Cardiac Arrhythmias at Long-Term Follow-Up of Patients with Grown-Up Congenital Heart Disease (GUCH). A New Arising Population

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Abstract

Due to the great improvement and successes of surgical management in childhood it could be expected that the 85% of patients with congenital heart disease (CHD) reach adulthood. Over the long-term follow-up of these patients with grown-up congenital heart disease (GUCH), cardiac arrhythmias are the major source of morbidity and mortality.

The electrical disturbances are often the consequence of a complex and unique anatomical substrate with sutured patches and scars from cardiac surgery, in combination with cyanosis and pressure or volume overload. In this population the complete spectrum of Heart Rhythm Disturbances can often be seen, including: bradyarrhythmias and atrial or ventricular tachyarrhythmias.

This higher complexity for arrhythmia management, is clearly described and listed in many international guidelines and consensus, where all the recommendations regarding humans and technical resources, that each regional institution must have for the correct evaluation and follow-up of the GUCH population. Thus, creation of multidisciplinary teams is mandatory.

The analysis of 1604 adults with CHD from the Multicenter Registry GUTI-GUCH shows a direct relation between arrhythmia type and the degree of complexity of CHD and patient age. Patients more than 40 years old present arrhythmias in 27% with mild CHD, 56% for those with moderate forms, and 70% in severe.

There is also a direct relation between the type of CHD and the possibility of developing supraventricular or ventricular arrhythmias, as well as the risk of AV or sinoatrial conduction disorders and the need for cardiac stimulation.

In the case of the univentricular hearts, a tachyarrhythmia episode that could go unnoticed or with very few symptoms under other circumstances, could present with significant hemodynamic impact, rapid deterioration of ventricular function and poor clinical tolerance.

Future technological advances will definitively improve the outcome on the treatment of arrhythmias in patients with GUCH diseases. Nevertheless, the profound knowledge of the anatomy and physiology of each of them, and the different repair or palliative surgical techniques that are used, endovascular therapeutic alternatives, and the natural history of the cardiopathy; are all essential for achievement better results in this new arising population of adult CHD.

Keywords: Cardiac Arrhythmias; Congenital Heart Disease (CHD); Grown-Up Congenital Heart Disease (GUCH)

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Abbreviations


Actually, due to the great improvement and successes of surgical management in childhood it could be expected that the 85% of patients with congenital heart disease reach adulthood.

Cardiac arrhythmias are a major source of morbidity and mortality in the long-term course of patients with grown-up congenital heart disease (GUCH).

Although rhythm disorders can often be observed in adults with natural history of heart disease, it is also observed in patients who have undergone prior intracardiac repairs, especially when this reparative surgery was performed relatively late in life.

Therefore, the electrical disturbances are often the consequence of a complex and unique anatomical substrate with sutured patches and scars from cardiac surgery, in combination with cyanosis and pressure or volume overload (Figure 1). In this population the complete spectrum of Heart Rhythm Disturbances can often be seen, including: bradyarrhythmias and atrial or ventricular tachyarrhythmias.

Figure 1: Schematic of factors leading to arrhythmias in patients with postoperative congenital heart disease.

The risk factors and consequently, the morbidity and mortality in children with congenital heart disease are related with early diagnosis, the complexity of its malformation, the appropriate use of available technologies and experience and advances in human resources knowledge.

Furthermore, the GUCH have a more complex profile where the ventricular dysfunction, heart failure, pulmonary hypertension and arrhythmias are the most likely risk elements that contribute with the prognosis. These factors are closely related with the severity of the congenital heart diseases, scars and residual defects due to the type of surgery, patient age, and years of follow-up.

This higher complexity, particular referred for arrhythmias, is clearly described in many international guidelines and consensus, where all the recommendations regarding humans and techniques resources that each regional institution must have for the correct evaluation and follow-up of the GUCH population:

- Cardiologist specializing in ACHD
  - At least 1 cardiologist 24h x 7 days
  - (24 hours the 7 days of the week)
- Congenital cardiac surgeon
  - At least 2 24/7
- Nurse/physician assistant/nurse practitioner
  - At least 1 24/7
- Cardiac anaesthesiologist
  - At least 1 24/7
- Echocardiography
  - Includes TEE, intraoperative TEE
  - At least 2 24/7
- Pediatric hemodynamist
  - At least 1 24/7
- Electrophysiology/pacing/ICD implantation
  - At least 1 24/7.

Also, the institution should ideally have:

- Ergometry, echocardiography, camera Gamma, Metabolic and cardiopulmonary test, Images (Cardiac MRI/CT scanning/Nuclear medicine).
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- System/technology (Database collection-Database support-Quality assessment review/protocols).
- The electrophysiology laboratory and post-procedure recovery unit should include:
  - Adult appropriate equipment
  - Nursing and technical staff certified in adult cardiac life support (ACLS) and trained in basic CHD anatomy
  - ACHD cardiothoracic surgical backup and operating room.

Finally, consensus also specify the requirements for electrophysiologists working with CHD:

- Complete trainee in adult and pediatrics electrophysiology with demonstrated acquisition of required full clinical competencies.
- Formal affiliation with an established ACHD center.
- Fundamental knowledge of congenital heart disease, including:
  - Anatomy and physiology of simple, moderate and complex forms of congenital heart disease
  - Surgical procedures for congenital heart disease
  - Natural and unnatural (postsurgical) short- and long-term arrhythmia sequelaes
  - Particularities essential to safely and effectively execute arrhythmia interventions, including an appreciation for complex access issues and displaced or malformed atrioventricular conduction systems.
- Experience and skills in managing adults with congenital heart disease and arrhythmias, including:
  - Noninvasive testing
  - Electrophysiologic studies
  - Catheter ablation, including with 3-dimensional electroanatomic mapping systems and large-tip/irrigated catheters
  - Intraoperative procedures
  - Cardiac rhythm management devices.

Types of arrhythmias in CHD

The electrophysiological mechanisms responsible for the arrhythmias in CHD do not differ from the rest of the population; however, the type of CHD, the palliative or reparative cardiac surgery, pharmacological treatment and the age, among others can influence the type of arrhythmias that can appear more frequently in each patient.

The analysis of 1604 adults with CHD from the Multicenter Registry GUTI-GUCH shows a direct relation between arrhythmia type and the degree of complexity of CHD and patient age. Patients more than 40 years old present arrhythmias in 27% with mild CHD, 56% for those with moderate forms and 70% in severe (Figure 2).
There is also a direct relation between the type of CHD and the possibility of developing supraventricular or ventricular arrhythmias, as well as the risk of AV or sinoatrial conduction disorders and the need for cardiac stimulation (Table 1).

<table>
<thead>
<tr>
<th>Complexity of CHD</th>
<th>Type CHD</th>
<th>Prevalence (CHD population)</th>
<th>Atrial Arrhythmias</th>
<th>Other Pacing Needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>Patent ductus</td>
<td>6 - 8%</td>
<td>AT</td>
<td>++ ++ +</td>
</tr>
<tr>
<td></td>
<td>Pulmonary stenosis</td>
<td>6 - 8%</td>
<td>AF</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Ventricular septal defect</td>
<td>30 - 32%</td>
<td>Other</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Secundum atrial septal defect</td>
<td>8 - 10%</td>
<td>AT AF Other</td>
<td>++ ++ ++ ++ ++</td>
</tr>
<tr>
<td>Moderate</td>
<td>Aortic coarctation</td>
<td>5 - 7%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++ +</td>
</tr>
<tr>
<td></td>
<td>Anomalous pulmonary venous return</td>
<td>0,5 - 2,5%</td>
<td>VA</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Atrioventricular septal defect</td>
<td>3 - 5%</td>
<td>AT AF</td>
<td>+ +</td>
</tr>
<tr>
<td></td>
<td>Aortic stenosis</td>
<td>3 - 5%</td>
<td>VA</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Ebstein’s anomaly</td>
<td>0,5 - 1,5%</td>
<td>VA</td>
<td>++ ++</td>
</tr>
<tr>
<td></td>
<td>Tetralogy of fallot</td>
<td>8 - 10%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++</td>
</tr>
<tr>
<td></td>
<td>Primum atrial septal defect</td>
<td>2 - 3%</td>
<td>VA</td>
<td>+ +</td>
</tr>
<tr>
<td>Severe</td>
<td>Truncus arteriosus</td>
<td>1,5 - 2%</td>
<td>VA</td>
<td>++ + + + ++</td>
</tr>
<tr>
<td></td>
<td>Pulmonary atresia</td>
<td>2 - 2,5%</td>
<td>VA</td>
<td>++ + + ++ ++ + ++</td>
</tr>
<tr>
<td></td>
<td>Double outlet right ventricle</td>
<td>1,5-2%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++ ++</td>
</tr>
<tr>
<td></td>
<td>D-transposition of great arteries</td>
<td>6 - 7%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++ ++</td>
</tr>
<tr>
<td></td>
<td>L-transposition of great arteries</td>
<td>1 - 2%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++ ++ ++</td>
</tr>
<tr>
<td></td>
<td>Hypoplastic left heart syndrome</td>
<td>3 - 4%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++ ++ ++</td>
</tr>
<tr>
<td></td>
<td>Other (heterotaxy, other single ventricle)</td>
<td>7 - 10%</td>
<td>VA</td>
<td>++ ++ ++ ++ ++ ++ ++</td>
</tr>
</tbody>
</table>

**Table 1:** Approximate risk estimates for atrial tachycardia (AT), atrial fibrillation (AF), other supraventricular arrhythmias, ventricular arrhythmia (VA), sinus node dysfunction (SND), atrioventricular (AV) block, and ventricular dyssynchrony are shown across various congenital heart defects (CHD) of simple, moderate, and severe complexity. The coded pattern ranges from minimal (no mark) to mild (+), moderate (++), and high (+++) risk.
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It is worth mentioning that some heart diseases could have a significant hemodynamic impact when a tachy or bradyarrhythmias develops. The best example is the case of the univentricular hearts where a tachyarrhythmia episode, that could go unnoticed or with very few symptoms under other circumstances, in patients with Fontan-Kreutzer Procedure, could present with a severe impact in the ventricular function and poor clinical tolerance.

On the other hand, supraventricular tachycardia (SVT) represents a set of different substrates or arrhythmogenic mechanisms that are different from each other. Accordingly, it is interesting that each CHD presents distinctive features that should be known because it could conditioned the arrhythmia mechanism that can appear in the future.

Accessory AV pathways, arrhythmogenic foci, intra-atrial reentry circuits, dual AV nodal physiology, pressure or volume atrial over-load, namely:

- **ASD**
  - Intra-atrial reentry/AF (long-term and late closure).
- **VSD**
  - Intra-atrial reentry/AF (post-surgery).

- **Ebstein's anomaly**
  - Intra-atrial reentry/Accessory AV pathways/Mahaim/Atrial flutter-AF.
  - Sudden death risk with multiple pathways.
  - **Left-sided obstructive lesions**
  - Intra-atrial reentry/AF.
  - **D-TGA (Senning-Mustard)**
  - Intra-atrial reentry/AF/Atrial tachycardia.
  - VT/VF due to rapid AV conduction during rapid atrial arrhythmia.
- **L-TGV**
  - Accessory AV pathways with sistemic AV valve Ebstein like.
  - **Tetralogy of fallot**
  - Intra-atrial reentry/Focal AT.
- **Heterotaxy**
  - AV Nodal Reentry Tachycardia (duplicated AV node system).
Fontan-kreutzer

- Intra-atrial reentry/Focal AT/AF with poor tolerance.

Eisenmenger physiology

- Intra-atrial reentry/AF/multifocal AT.

Wolff-Parkinson-White syndrome

Ebstein’s anomaly is a congenital cardiomyopathy that is most frequently associated with the presence of accessory pathways, and occasionally presents with multiples fibers in the posteroseptal/posterolateral region of the tricuspid valve. AV reentry is the typical form in early and mild stages, but SVT in childhood or in adulthood can occur when scars or atrial dilation predisposes for flutter or atrial fibrillation with preferential and rapid passage through the accessory pathway. Radiofrequency ablation is well established as the curative and definite treatment for this condition. However, when compared to cases without structural cardiomyopathy, the success rate is somewhat lower and the likelihood of recurrence is higher due to the disrupted anatomy, abnormal location of the atrio-ventricular node (AVN) and the higher prevalence of multiple pathways in these cases. Intraoperative ablation may be considered when the patient has an indication for surgical management of tricuspid valve disease.

Atrial flutter

Atrial flutter is the most common arrhythmia and may be associated with chronotropic incompetence. The highest incidence (between 30% and 50%) is seen during follow-up after the Senning, Mustard or Fontan-Kreutzer procedures. It is called IART (Intra-Atrial Reentry Tachycardia) to differentiate it from the flutter observed in patients with a structurally normal heart. Although the typical forms of flutter evidence a typical 12-lead surface ECG predicting a well defined circuit around the tricuspid ring, flutter in GUCH may include different circuits involving scars and patches, generating a wide spectrum ECG manifestations, with different F waves morphologies.

Figure 3: 12-lead surface ECG showing a typical atrial flutter with 2:1 AV conduction. These finding correlates with a macro-reentry over the right atrium with anti-clockwise activation sequence.
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These reentries typically showed slower frequencies (longer cycle length due to atrial enlargement and/or prolonged conduction velocities), that in cases with preservation of AV conduction may allow for AV 1:1 conduction and bad tolerance, syncope and even death. Also, IART may be responsible for thrombus formation and embolic events in the long term follow up.

The acute forms may be easily reversed with drug therapy, electrical cardioversion or overdrive pacing maneuvers. However, preventing recurrence and the correct identification of the anatomic or hemodynamic substrate predisposing for recurrent tachycardia is the real challenge. In this sense, the experience with anti-arrhythmic drugs has been discouraging and many centers prefer to use non-pharmacological interventions. Pacemaker implantation may be useful for patients presenting concomitant with sinus dysfunction, whether as an important clinical component or for the safe use of negative chronotropic agents against recurrence.

Radiofrequency ablation has been adopted for the management of recurrent and refractory forms of IART. The inclusion of 3D mapping systems and the use of irrigated-tip catheters have led to success rates close to 90%; however, long term recurrence (mainly related to the Fontan-Kreutzer procedure) is still remarkable due to the presence of multiple circuits and severe atrial enlargement.

Atrial fibrillation

Similar to IART. Consider anticoagulant therapy (ACT) for the prevention of thromboembolic events. Consider heart rate control when necessary in specific cases.

Maze surgical ablation may be considered for patients requiring surgery due to hemodynamic factors. The results are encouraging with low recurrence rates; however, the surgical risk must be included in the decision making process.

Ventricular tachycardia

The scenario of ventricular arrhythmias in GUCH occurs in cases of ventriculotomy and/or patches for closure of the ventricular septal defect (VSD) as in the case Tetralogy of Fallot. VT occurs due to reentries in region of fibrosis or scars in the RV outflow tract (RVOT), particularly in border zones where sick myocardium is adjacent to more healthy areas. The incidence of sudden cardiac death (SCD) ranges between 0.5% and 6%. Two of the most important variables associated with an increased risk of SCD are surgical repair at older age and a QRS > 180 msec. An electrophysiology (EP) study may be useful to discriminate populations at high and low risk but has a poor positive predictive value when used as a systematic evaluation tool. Thus, EP study could only be performed in selected patients with intermediate risk, whether with suggestive symptoms (palpitations, dizziness and unexplained syncope) or Holter findings of suspicious malignant ventricular arrhythmia.

Other GUCH diseases predisposing to ventricular arrhythmias include those where the right ventricle functions as a systemic ventricle (d-TGV, L-TGV, univentricular heart, VSD with pulmonary hypertension).

Figure 4: Episode of sustained monomorphic ventricular tachycardia in a patient with surgical repair of tetralogy of Fallot 18 years ago. QRS morphology analysis is consistent with an arrhythmia substrate in the right ventricular outflow tract region.
Bradycardia

Sinus node dysfunction after a surgical intervention has been commonly reported for those cases of Mustard, Senning, Glenn and Fontan-Kreutzer procedures due to direct trauma, or damage of arterial flow at that level. The presence of chronotropic incompetence in patients with sub-optimal hemodynamics status may cause important symptoms. The tachycardia-bradycardia syndrome is the most common clinical presentation at the long term after performing the Mustard or Senning procedure for d-TGV correction, and sinus dysfunction is present in 50% of these cases. Patients may be severely symptomatic due to their bradycardia or tachycardia and they may even be at risk of SCD due to rapid ventricular response during any fast atrial tachycardia.

The indication of a definite cardiac pacemaker implant is Class I evidence for the management of symptomatic sinus dysfunction in all cases. This includes patients with tachycardia-bradycardia syndrome and symptoms due to recurrent tachycardia, as well as patients with pause-dependent VT. It is a Class IIb indication for asymptomatic patients with a HR under 40 bpm and pauses longer than 3 seconds.

AV block

The occurrence of spontaneous AV block during follow-up has been described in some GUCH diseases, since the tissue in the AV node is congenitally abnormal in terms of either function or location. Patients with L-TGV and AV septal defects (Down Syndrome patients even more) must be closely followed with ECG and 24 hour Holter recordings for AV conduction monitoring. The occurrence and development of persistent 2nd or 3rd degree AV block within 7 - 10 days of surgery must be assessed for definite pacemaker implantation.

Also, cardiac stimulation might be considered and indicated for patients presenting post-operative AV block recovery but who remains with any form of bifascicular block pattern.

Prevention of sudden cardiac death

The prevalence of SCD in patients with Fallot tetralogy is 2.5% per decade of follow up and less than 0.2% per year/follow up.

In patients who survived after an episode of sudden cardiac death or an episode of symptomatic VT, there is clear consensus to reach on the indication of an ICD for the prevention of future events. However, the prevention of a first and potentially fatal ventricular arrhythmia and the implant of an ICD for primary prevention is a challenging scenario.

No risk factor with sufficient sensitivity and specificity to guide therapeutic decisions has been identified yet, and no perfect risk stratification scheme is available to date.

However, some isolated variables as predictors of malignant arrhythmias have been identified for Tetralogy of Fallot, patients as follows:

- Residual connections.
- Repair surgery at older age, number of surgeries.
- Hemodynamic abnormalities of the RV (severe pulmonary valve regurgitation, trans-annular patch, right ventricular outflow tract obstruction).
- High grade ventricular ectopic activity, NSVT in a 24-hs Holter recording.
- VT inducible in the EP study.

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- QRS > 180 msec.
- Remarkable fibrosis on MRI.

Asymptomatic patients with Tetralogy of Fallot are a topic for continuous debate. No doubt, non-invasive periodic assessments are crucial. Several options are available for the management of NSVT, including the addition of antiarrhythmic drugs, invasive arrhythmia induction, and ICD implantation; even RV function assessment, and consider pulmonary valve replacement surgery in the presence of severe regurgitation. Management must be individualized and based on the findings and the hemodynamic parameters of each particular patient.

The occurrence of symptoms such as palpitations, dizziness and syncope may drive an invasive evaluation including catheterization and electrophysiology studies. The induction of monomorphic, sustained and stable VT may enable mapping to then consider RF ablation. The induction of a reentrant atrial arrhythmia may be responsible for the symptoms and might also be a setting for RF ablation. Catheter-ization may be useful to identify any significantly hemodynamic defect likely to be managed with closure or surgical repair.

Although it is proven that residual lesions of severe pulmonary valve regurgitation may be responsible for the onset or worsening of arrhythmias, the impact of the surgical correction does not necessarily modify the electrical substrate and the risk.

The strategy of pulmonary valve replacement does not suffice to prevent the occurrence of arrhythmias; however, the optimal treatment approach and the impact in SCD have not been yet elucidated.

ICD placement is indicated for secondary prevention. Radiofrequency ablation may also be used in this patient with recurrent VT to reduce or prevent the number of appropriate ICD shock. The appropriate ICD therapies rate for Fallot patients has been reported in the range of 8% to 10% per year. In a retrospective multicenter study, patients with an ICD for primary prevention reported 44% of appropriate shocks during follow up.

In patients with d-TGV undergoing atrial switch (Senning or Mustard procedures) ventricular arrhythmia occurs in the setting of contractile damage of the systemic ventricle, and low ejection fraction. The presence of ventricular dysfunction and a history of atrial tachy-arrhythmias are the variables associated with SCD. The treatment strategy includes a combination of drugs, pacemaker implantation, mapping and ablation of the arrhythmic circuit. An ICD placement is indicated for secondary prevention and for high risk patients.

Univentricular hearts. Fontan-Kreutzer procedure

The univentricular heart deserves to be mentioned separately because its presents a special anatomy and physiology. For that reason, symptomatic atrial tachyarrhythmias must be considered at high risk in GUCH with Fontan-Kreutzer operation. Sustained arrhythmias may precipitate rapid haemodynamic deterioration, may predispose to thrombus formation, and should be considered a medical emergency. Treatment is difficult and challenge, so CHD experienced Electrophysiologist should be consulted when a recurrent intra-atrial reentrant tachycardia (IART) is detected. The 50% of the patients with atripulmonary connection can develop IART during long-term follow up. Comparatively, just the 10% of these patients developed IART with intracardiac or an extracardiac conduit technique known as total cavopulmonary connection (TCPC) or modified Fontan Procedure. Every time a patient presents with an atrial tachycardia episode, there must be a quick evaluation to identify presence of thrombus, anatomic abnormalities of the conduits, of the flow, or ventricular dysfunction. The therapeutic management of arrhythmias should involved the whole cardiovascular areas, especially potentially hemodynamic treatments or reparative cardiac surgery if required.

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Any consideration for electrophysiology study or pacemaker implant must include an accurate understanding of the congenital heart defect and cardiothoracic surgical procedures performed. Meticulous attention should be given to previous operative reports, noninvasive imaging and angiography with venous patency for the particular and unique anatomy of the patient. It is particularly challenging invasive procedures in these patients due to difficulty in finding vascular accesses as to reach each cardiac chamber according to the interest and therapeutic objective [1-10].

Conclusion

Future technological advances will definitively improve the outcome on the treatment of arrhythmias in patients with GUCH diseases. Nevertheless, the profound knowledge of the anatomy and physiology of each of them, and the different repair or palliative surgical techniques that are used, endovascular therapeutic alternatives, and the natural history of the cardiopathy; are all essential for achievement better results in this new arising population.

Bibliography


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