, we also pointed our attention to evaluation of results in terms of clinical outcome and status of these patients in the mid term .In literature, limited knowledge exists on optimal timing for reoperations, perioperative risk factors and long term benefits. As reported elsewhere, [4,5,7,11,106] these patients are often in a very compromised preoperative clinical status, and, as expected, they presented a high frequency of postoperative complications (ranging from 36.4% to 42.4%). As also outlined elsewhere, [103] in our experience postoperative low cardiac output syndrome has been main cause of death in this series. When we analyzed clinical late outcomes, we referred to clinical conditions as described at follow up controls by means of NYHA and Ability index assessement. These indexes are commonly recognized to be equally suitable for the judgement of heart failure in post surgical patients.[102] Our statistic elaboration has shown that a

patient with preoperative NYHA class >1 is likely to have greater morbidity in the late term, defined as NYHA Class and Ability Index greater than 1 at follow up (since Hazard Ratios are calculated to be 1.573, p-value 0.076, and 2.454, p-value < 0.001, respectively-Table 13 and 14). In addition, as for patients with acquired heart disease, aging may play a role in risk for "bad" late outcome intended as above: in fact our study demonstrates a significant incremental risk in patients older than 40 years (HR 1.466, p-value 0.042).

These data, together with reported experiences in literature, may support the current opinion that ACHD patients may benefit from earlier intervention before irreversible myocardial deterioration is established. The concept of early intervention in ACHD patients after primary repair has been outlined by Judith Therrien and the Toronto group,[110] who reported experience of pulmonary valve replacement after repair for tetralogy of Fallot in 25 consecutive adult patients. In this series, a preoperative echocardiographic ejection fraction greater than 40% was significantly associated with a better postoperative ventricular function and, thus, hopefully to a better long term outcome. Diller and associates have pointed out that adults with CHD, even when asymptomatic, present with a decreased exercise capacity, and, thus, they hide a suboptimal cardiac fuction.[111] This retrospective analysis performed in 335 patients with heterogeneous CHD points out the concept that ACHD patients represent a very complex group of patients, that even when asymptomatic, they hide a less than normal cardiac situation. In our opinion, all caregivers devoted to CHD in adults should be aware of these informations and should pay more attention to the clinical status of these patients. All these data support the fact that early diagnosis and referral to surgical treatment (before irreversible cardiac decompensation and onset of severe symptoms occurs) may be a rational strategy to improve surgical results. This concept may be considered an extension of what Castaneda[112] suggested in 1989 for repair of neonates with CHD: as CHD causes in neonates progressive and severe multiple organ damage due to abnormal physiology, and repair is advocated to avoid irreversible pathophysiological changes, a chronic pathologic circulation persisting for years is doomed to produce multiple organ injuries, included lungs, heart and brain. For this reason, we believe that if surgery in ACHD is meant to be safe and effective, surgical timing remains

crucial. Thus, when diagnosis of CHD or residual defect after CHD surgery is made in an adult, surgery should be performed "before is too late", and surgical indication should be precocious, so as to have better hospital outcome.[113] For this reason, we think that if surgery is meant to be of some help for these patients, it should be performed before is too late, so surgical indication should be precocious. In addition, as outlined by several authors,[14-17] it is legitimate to think that postoperative intensive care knowledge in this field needs to be improved to be ready to face this increasing group of demanding patients. A devoted team of caregivers have to be well trained to treat these complex patients appropriately. This complex population is estimated to grow 5% per year. [114] Thus it is imperative that the medical community soon structures a functional care network for ACHD based on clinicians and surgeons with an adequate training and knowledge on congenital heart disease and physiology, together with the knowledge of problems of adult patients. As above mentioned and described by several authors,[16,17] care should be specialized in devoted hospital units where a complete team of cardiologists, congenital cardiac surgeons, heart and heart lung transplant team, intensive care specialists, anesthesiologists, but also endocrinology, gynecology and psychiatry specialists should be involved.

Major arrhythmias, as well as atrial fibrillation or atrioventricular block or atrial flutter, are more common among adult congenital patients instead of the pediatric population.[16] Several multi-center studies have described improvement in cardiac rhythm after operation.[72,113] Our study does show a trend of improvement in early postoperative course and at discharge, but most importantly underlines a significant impact of pre-operative alterations of cardiac rhythm on postoperative late outcome (Table 13 and 14). This confirms the common assumption that the most common reason for hospitalization in ACHD is for arrhythmias.

Finally, as previously reported,[72] preoperative cyanosis is an incremental risk factor related to worse late term outcome, described either as NYHA class > 1 (HR 1.55, p-value 0.034),or as Ability Index > 1 (HR 1.096, p-value 0.011), due to the above mentioned problems inherent with cyanosis itself.[45,48,107]

In conclusion, surgical treatment of congenital heart disease in adults is a safe and feasibòe procedure. Our analysis predicts a good mid term postoperative outcomes in terms of either survival or clinical status, with survival greater than 90% at 5 years for repair and reoperation categories. This allows the surgeons to be relatively optimistic in proposing surgical treatment to these difficult category of patients. However, survival is affected negatively by preoperative NYHA classes III and IV, diagnosis of single ventricle, while ASD diagnosis and left heart lesions are resulted to be decremental risk factors. Preoperative cyanosis is a negative prognostic factor either on early survival or on quality of life after surgery. In addition, our study has confirmed a significant influence of preoperative condition on clinical late outcome. We believe that closer follow up of these patients and learning the optimal surgical timing will improve clinical results and quality of life in the long term.

References

1. European Cardio-Thoracic Surgery Association Congenital Database, http://www.eactscongenitaldb.org

2. MacMahon B, Mckeown T, Record RG. The incidence and life expectation of children with heart disease. Br Heart J 1953; 15:121.

3. Moller JH, Taubert KA, Allen HD, Clark EB, Lauer RM. Cardiovascular health and disease in children: current status. A Special Writing Group from the Task Force on Children and Youth, American Heart Association. Circulation. 1994 Feb;89(2):923-30.

4. Webb GD. Care of adults with congenital heart disease. A challenge for the new millennium. Thorac Cardiovasc Surg 2001; 49:30-34.

5. Somerville J. Management of adult with congenital heart disease. An emerging increasing problem. Ann Rev Med 1997; 48:283-293.

6. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, Somerville J, Williams RG, Webb GD. Task force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol 2001;37:1170-5.

7. Williams WG, Webb GD. The emerging population with congenital heart disease. Pediatr Card Surg Annu Semin Thorac Cardiovasc Surg 2000; 3:227-233.

8. Wren C, O'Sullivan JJ. Survival with congenital heart disease and need for follow up in adult life. Heart 2001; 85: 438-443.

9. Chessa M, Cullen S, Deanfield J, Frigiola A, Negura DG, Butera G, Giamberti A, Bossone E, Carminati M. The care of adult patients with congenital heart defects: a new challenge. Ital Heart J 2004; 5:178-182.

10. British Cardiac Society. Current needs and provision of service for adolescents and adults in the United Kingdom. 2002.

11. Warnes CA. The adult with congenital heart disease. Born to be bad? JACC 2005; 46: 1-8.

12. Daliento L, Mazzotti E, Mongillo E, Rotundo M, Dalla Volta S. Life expectancy and quality of life in adult patients with congenital heart disease. Ital Heart J 2002; 339-347.

13. Cetta F, Warnes CA. Adults with congenital heart disease: patient knowledge of endocarditis prophilaxis. Mayo Clin Proc 1995; 70:50-4.

14. Connelly MS, Webb GD, Somerville J, Warnes CA, Perloff JK, Liberthson RR, Puga FJ, Collins-Nakai RL, Williams WG, Mercier LA, Huckell VF, Finley JP, McKay R.Canadian Consensus Conference on Congenital Heart Defects in the Adult 1996.Can J Cardiol. 1998;14:533-97

15. Therrien J, Gatzoulis M, Graham T, Bink-Boelkens M, Connelly M, Niwa K, Mulder B, Pyeritz R, Perloff J, Somerville J, Webb GD. Canadian Cardiovascular Society Consensus Conference 2001 update: Recommendations for the Management of Adults with Congenital Heart Disease—Part II. Can J Cardiol. 2001;17:1029-50.

16. Deanfield J, Thaulow E, Warnes C, Webb G, Kolbel F, Hoffman A, Sorenson K, Kaemmerer H, Thilen U, Bink Boelkens M, Iserin L, Daliento L, Silove E, Redington A, Vohue P. Management of Grown up congenital heart disease. The task force on the management of grown up congenital heart disease of the European society of cardiology. Eur Heart J 2003; 24:1035-1084.

17. Webb GD, Williams RG, et al.32nd Bethesda Conference: Care of the adults with congenital heart disease. Am Coll Cardiol 2001; 37:1161-1198.

18. Viner R. Transition from pediatric to adult care. Bridging the gaps or passing the buck? Arch Dis Child 1999; 81: 271-275.

19. Foster E, Graham TP, Driscoll DJ, Reid GJ, Reiss JG, Russel IA, Sermer M, Siu SC, Uzark K, Williams RG, Webb GD. Task force 2: special health care needs of adult with congenital heart disease. J Am Coll Cardiol 2001;37:1176-1183.

20. Stark J. Glenn Lecture. How to choose a cardiac surgeon. Circulation 1996; 94 (Suppl 9): II1-4.

21. Gatzoulis MA, Webb GD. Adults with congenital heart disease: a growing population. Section one, Chapter 1, in: Gatzoulis MA, Webb GD, Daubeney PEF. Diagnosis and Management of Adult Congenital Heart Disease. Churchill Livingstone. 1st Ed 2003.

22. Child JS, Collins Nakai RL, Alpert JS, Deanfield JE, Harris L, McLaughlin P, Miner PD, Webb GD, Williams RG. Task force 3: workforce description and educational requirements for the care of adults with congenital heart disease. J Am Coll Cardiol 2001; 37: 1183-1187.

23. Studio per la qualità nel trattamento delle cardiopatie in età pediatrica e nelle cardiopatie congenite nell'adulto. Progetto Baby Heart. www.sicch.it

24. Di Salvo G, Pacileo G, Caso P, Verrengia M, Rea A, Santoro G, Giovanna Russo M, Calabro R. Strain rate imaging is a superior method for the assessment of regional myocardial function compared with Doppler tissue imaging: a study on patients with transcatheter device closure of atrial septal defect.J Am Soc Echocardiogr. 2005;18: 398-400.

25. Nienaber CA, Rehders TC, Fratz S. Detection and assessment of congenital heart disease with magnetic resonance imaging techniques. J Cardiovasc Magn Reson 1999; 1:169-184.

26. Moon JC, Mc Kenna WJ, McCrohon JA, Elliot PM, Smith PC, Pennell DJ. Toward clinical risk assessment in hypertrophic cardiomiopathy with gadolinium cardovascular magnetic resonance. J Am Coll Cardiol 2003;41:1561-1567.

27. Moon JC, Reed E, Sheppard MN, Elkington AG, Ho SY, Burke M, Petrou M, Pennell DJ. The histologic basis of late gadolinium enhancement cardiovascula magnetic resonance in hypertrofic cardiomiopathy. J Am Coll Cardiol 2004; 43:2260-2264.

28. McCrohon JA, Moon JC, Prasad SK, Mc Kenna WJ, Lorenz CH, Coats AJ, Pennell DJ. Differentiation of heart failure related to dilated cardiomiopathy and coronary artery disease using gadolinium enhanced cardiovascular magnetic resonance. Circulation 2003; 108: 54-59. Dowdle SC, Human DG, Mann MD.

29. Pulmonary ventilation and perfusion abnormalities and ventilation perfusion imbalance in children with pulmonary atresia or extreme tetralogy of Fallot. J Nucl Med. 1990; 31:1276-9.

30. Chiou CW, Chen SA, Chang CE, et al. Radiofrequency catheter ablation of paroxysmal supraventricular tachycardia in patients with congenital heart disease. In J Cardiol 1995; 50:143.

31. Deal BJ, Mavroudis C, Backer CL,et al. New directions in surgical therapy of arrhythmias. Pediatr Cardiol 2000; 21: 576.

32. Sarkar D, Bull D, Yates R, et al. Comparison of long term outcomes of atrial repair of simple transposition with implications for a late arterial switch strategy. Circulation 1999;100(S 19):II187-192.

33. Julsrud PR, Weigel TJ, Van son JA, et al. Influence of ventricular morphology on outcome after the Fontan procedure. Am J Cardiol 2000; 86: 19-23.

34. Gatzoulis MA, Balaji S, Webber SA, Siu SC, Hokanson JS, Poile C, Rosenthal M, Nakazawa M, Moller JH, Gillette PC, Webb GD, Redington AN. Risk factors for arrhythmias and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet 2000; 356: 975-981.

35. Silka MJ, Hardy BG, Menashe VD, Morris CD. A population based prospective evaluation of risk of sudden death after operation for common congenital heart defects. J Am Coll Cardiol 1998; 32: 245-251.

36. Gatzoulis MA, Till JA, Somerville J, et al. Mechanoelectrical interaction in tetralogy of Fallot. QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. Circulation 1995; 92: 231-237.

37. Thorne SA, Barnes I, Cullinan P et al. Amiodarone associated thyroid dysfunction: risk factors in adults with congenital heart disease. Circulation 1999; 100: 149-154.

38. van Hare GF. Radiofrequency ablation of accessory pathways associated with congenital heart disease. Pacing Clin Electrophysiol 1997; 20: 2077-2081

39. Triedman JK, Bergau DM, Saul JP, et al. Efficacy of radiofrequency ablation for control of intraatrial reentrant tachycardia in patients with congenital heart disease. J AM Coll Cardiol 1997; 30: 1032-1038.

40. Westermann GR, Van Devanter SH. Surgical management of difficult pacing problems in patients with congenital heart disease. J Card Surg 1987; 2: 351-360.

41. Yap SC, Roos Hesselink JW, Hoendermis ES, Budts W, Vliegen HW, Mulder BJ, van Dijk AP, Schalij MJ, Drenthen W. Outcome of implantable cardioverter defibrillators in adults with congenital heart disease: a multi center study. Eur Heart J 2006; 28: 1854-1861.

42. Dore A, Santagata P, Dubuc M, Mercier LA. Implantable cardioverter defibrillators in adults with congenital heart disease: a single center experience. Pacing Clin Electrophysiol 2004; 27: 47-51.

43. Khairy P, Harris L, Landzberg MJ, Viswanathan S, Barlow A, Gatzoulis MA, Fernandes SM, Beauchesne L, Therrien J, Chetaille P, Gordon E, Vonder Muhll I, Cecchin F. Implantable cardioverter defibrillators in tetralogy of Fallot. Circulation 2008; 117: 363-370.

44. Findlow D, Doyle E. Congenital heart disease in adults. Br J Anesth 1997; 78: 416.

45. Rosove MH, Perloff JK, Hockin g WG, et al. Chronic hypoxemia and decompensated erythrocytosis in cyanotic congenital heart disease. Lancet 1986; 2:313.

46. Henriksson P, Varendh G, Lundstrom NR. Haemostatic defects in cyanotic congenital heart disease. Brit Heart J 1973; 41:23.

47. Spear GS. The glomerular lesion of cyanotic congenital heart disease. John Hopkins Med J 1977; 140: 185.

48. Perloff JK. Systemic complications of cyanosis in adults with congenital heart disease. Hematologic derangements, renal function, and urate metabolism. Cardiol Clin 1993; 11: 689-699.

49. Perloff JK, Child JS. Non cardiac surgery. In: Congenital heart disease in adults, 2nd Edn. Perloff JK, editor.Philadelphia Sanders 1998; 291-299

50. Eisenmenger V. Die angeborenen defecte der kammerscheidenwand des herzens. Z Klin Med 1897; 32: 1-28.

51. Wood P. The Eisenmenger syndrome or pulmonary hypertension with reversed central shunt. BMJ 1958; ii: 701-709, 755-762.

52. Daliento L, Somerville J, Presbitero P et al. Eisenmenger sindrome. Factors relating to deterioration and death. Eur Heart J 1998; 19: 1845-1855.

53. Avila WS, Grinberg M, Snitcowsky R et al. Maternal and fetal outcome in pregnant women with Eisenmenger's syndrome. Eur Heart J 1995; 96: 460-464.

54. Hosenpud JD, Bennet LE, Keck BM aet al. The registry of the international society for heart and lung transplantation: sixteenth official report-1999. J Heart Lung Transplant 1999; 18: 611-626.

55. Wei Li. Infective endocarditis. Section one, Chapter 15, in: Gatzoulis MA, Webb GD, Daubeney PEF. Diagnosis and Management of Adult Congenital Heart Disease. Churchill Livingstone. 1st Ed 2003.

56. ESC Task Force on Infective Endocarditis. Eur Heart J 1999

57. American College of Cardiology/American Heart Association Task Force on Practical Guideline. Joint Guidelines for the management of patients with valvular Heart disease:executive summary. Circulation 1998; 98: 1949-1984.

58. Warnes CA. Congenital heart disease and pregnancy. In: Elkayam U, Gleicher N, Editors. Cardiac problems in pregnancy. New york: John Wiley and asociates, 1988.

59. Siu SC, Sermer M, Harrison DA et al. Risk and predictors for pregnancy related complications in women with heart disease. Circulation 1997; 96: 2789-2794.

60. Clarkson PM, Wilson NJ, Neutze JM, et al.Outcome of pregnancy after the Mustard operation for transposition of the great arteries with intact ventricular septum. J Am Coll Cardiol 1994; 24: 190-193.

61. Ammash NM, Connolly HM, Abel MD, Warnes CA. Non cardiac surgery in Eisenmenger syndrome. J Am Coll Cardiol 1999; 33:222-227.

62. Canobbio MM, Mair DD, van der Velde M et al. Pregnancy outcomes after the Fontan repair. J Am Coll Cardiol 1996; 28: 763-767.

63. Vitale N, De Feo M, De Santo LS, et al. Dose dependent fetal complications of warfarin in pregnant women with mechanical heart valves. J Am Coll Cardiol 1999; 71: 1637-1641.

64. Sader L, McCowan L, White H et al. Pregnancy outcomes and cardiac complications in women with mechanical, bioprosthetic and homograft valves. Br J Obstet Gynecol 2000; 107: 245-253.

65. Presbitero P, Somerville J, Stone S, et al. Pregnancy in cyanotic heart disease. Outcome of mother and fetus. Circulation 1994; 89: 2673-2676.

66. Leonard H, O'Sullivan JJ, Hunter S. Family planning requirements in the adult congenital heart disease clinic. Heart. 1996;76:60–62.

67. Andersson K, Odlind V, Rybo G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial. *Contraception*. 1994;49(1):56–72.

68. Siu S, Chitayat D, Webb G. Pregnancy in women with congenital heart defects: what are the risks? Heart 1999; 81: 225–226.

69. Czeizel AE. Reduction of urinary tract and cardiovascular defects by periconceptional multivitamin supplementation. Am J Med Genet 1996; 62: 179–183.

70. Nora JJ. From generational studies to a multilevel genetic–environmental interaction. J Am Coll Cardiol 1994; 23: 1468–1471.

71. Fratz S, Kaemmerer H, Oechslin E et al. Emergency Hospital Admission of Adults with Congenital Heart Disease, a Multicentre Study. JACC. 2000;35(S2):503A.

72. Stellin G, Vida VL, Padalino MA, Rizzoli G. Surgical outcome for congenital heart malformations in the adult age. A multicentric European study. Ped Card Surg Ann Sem Thorac Cardiovasc Surg 2004; 7: 95-101.

73. Kristeller JL, Roslund BP, Stahl RF. Benefits and risks of aprotinin use during cardiac surgery. Pharmacotherapy. 2008; 28:112-124.

74. Backer CL, Kelle AM, Stewart RD, Suresh SC, Ali FN, Cohn RA, Seshadri R, Mavroudis C. Aprotinin is safe in pediatric patients undergoing cardiac surgery.J Thorac Cardiovasc Surg. 2007;134:1421-1426.

75. Naik SK, Knight A, Elliott MJ. A. A successful modification of ultrafiltration for cardiopulmonary bypass in children. Perfusion 1991; 6:41-50.

76. Maehara T, Novak I, Elliott MJ. Perioperative monitoring of total body water by bio-electrical impedance in children undergoing open heart surgery. Eur J Cardiothorac Surg 1991; 5: 258-265.

77. Naik SK, Balaji S, Elliott MJ. Modified ultrafiltration improves hemodynamics after cardiopulmonary bypass in children. [abstract]. J Am Coll Cardiol 1993;19:37.

78. Gaynor JW. The effect of modified ultrafiltration on the postoperative course in patients with congenital heart disease. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2003;6:128-39.

79. Perloff JK, Rosove MH, Child JS et al. Adults with cyanotic congenital heart disease: hematologic management. Ann Intern Med 1988;109:406–413.

80. Dajani AS, Taubert KA, Wilson W et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. Circulation. 1997; 96:358–366.

81. BaumVC, Perloff JK. Anesthetic implications of adults with congenital heart disease. Anesth Analg 1993; 76: 1342–1358.

82. Warner MA, Lunn RJ, P.W. O'Leary PW, Schroeder DR. Outcomes of noncardiac surgical procedures in children and adults with congenital heart disease. Mayo Perioperative Outcomes Group, Mayo Clin Proc 1998; 73: 728–734.

83. Lamour JM, Addonizio LJ, Galantowicz ME et al. Outcome after orthotopic cardiac transplantation in adults with congenital heart disease. Circulation. 1999;100(Suppl II):II200–II205.

84. Carey JA, Hamilton JRL, Hilton CJ et al. Orthotopic cardiac transplantation for the failing fontan circulation. Eur J Cardio-Thorac Surg. 1998;14:7–14.

85. Pigula FA, Gandhi S, Ritisch J et al. Cardipulmonary transplantation for congenital heart disease in the adult. J Heart Lung Transplant. 2000;19:94 (abstract).

86. Aaronson K, Schwartz JS, Chen T et al. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. Circulation. 1997;95:2660–2667.

87. Hosenpud JD, Bennett LE, Keck BM et al. The registry of the international society for heart and lung transplantation: Sixteenth official report — 1999. J Heart Lung Transplant. 1999;18:611–626.

88. Horner T, Liberthson R, Jellinek MS. Psychosocial profile of adults with complex congenital heart disease. Mayo Clin Proc. 2000;75:31–36.

89. Van Tongerloo A, De Paepe A. Psychosocial adaptation in adolescence and young adults with Marfan syndrome: An exploratory study. J Med Genet. 1998;35:405–409.

90. Gersony WM, Hayes CJ, Driscoll DJ et al. Second natural history, study of congenital heart defects: quality oflife of patients with aortic stenosis, pulmonary stenosis, or ventricular septal defect. Circulation. 1993;87(Suppl I):I-52–I-65.

91. Newburger J, Silbert A, Buckley L et al. Cognitive function and age at repair of transposition of the great arteries in children. N Eng J Med. 1984;310:1495–1499.

92. Miller G, Vogel H. Structural evidence of injury or malformation in the brains of children with congenital heart disease. Semin Pediatr Neurol. 1999;6(1):20–26.

93. McGrath KA, Truesdell SC. Employability and career counseling for adolescents and adults with congenital heart disease. Nurs Clin North Am. 1994;29:319–330.

94. Manning J. Insurability and employability of young cardiac patients. Engle M. Paediatric Cardiovascular Disease. 2nd Edn. Philadelphia: Davis; 1981, 117–127.

95. Celermajer DS, Deanfield JE. Employment and Insurance for Young Adults with Congenital Heart Disease. Br Heart J. 1993;69:539–543.

96. Kaemmerer H, Tintner H, Konig U et al. Psychosocialproblems of adolescents and adults with congenital heart defects. Z Kardiol. 1994;83(3):194–200.

97. Opocher F, Varnier M, Sanders SP, Tosoni A, Zaccaria M, Stellin G, Milanesi O. Effects of aerobic exercise training in children after the Fontan operation. Am J Cardiol. 2005; 95: 150-2.

98. Cullen S, Celermajer DS, Deanfield JE. Exercise in Congenital Heart Disease. Cardiol in the Young. 1991;1:129–135.

99. Fredriksen PM, Veldtman G, Hechter S et al. Aerobiccapacity in adults with various congenital heart diseases. Am J Cardiol. 2001;87:310–314.

100. Maron BJ, Isner JM, McKenna W. 26th Bethesda Conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. Task Force 3: Hypertrophic cardiomyopathy, myocarditis and other myopericardial diseases and mitral valve prolapse. J Am Coll Cardiol. 1994;24:880–885.

101. Meijboom F, Szatmari A, Deckers JW et al. Cardiacstatus and health-related quality of life in the long term after surgical repair of tetralogy of Fallot in infancy and childhood. J Thorac Cardiovasc Surg. 1995;110:883–891.

102. Norozi K, Wessel A, Buchhorn R, Alpers V, Arnhold JO, Zoege M, Geyer S. Is the ability index superior to the NYHA classification for assessing heart failure? Comparison of two classification scales in adolescents and adults with operated congenital heart defects. Clin Res Cardiol 2007; 96: 542-7.

103. Srinathan SK, Bonser RS, Sethia B, Thorne SA, Brawn WJ, Barron DJ. Changing practice of cardiac surgery in adult patients with congenital heart disease. Heart 2004; 91: 207-212.

104. Butera G, Carminati M, Chessa M, Youssef R, Drago M, Giamberti A, Pome G, Bossone E, Frigiola A. Percutaneous versus surgical closure of secundum atrial septal defect: comparison of early results and complications. Am Heart J. 2006 Jan;151(1):228-34.

105. Murphy JG, Gersh BJ, McGoon MD, et al. Long term outcome after surgical repair of isolated atrial defect. Follow up at 27 to 32 years. N Eng J Med 1990;333:469-73.

106. Berdat PA, Immer F, Pfammatter JP, Carrel T. Reoperations in adults with congenital heart disease: analysis of outcome. Intern J Cardiol 2004; 93:239-245.

107. Dore A, Luke Glancy D, Stone S, Menasche VD, Somerville J. Cardiac surgery for Grown Up Congenital heart patients: survey of 307 consecutive operations from 1991 to 1994. Am J Cardiol 1997; 80:906-913.

108. Isomura T, Hisatomi K, Andoh F, et al. Reoperation following total repair of congenital heart disease. Jpn Circ J, 1991; 55:453-458.

109. Geissler HJ, Sudkamp M, Nowak J, de Vivie ER. Congenital heart defects in adolescence and adulthood: fatalities and morbidity in primary and reoperation. Z Kardiol 1996; 85: 782-789.

110. Therrien J, Siu SC, McLaughlin PR, Liu PP, Williams WG, Webb GD. Pulmonary valve replacement in adults late after repair of tetralogy of Fallot: are we operating too late? J Am Coll Cardiol 2000; 36: 1670-1675.

111. Diller GP, Dimopoulos K, Okonko D, Li W, Babu Narayan SV, Broberg CS, Johansson B, Bouzas B, Mullen MJ, Poole Wilson PA, Francis DP, Gatzoulis MA. Exercise intolerance in adult congenital heart disease. Comparative severity, correlates and prognostic implications. Circulation, 2005;112:828-835.

112. Castaneda AR, Mayer JE, Jonas RA, Lock JE, Wessel DL, Hickey PR. The neonate with critical congenital heart disease: Repair – A surgical challenge. J Thorac Cardiovasc Surg 1989;98:869-75.

113. Vida VL, Berggren H, Brawn WJ, Daenen W, Di Carlo D, Di Donato R, Lindberg HL, Corno AF, Fragata J, Elliott MJ, Hraska V, Kiraly L, Lacour-Gayet F, Maruszewski B, Rubay J, Sairanen H, Sarris G, Urban A, Van Doorn C, Ziemer G, Stellin G. Risk of surgery for congenital heart disease in the adult: a multicentered European study.Ann Thorac Surg. 2007 Jan;83(1):161-8.

114. Brickner ME, Hillis LD, Lange RA. Congenital heart disease in adults. First of two parts. N Engl J Med 2000; 342: 256-263.

TABLES

Table 1. Congenital heart lesions defined as complex are listed and indication to a regular clinical follow up is given.

Table 1. Type of Adult Patients with Complex Congenital Heart Disease*
Conduits, valved or non valved
Cyanotic congenital heart disease (all forms)
Double outlet ventricles
Pulmonary vascular obstructive disease and Eisenmenger syndrome
Fontan procedure
Mitral atresia
Single ventricle physiology anomalies
Pulmonary atresia (all forms)
D-Transposition of the great arteries
L-Transposition of the great arteries (*corrected*)
Tricuspid atresia
Truncus arteriosus/henitruncus
Other anomalies of atrioventricular or ventriculoarterial connection not included above (i.e. criss cross heart, heterotaxy syndromes, ventricular inversion)
*These patients should be seen regularly at a regional adult congenital heart disease center.

Modified from Warnes et al, JACC 2001,37:1161-1198.

Table 1. Congenital heart lesions defined as moderately severe are listed and indication to a periodical clinical follow up is given.

Table 2. Type of Adult Patients with Congenital Heart Disease of Moderate Severity*
Aorto-left ventricular fistulae
Anomalous pulmonary venous drainage, partial or total
Atrioventricular septal defects (partial or complete)
Coarctation of the aorta
Ebstein's anomaly
Significant infundibular right ventricular outflow obstruction
Atrial septal defects: Ostium primum and large Ostium secundum (unrepaired)
Patent ductus arteriosus (not closed)
Pulmonary valve regurgitation (moderate to severe)
Pulmonary valve stenosis (moderate to severe)
Sinus of Valsalva fistula/aneurysm
Sinus venosus atrial septal defect
Subvalvar or supravalvar aortic stenosis (excluded hypertrofic obstructive cardiomiopathy)
Tetralogy of Fallot
Ventricular septal defect with • Absent valve or valves • Aortic regurgitation • Coarctation of the aorta • Mitral disease • Right ventricular outflow tract obstruction • Straddling tricuspid/mitral valve • Subaortic stenosis
*These patients should be seen periodically at a regional adult congenital heart disease center.

Modified from Warnes et al, JACC 2001,37:1161-1198.

Table 3. Congenital heart lesions defined as simple are listed and indication to general medical follow up is given.

Table 3. Type of Adult Patients with Simple Congenital Heart Disease*
Native disease • Isolated congenital aortic valve disease • Isolated congenital mitral valve disease • Isolated mild pulmonary valve stenosis • Isolated patent foramen ovale or small atrial septal defect • Isolated small ventricular septal defect (with no associated lesions)
Repaired conditions • Previously ligated or occluded ductus arteriosus • Repaired secundum or sinus venosus septal defect without residual lesions • Repaired ventrcular septal defects without residula lesions
*These patients may be cared for in a general medical community.

Modified from Warnes CA et al, JACC 2001,37:1161-1198.

Table 4. Most commonly encountered syndromes associated to congenital cardiac lesions and mental deficits in adults.

Table 4. Syndromes associated with mental deficits*		
Syndrome	***General features***	***Cardiac defect***
Alcohol Syndrome	Facial and growth anomaly, mental retardation	ASD, VSD (30%)
Down (trisomy 21)	Mental retardation, typical facies, lymphedema	AVSD (VSD, aortic valve anomaly) in 40%
Noonan	Turner like phenotype, normal chromosomes, mental retardation	Coarctation, HCM, ASD, PS
Turner	Chromosome XO, skeletal and mental deficits	Coarctation in 35%, ±bicuspid aortic valve
Williams Beuren	Facial displasia, Hypervitaminosis D, hypocalcemia, mental retardation	Supravalvar aortic stenosis, somtimes with multiple pulmonary artery stenoses

Legend: ASD: atrial septal defect; AVSD: atrioventricular septal defect; HCM: hypertrophic cardiomiopathy; PS: pulmonary stenosis; VSD: ventricular septal defect.

***Modified from Deanfield J et al. Eur Heart J 2003; 24:1035-1084.**

Table 5a. Anatomical diagnoses (*i.e. the basic heart malformations*)		
Diagnosis	***n.***	***%***
Atrial septal defect	321	26,84
Aortic Regurgitation	98	8,19
Tetralogy of Fallot	73	6,10
Partial Anomalous Pulmonary Venous Connection	70	5,85
Tricuspid Valve Disease	65	5,43
Ventricular Septal Defect	60	5,02
Atrioventricular Septal Defect	54	4,52
Sub –aortic Stenosis	43	3,60
Arrhythmia	41	3,43
Functional single ventricle	34	2,84
Aortic coarctation	25	2,09
Pulmonary valve regurgitation	20	1,67
Pulmonary Atresia	18	1,51
Pulmonary Stenosis	11	0,92
Corrected Transposition of the great arteries	9	0,75
Miscellaneous	265	21,24

Table 5b. Leading to surgery diagnoses (*Indications for surgery*)		
Leading to surgery diagnosis	***n.***	***%***
Atrial septal defect	307	28,8
Aortic Regurgitation	99	9,29
Partial Anomalous Pulmonary Venous Connection	65	6,10
Aortic Stenosis	63	5,91
Tricuspid Valve Disease	60	5,63
Ventricular Septal Defect	53	4,97
Atrioventricular Septal Defect	48	4,50
Arrhythmia	44	4,39
Tetralogy of Fallot	34	3,19
Pulmonary Artery Stenosis	31	2,91
Conduit failure	31	2,91
Mitral Valve Regurgitation	31	2,91
Pulmonary stenosis	29	2,72
Aortic Aneurysm	27	2,53
Functional Single Ventricle – Fontan	26	2,44
Aortic Coarctation	24	2,25
Pulmonary Atresia	6	0,76
Corrected Transposition of the great arteries	2	0,20
Others	81	7,60

Table 6. Palliative procedures *(any operation performed to improve the patient's clinical status, without restoring normal anatomy or physiology)*	
Palliative Procedure	***%***
Bidirectional Cavopulmonary Anastomosis (Glenn procedure)	20.7
Pulmonary Artery Banding	13.8
Surgical Ablation	10.3
Blalock-Taussig Shunt	10.3
Systemic to pulmonary artery shunt ligation and take down	3.4
Other procedures (miscellaneous)	41.4

Table 7. Repair procedures

(any operation designed to achieve an anatomical or physiological correction resulting in a separation of the pulmonary from the systemic circulation)

Surgical Procedure	***%***
Atrial Septal Defect Closure	36.1
Partial Anomalous Pulmonary Venous Connection Repair	7.2
Ventricular Septal Defect Closure	5.4
Ross operation	5.3
Atrioventricular Septal Defect-Partial type, repair	5.1
Tricuspid Valve Plasty	4.8
Aortic Valve Replacement	3.7
Subaortic Stenosis Resection	3.2
Aortic Repair	2.4
Mitral Valve Plasty	2.2
Surgical Ablation	2.2
Right Ventricular Outflow Tract Procedure	2.1
Aortic Coarctation Repair	2
Tetralogy of Fallot Repair	1
Mitral Valve Replacement	0.7
Other Procedures	16.6

Table 8. Re-operations

(any cardiac surgical procedure after either physiologic or anatomic repair, or palliation)

Reoperation	***%***
Conduit reoperation	9.9
Aortic Valve Replacement	7.7
Pulmonary Valve Replacement	6.8
Ventricular Septal Defect	4.6
Tricuspid Valve Plasty	4.3
Right Ventricular Outflow Tract Procedure	4
Sub-aortic Stenosis Resection	3.7
Aortic Aneurysm Repair	3.7
Atrial Septal Defect Closure	3.4
Mitral Valve Replacement	3.1
Heart Transplant	2.5
Pulmonary Arteries Plasty	2.2
Right Ventricle-Pulmonary Artery Conduit	2.2
Aortic Coarctation Repair	1.9
Ross Procedure	1.5
Mitral Valve Plasty	1.5
Other	25.3

Table 9. Early outcome per groups. *Main causes of death and postoperative complications are listed*				
	Palliation (18 pts)	***Repair (628 pts)***	***Reoperation (210 pts)***	***Total (856 pts)***
Early death	3 (16.6%)	8 (1.27%)	16 (7.6%)	27 (3.1%)
Early death, LCO Sdr	1	3	9	13
Major postop. Complications	13	138	81	247
Arrhythmias	1	53	10	64
LCO sdr	5	10	13	28
Bleeding	0	13	11	24
Sternum left opened	0	1	6	7
Unplanned reoperation during same admission	1	8	1	10
Postop. VAD/ECMO	1	2	4	7
Postop. AV block requiring perm. PM	0	7	3	10
Prolonged mech. Ventilation	1	6	10	17
Postop. cardiac arrest	1	2	1	4
Acute renal failure requiring temporary dialysis	1	0	0	1
Pleural effusion requiring drainage	2	8	9	19
Pneumothorax	0	10	0	10
Other minor	15	18	13	46
ICU stay (mean, days)	5.2	1.8	3.5	2.3

Table 10. Preoperative and postoperative ECG findings		
ECG Rhythm	***Preoperative (%)***	***Postoperative (%)***
Sinus	83	90.5
Atrial fibrillation	6.4	2.5
A-V block 3rd degree	1.1	0.8*
Atrial flutter	0.7	0.2
No avalable data	8.8	6.0

*3 patients affected died at operation

Table 11. Late outcome per groups. *Main late adverse events(included late deaths) are listed*			
Adverse events	***Palliation (17 survivors)***	***Repair (620 survivors)***	***Reoperation (194 survivors)***
Late death, cardiac	/	3	1
Late death, non cardiac	/	0	1
Reoperation	2	4	3
Interventional	1	2	2
Other (arrhythmias, pleural effusions, etc)	5	21	3
Total	8	30	10

Table 12. Incremental and decremental risk factors for survival according to Multivariate Cox analysis		
Variate	***Hazard Ratio***	***p-value***
Preoperative NYHA IV+cyanosis	8.6	0.0001
Preoperative NYHA III	2.7	0.023
Single ventricle	2.6	0.032
Reoperation	2.3	0.029
ASD	0.08	0.0018
Left heart lesion	0.16	0.0014

Table 13. Incremental risk factors for postoperative NYHA class >1 according to multivariate Cox analysis

Variate	*Hazard Ratio*	*95% CI*	*p-value*
ICU stay	1.037	1.002-1.072	0.036
Number of operations	1.445	1.1213-1.721	< 0.001
Alteration of cardiac rhythm before surgery	1.124	1.040-1.215	0.03
Cyanosis	1.555	1.035-2.335	0.034
Pre-operative NYHA class>1	1.573	0.954-2.593	0.076
Age > 40y	1.466	1.014-2.119	0.042

Table 14. Incremental risk factors for postoperative Ability Index >1 according to multivariate Cox analysis

Variate	*Hazard Ratio*	*95% CI*	*p-value*
Number of operations	1.197	1.030-1.391	<0.019
Alteration of cardiac rhythm before surgery	1.649	1.178-2.307	0.004
Cyanosis	1.096	1.021-1.117	0.011
Pre-operative NYHA class>1	2.454	1.565-3.847	<0.001

FIGURES

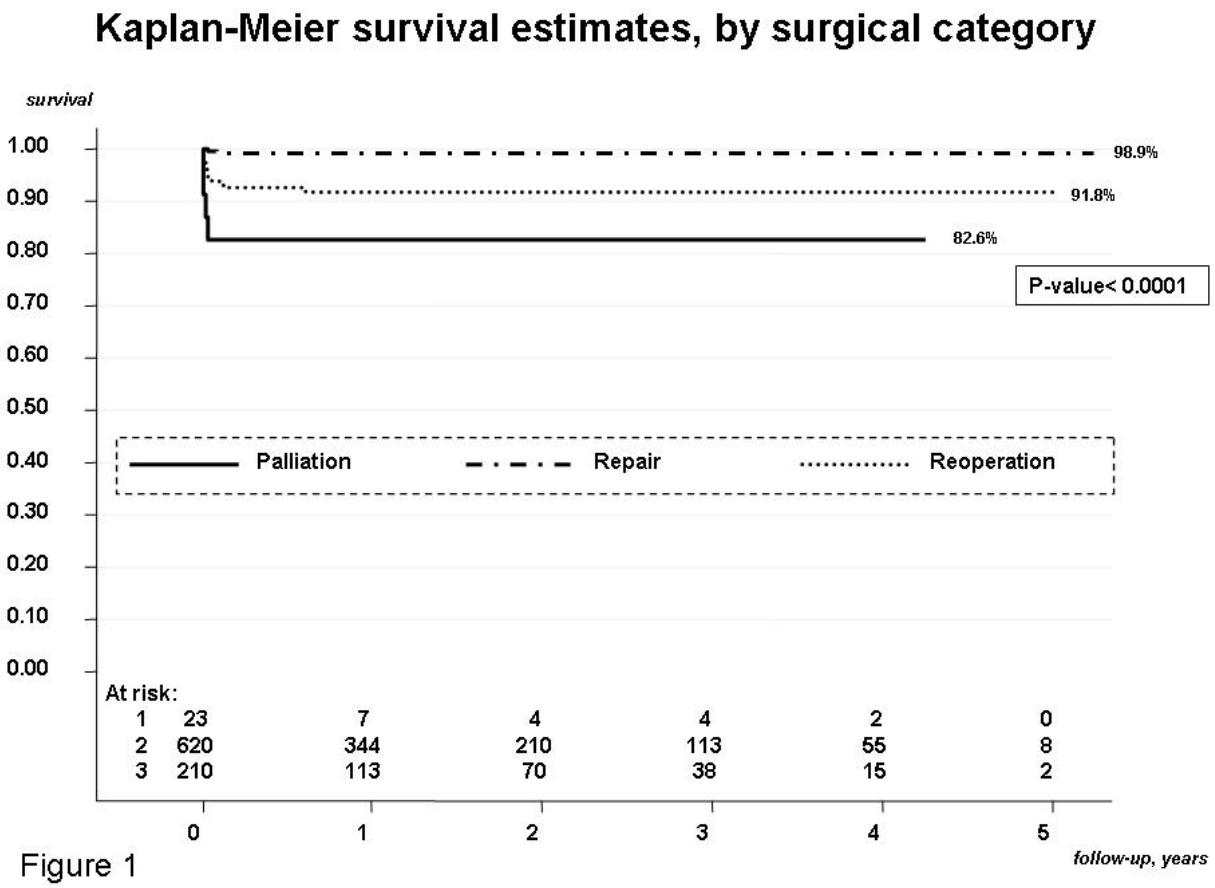

Figure 1

Figure 1. Survival estimate is 82.6% at 4 years for palliation procedures, 98.9% for repair and 91.8% for reoperation at 5 years, p value < 0.0001.

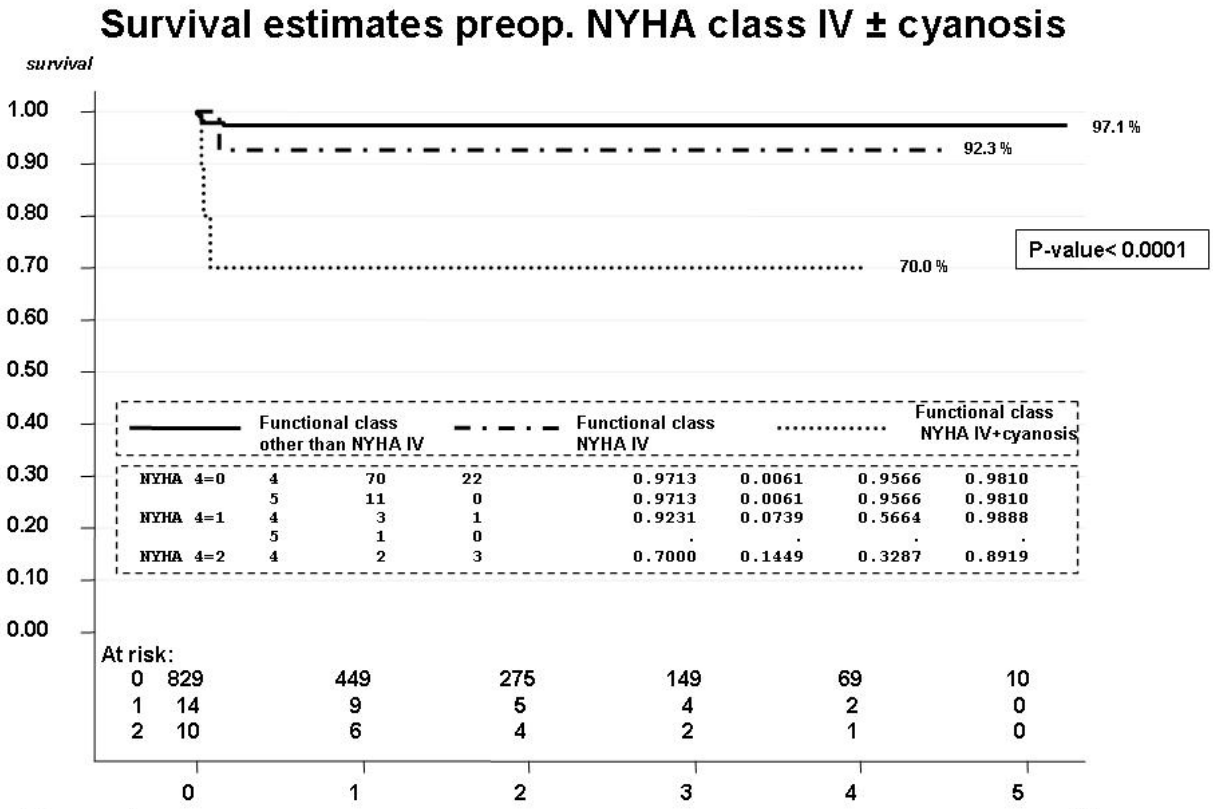

Figure 2

Figure 2. Survival estimate for patients in preoperative NYHA class IV associated or not to cyanosis is significantly lower vs other patients, 70% and 92.3% vs 97.1, p value < 0.0001.

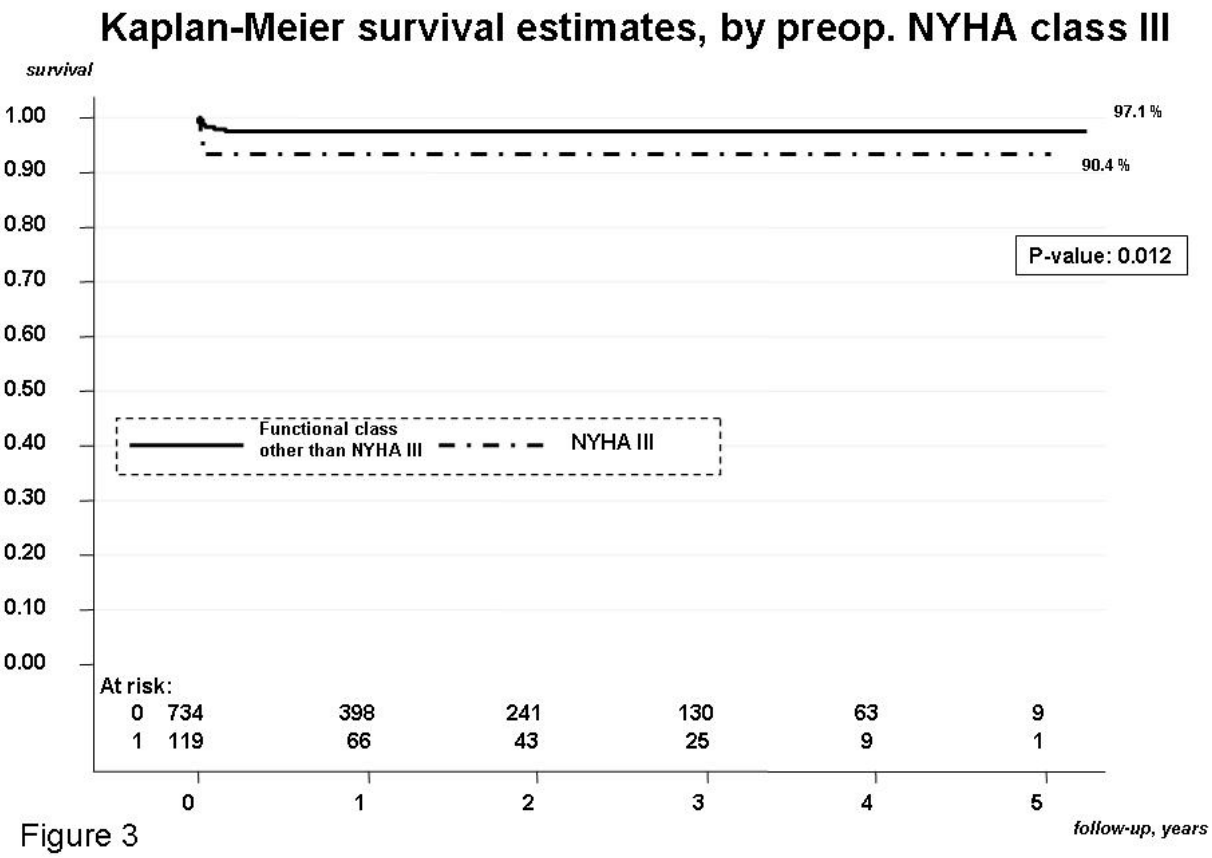

Figure 3

Figure 3. Survival estimate for patients in preoperative NYHA class III is significantly lower vs other patients, 97.1% vs 90.4%, p value = 0.012.

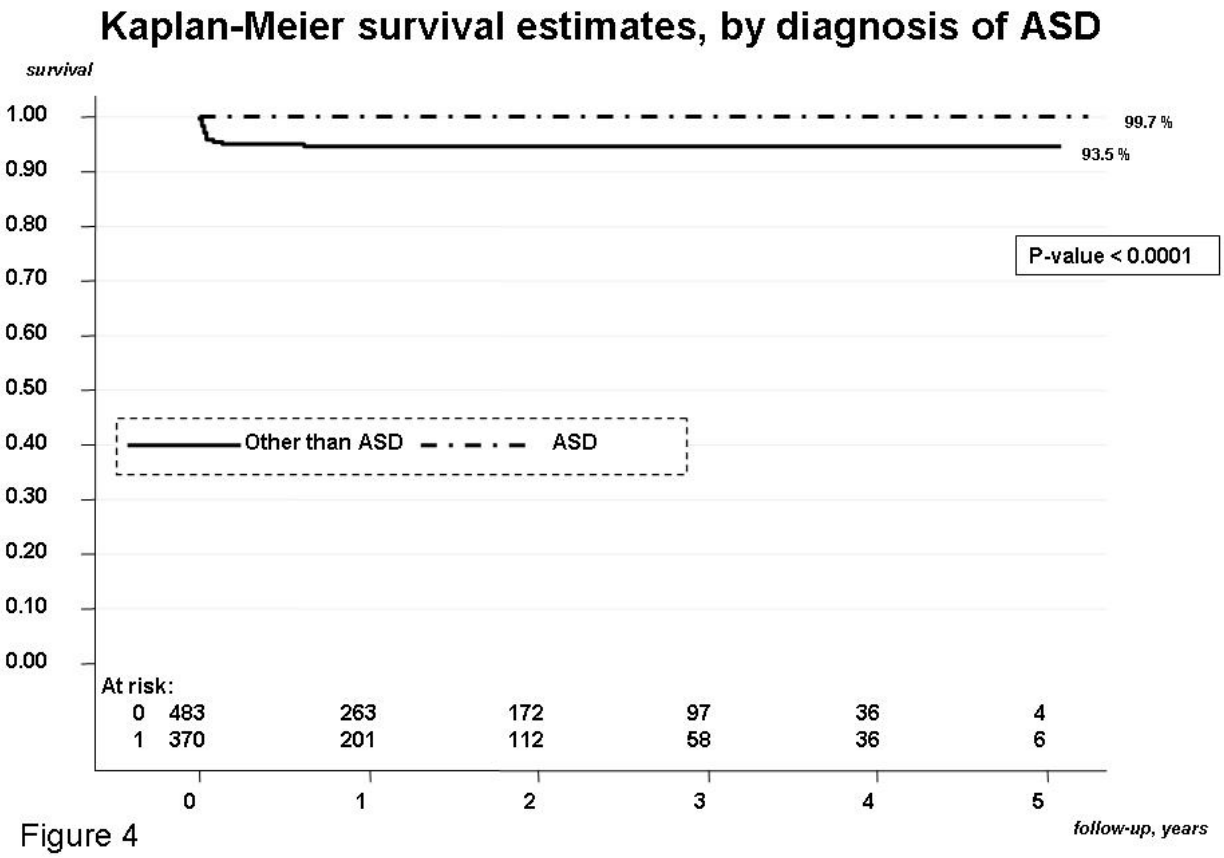

Figure 4

Figure 4. Survival estimates is 99.7% at 5 years for ASD and 93.5% at 5 years for all the other pathologies, p value<0.0001.

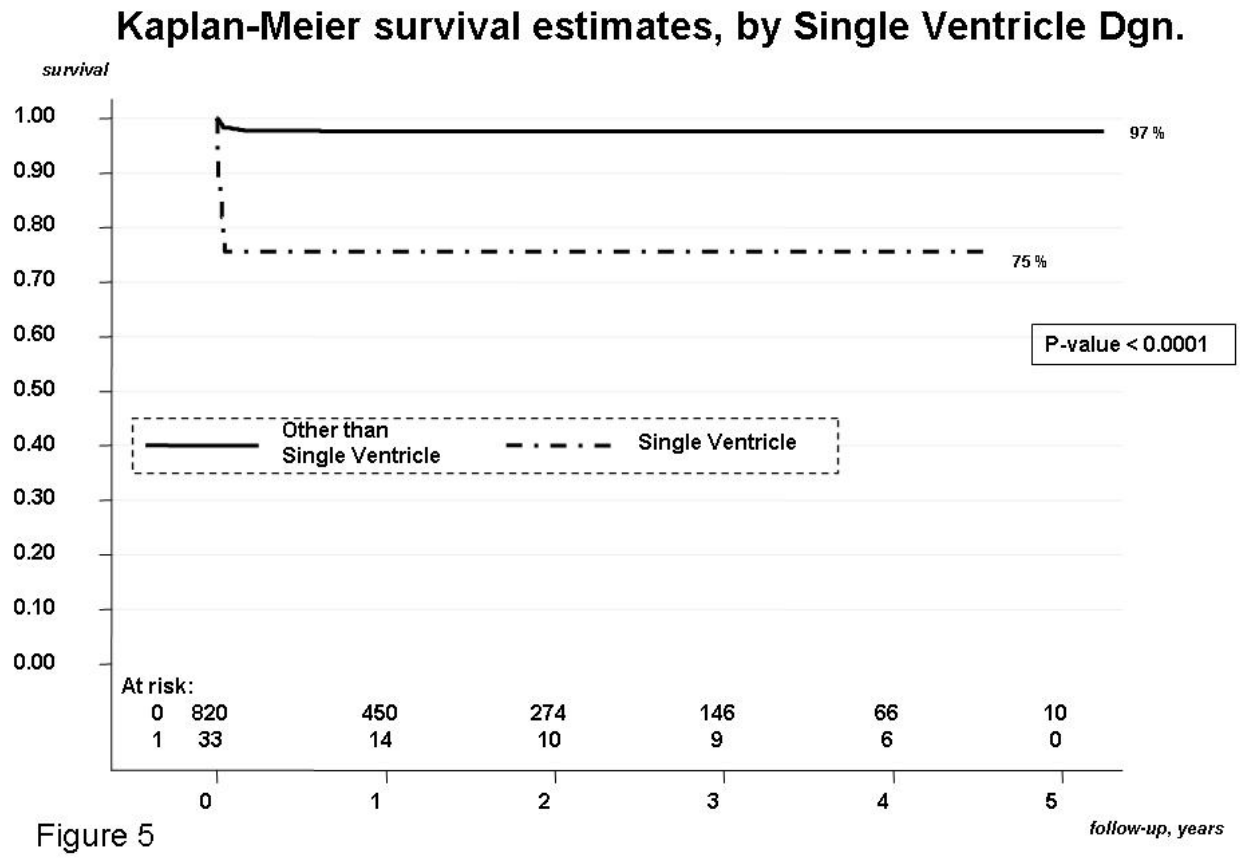

Figure 5

Figure 5. Survival estimate for patients with single ventricle is 75% vs 97% for non single ventricle patients, p value < 0.0001.

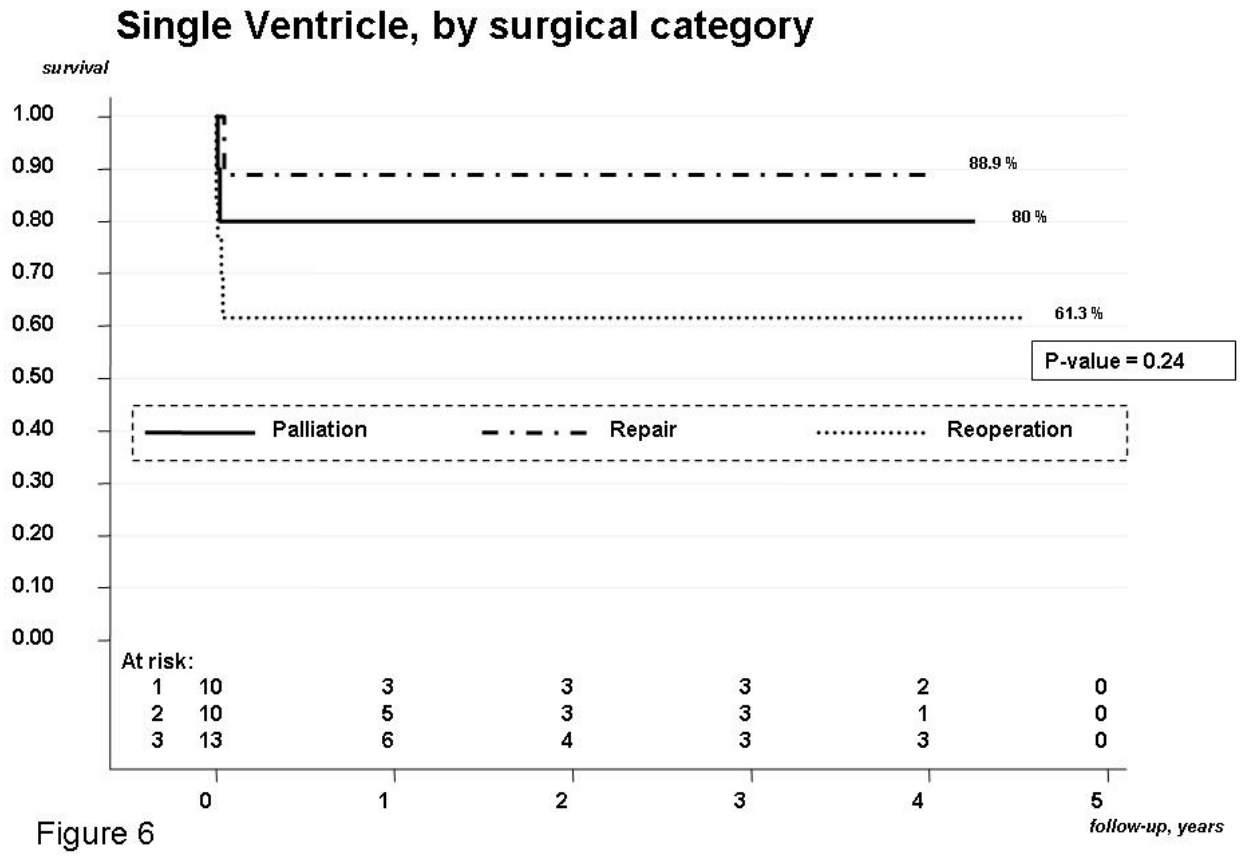

Figure 6

Figure 6. No statistically significant difference is found in survival estimates for patients with diagnosis of single ventricle, when considered by surgical category, p value= 0.24.

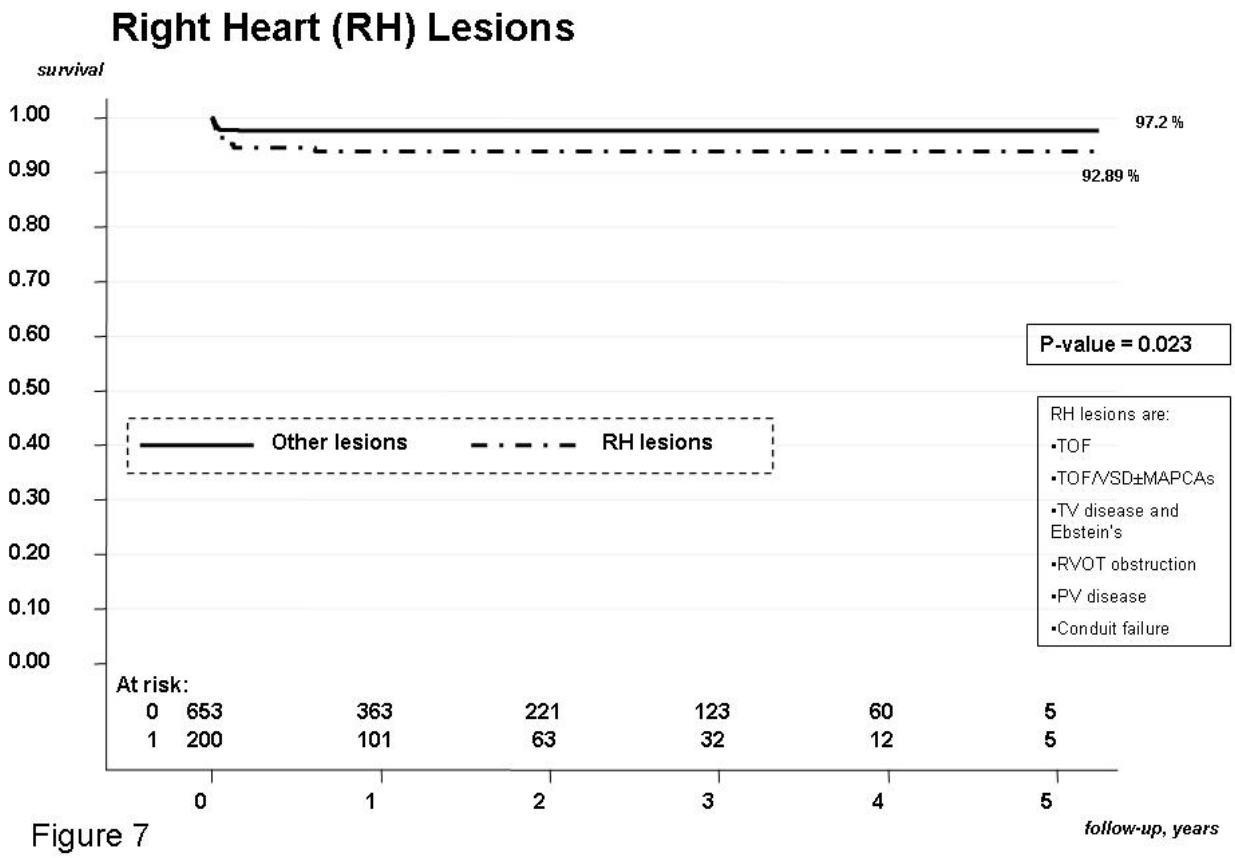

Figure 7

Figure 7. Survival estimate for patients with a right heart lesion is 92.8% vs 97.2% for patients without , p value = 0.023.

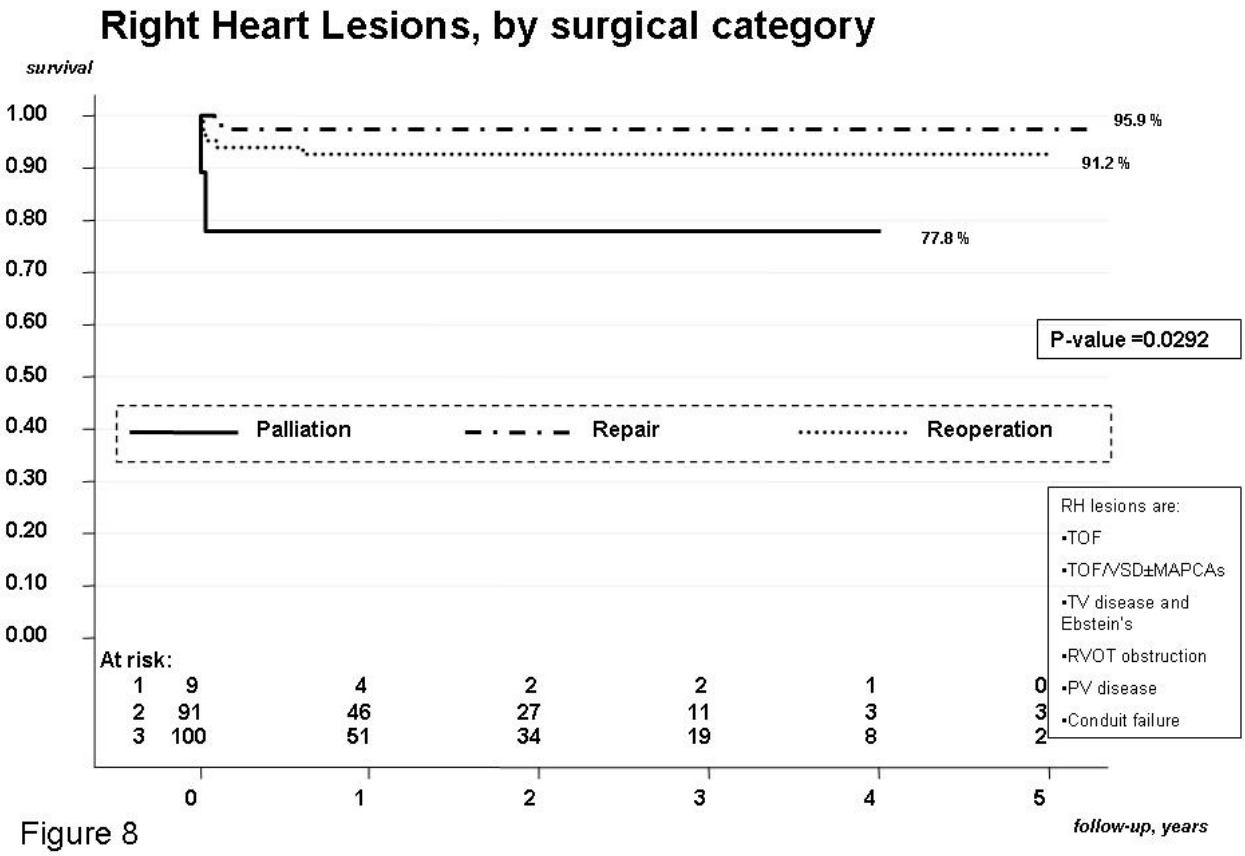

Figure 8

Figure 8. Survival in patients with a right heart lesion by category is 77.8% for palliation, 95.9% for repair, 91.2% in reoperation, p value = 0.0292,

Figure 9

Figure 9. Survival estimate for patients with left heart lesion is 98.9% vs 95.3% for patients without, p value 0.05.

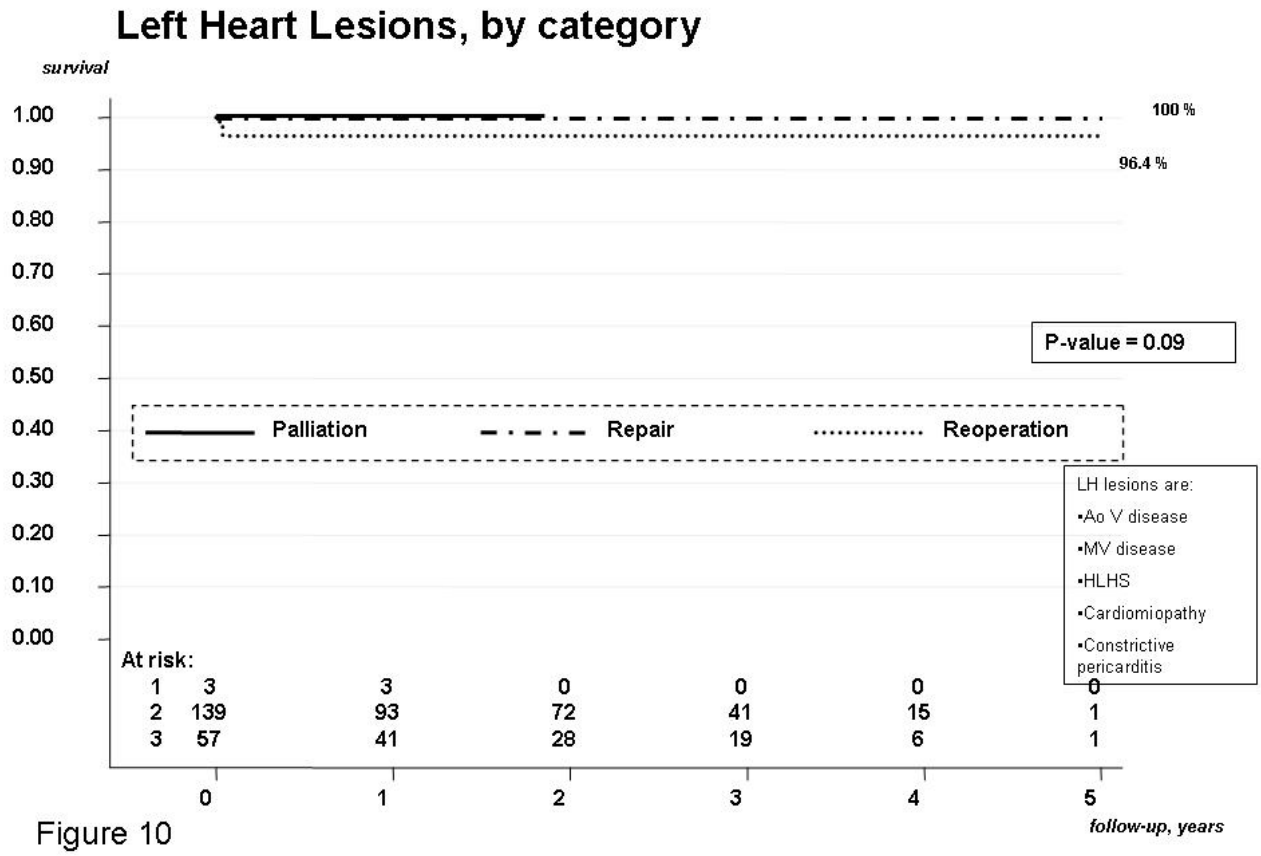

Figure 10

Figure 10. There is no significant difference for patients with diagnosis of left heart lesions, when considered by category (p value = 0.0884).

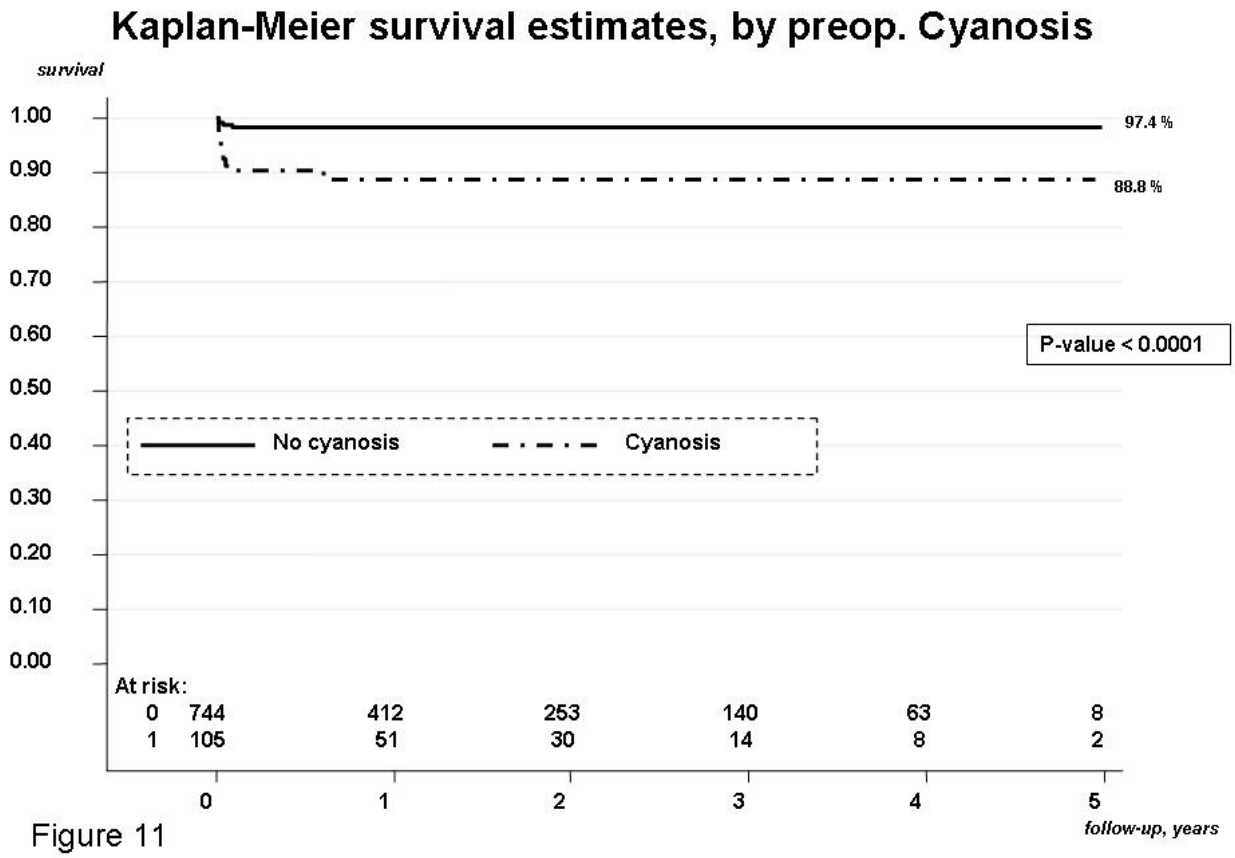

Figure 11

Figure 11. Survival estimate is 97.4% at 5 years for preoperative acyanotic patients and 88.8 % at 5 years for preoperative cyanotic patients, p value <0.0001

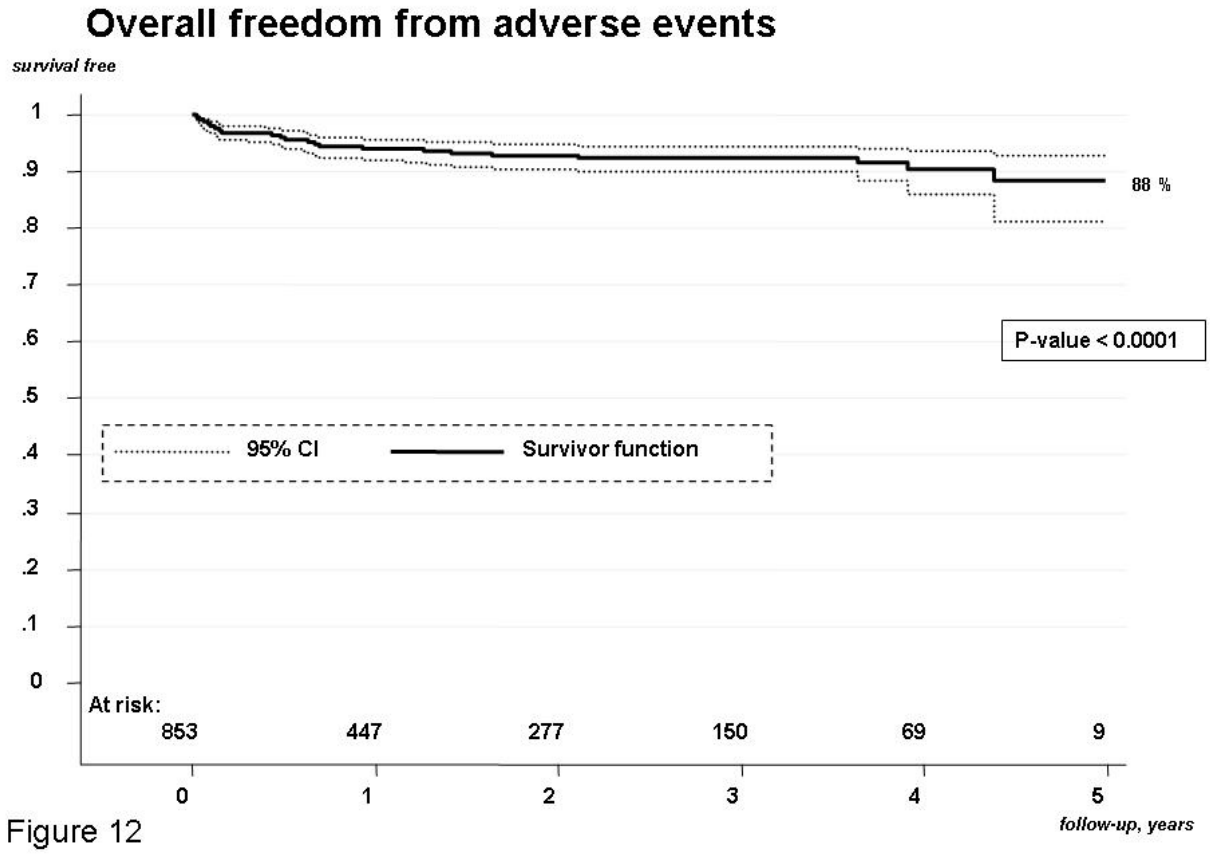

Figure 12

Figure 12. Overall freedom from adverse events is 88% at 5 years, CI 95%

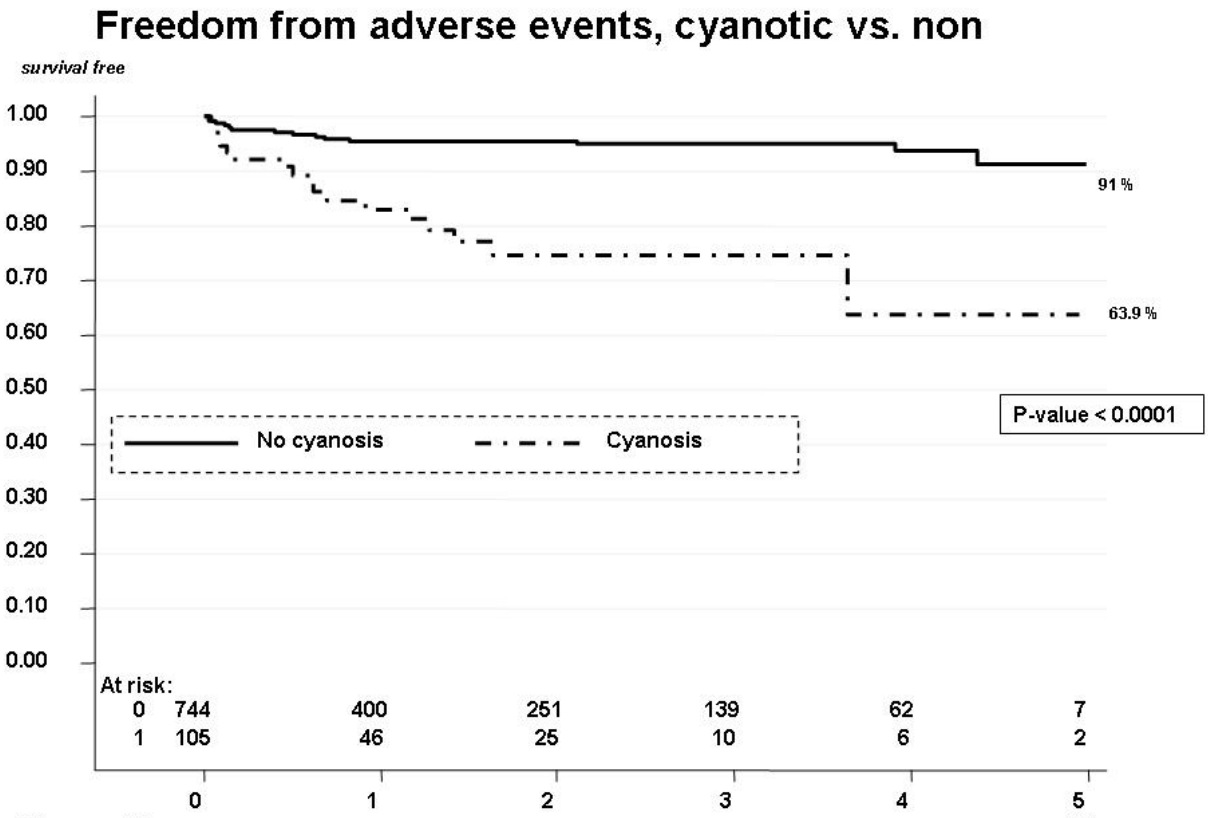

Figure 13

Figure 13. Freedom from any kind of adverse event is 91% for non cyanotic vs 63.9% at 5 years, p value < 0.0001.