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Management of Arrhythmias among Pediatric Patients in the PICU

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Abstract: Background: It's important to note that arrhythmias can be asymptomatic or have subtle clinical presentations, particularly in patients with chronic or subclinical conditions. Therefore, continuous cardiac monitoring and vigilant assessment of heart rate and rhythm are essential in detecting arrhythmias, especially in the PICU setting. The clinical presentation and diagnosis of pediatric arrhythmias may vary depending on the type and severity of the arrhythmia. Here is a general overview. Arrhythmias in the pediatric population, especially in an intensive care unit (ICU) setting, can present in various ways. The clinical manifestations often depend on the type of arrhythmia, the age of the child, the presence of any underlying heart disease, and the child's overall health status. Pediatric arrhythmias in the PICU can be associated with complications that can impact outcomes. The diagnosis of pediatric arrhythmias in the pediatric intensive care unit (PICU) involves a combination of clinical assessment, electrocardiographic (ECG) evaluation, and additional diagnostic tests. The management approach for pediatric arrhythmias in the intensive care unit (ICU) aims to stabilize the child's condition, correct the underlying cause if possible, and prevent complications. The specific management strategies depend on the type and severity of the arrhythmia, as well as the child's overall clinical status. As soon as an arrhythmia is suspected, a rapid assessment of the patient's clinical status should be performed. This includes evaluating vital signs, oxygen saturation, level of consciousness, and signs of hemodynamic compromise. Immediate intervention is required for life-threatening arrhythmias or those associated with hemodynamic instability. Pharmacological therapy may be initiated to control arrhythmias in the PICU. Specific antiarrhythmic medications are selected based on the type of arrhythmia and the patient's clinical condition, used to terminate or control certain arrhythmias and restore normal heart rhythm or prevent recurrent arrhythmias

Keywords: Arrhythmia, Pediatric, PICU

Introduction

It's important to note that arrhythmias can be asymptomatic or have subtle clinical presentations, particularly in patients with chronic or subclinical conditions. Therefore, continuous cardiac monitoring and vigilant

assessment of heart rate and rhythm are essential in detecting arrhythmias, especially in the PICU setting. The clinical presentation and diagnosis of pediatric arrhythmias may vary depending on the type and severity of the arrhythmia. Here is a general overview. **(1)**

Arrhythmias in the pediatric population, especially in an intensive care unit (ICU) setting, can present in various ways. The clinical manifestations often depend on the type of arrhythmia, the age of the child, the presence of any underlying heart disease, and the child's overall health status. Key elements of the clinical presentation may include:

- Asymptomatic
- Palpitations (sensation of a rapid or irregular heartbeat)
- Chest pain or discomfort
- Fatigue, shortness of Breath or exercise intolerance
- Dizziness or lightheadedness
- Fainting or near-fainting episodes
- Cyanosis (bluish discoloration of the lips or extremities)
- Decreased Consciousness or Seizures
- Cardiac Arrest
- Failure to Thrive

1. Asymptomatic: Some children with arrhythmias may not exhibit any symptoms. The arrhythmia may be discovered incidentally during a routine physical examination or electrocardiogram (ECG). **(1)**

2. Palpitations: This is a common symptom of arrhythmias. The child or their parents may report sensations of a racing or irregular heartbeat. **(2)**

3. Chest Pain or Discomfort: While less common in children than in adults, some pediatric patients may experience chest pain or discomfort during an arrhythmia. **(3)**

4. Fatigue, Shortness of Breath or Exercise Intolerance: Arrhythmias can cause feelings of breathlessness or a decreased ability to exercise. In infants, this may present as difficulty feeding.

Cardiorespiratory Distress: Certain arrhythmias, particularly those associated with hemodynamic compromise, can lead to significant cardiorespiratory distress. This may present as severe respiratory distress, cyanosis (bluish discoloration of the skin), or signs of respiratory failure. Prompt recognition and intervention are crucial in these situations. **(3).**

5. Dizziness or lightheadedness due to Hemodynamic Instability: Children with arrhythmias in the ICU may show signs of hemodynamic instability, such as hypotension (low blood pressure), tachycardia (high heart rate), or poor perfusion (poor blood flow to the body's tissues). **(3).**

6. Syncope or Near-Syncope: Syncope (fainting) or near-syncope (almost fainting) can occur if the arrhythmia causes a significant decrease in the blood flow to the brain. **(3)**

7. Decreased Consciousness or Seizures: In severe cases, arrhythmias can cause a decrease in consciousness or even seizures due to inadequate blood flow to the brain. **(2)**

8. Cardiac Arrest: The most serious arrhythmias can cause cardiac arrest, where the heart stops beating effectively.

Sudden Cardiac Arrest: In some cases, arrhythmias can lead to sudden cardiac arrest, where the heart suddenly stops beating effectively. This is a life-threatening emergency and may present with sudden loss of consciousness, absence of pulse, and absence of breathing. Immediate cardiopulmonary resuscitation (CPR) and defibrillation are required to restore circulation. **(3)**

9. Failure to Thrive: In infants and young children, persistent arrhythmias can cause failure to thrive, which is characterized by inadequate weight gain and growth. **(4)**

The specific presentation depends on the type and severity of the arrhythmia, the underlying cardiac condition, and the overall clinical status of the patient, and there are symptoms according to type of arrhythmia:-

***Irregular Heart Rhythm:** Arrhythmias that cause an irregular heart rhythm can present with palpitations, a sensation of "skipped beats," or a feeling of an irregular pulse. Depending on the underlying arrhythmia, the irregular rhythm may be intermittent or sustained . **(2)**

***Tachycardia:** Tachycardia refers to an abnormally fast heart rate. It can present as sustained or episodic episodes of rapid heart rate. The clinical presentation may include palpitations, chest discomfort, shortness of breath, dizziness, or syncope (fainting). Tachycardia can be further classified based on the origin of the rhythm disturbance, such as supraventricular tachycardia (SVT) or ventricular tachycardia (VT). **(3)**

***Bradycardia:** Bradycardia is characterized by a slow heart rate. In pediatric patients, bradycardia is typically defined as a heart rate below the normal range for age. Bradycardia can manifest as fatigue, weakness, dizziness, poor feeding, or syncope. Severe bradycardia may result in hemodynamic instability and require immediate intervention. **(1)**

The diagnosis of pediatric arrhythmias in the pediatric intensive care unit (PICU) involves a combination of clinical assessment, electrocardiographic (ECG) evaluation, and additional diagnostic tests. **(5)**

Here are the key steps involved in diagnosing pediatric arrhythmias in the PICU:

1.Clinical Evaluation: The first step in diagnosing pediatric arrhythmias is a thorough clinical evaluation of the patient. This includes a detailed medical history, physical examination, assessment of symptoms (such as palpitations, dizziness, or syncope), and evaluation of overall cardiac status. The presence of any underlying cardiac conditions or risk factors should be identified. **(5)**

2. Electrocardiogram (ECG): An ECG is a fundamental diagnostic tool for evaluating arrhythmias. It records the electrical activity of the heart and can provide valuable information about the type, duration, and characteristics of the arrhythmia. If the ECG is not definitive, the cardiologist might supplement it with another diagnostic test. Continuous monitoring with telemetry or Holter monitoring may be necessary for 24-48 hours to record the heart rhythm during usual activities, or performing an electrophysiologic study to determine the electrical signal type causing the issue. A tilt table test may be done to assess the heart rate and blood pressure while the child is in different positions,for capturing intermittent or paroxysmal arrhythmias. **(6)**

3. Laboratory Tests: Laboratory tests are often performed to assess electrolyte levels, cardiac enzymes, and other parameters that may influence arrhythmia development or management. These tests can help identify potential underlying causes or contributing factors, such as electrolyte imbalances or myocardial injury. **(7)**

4. Echocardiography (ECHO): Echocardiography, including transthoracic or transesophageal echocardiography, is commonly used to evaluate the structure and function of the heart. It helps assess cardiac anatomy, chamber size, ejection fraction, valve function, and the presence of any congenital or acquired heart abnormalities that may contribute to arrhythmias. **(8)**

A transesophageal echocardiogram is an imaging test that uses ultrasound to create an image of the heart. In this test, the doctor guides a small probe through the nose and into the esophagus the tube through which food travels from the throat into the stomach to the upper part of the chest near the heart. This test, which is performed in less than an hour using mild sedation, can provide a more detailed image of the heart than a conventional echocardiogram performed on the surface of the chest. **(9)**

5. Electrophysiological Studies (EPS): In some cases, electrophysiological studies may be required to further evaluate complex or refractory arrhythmias. EPS involves the introduction of catheters into the heart to assess the electrical properties and conduction pathways. It can help identify the specific site and mechanism of arrhythmia and guide treatment decisions, such as catheter ablation. **(10)**

6. Imaging Studies: Additional imaging studies, such as cardiac magnetic resonance imaging (MRI) or computed tomography (CT), may be necessary to provide detailed anatomical information or evaluate specific cardiac structures, especially in complex cases or when structural abnormalities are suspected. **(11)**

7. Genetic Testing: In certain situations, genetic testing may be considered, especially in patients with suspected or known genetic conditions associated with arrhythmias. Genetic testing can help identify specific genetic mutations or abnormalities that may contribute to the arrhythmia and guide further management or family screening. **(12)**

8. Consultation with Pediatric Cardiology Specialists: In the PICU, close collaboration with pediatric cardiology specialists is essential for the accurate diagnosis of pediatric arrhythmias. Pediatric cardiologists have expertise in interpreting ECGs, echocardiograms, and other diagnostic tests, and they can provide guidance on treatment options and long-term management strategies. **(6)**

Management of cardiac arrhythmias

The management approach for pediatric arrhythmias in the intensive care unit (ICU) aims to stabilize the child's condition, correct the underlying cause if possible, and prevent complications. The specific management strategies depend on the type and severity of the arrhythmia, as well as the child's overall clinical status. Here are some common approaches : **(2)**

1.Immediate Assessment: As soon as an arrhythmia is suspected, a rapid assessment of the patient's clinical status should be performed. This includes evaluating vital signs, oxygen saturation, level of consciousness, and signs of hemodynamic compromise. Immediate intervention is required for life-threatening arrhythmias or those associated with hemodynamic instability. **(2)**

Supportive Care: Initially, the focus is on providing supportive care to stabilize the child. This may include ensuring adequate oxygenation, ventilation, and hemodynamic support, such as fluid resuscitation or inotropic medications, as needed. Close monitoring of vital signs and continuous ECG monitoring are essential. **(4)**

Cardiopulmonary Resuscitation (CPR): If the patient presents with cardiac arrest or severe hemodynamic instability, immediate initiation of CPR is essential. High-quality CPR, including chest compressions and assisted ventilation, should be initiated while preparations are made for advanced life support interventions. **(4)**

Oxygenation and Ventilation: Ensuring adequate oxygenation and ventilation is crucial in stabilizing pediatric arrhythmias. Supplemental oxygen should be provided to maintain oxygen saturation within the target range. In cases of respiratory distress or failure, assisted ventilation or mechanical ventilation may be necessary to optimize oxygenation and ventilation. **(4)**

Hemodynamic Support: Hemodynamically unstable arrhythmias require prompt intervention to restore cardiac output and perfusion. Depending on the specific situation, intravenous fluids, vasopressor medications (e.g., epinephrine, dopamine), or inotropic agents (e.g.,dobutamine) may be administered to support blood pressure and improve cardiac function. **(4)**

2.Medications: Pharmacological therapy may be initiated to control arrhythmias in the PICU. Specific antiarrhythmic medications are selected based on the type of arrhythmia and the patient's clinical condition, used to terminate or control certain arrhythmias and restore normal heart rhythm or prevent recurrent arrhythmias. **(13)**

Antiarrhythmic drugs classified into classes:

1) Class 1 antiarrhythmics: These medications primarily inhibit sodium channels in cardiac cells. They were divided into subclasses according to their effects on sodium channels (e.g., Classes IA, IB, and IC). However, their proarrhythmic potential and limited efficacy in certain cases necessitated their use with caution. For instance, while procainamide (Class IA: Quinidine, Procainamide and Disopyramide) and lidocaine (Class IB: lidocaine, mexilitine, phenytoin, tocainide and moricizine) were widely employed, they each had specific limitations **(14)**

2) Class 2 antiarrhythmics: These are agents with beta adrenergic blocking properties. These include beta-1 (cardiac) selective (atenolol, metoprolol), non selective (propranolol, nadolol) and drugs that have intrinsic sympathomimetic activity (ISA) (Pindolol), highly effective in the management of arrhythmias, particularly in preventing episodes of AF and VT. These medications decrease heart rate and myocardial oxygen consumption, benefiting both rate and rhythm control **(15)**.

3) Class 3 agents: These agents effect the membrane repolarization and thus prolong the refractory period. The drugs have predominant K channel effects with some Na and Ca channel blocking properties. These result in reduction in membrane excitability of all myocardial tissue. Amiodarone, sotalol, ibutilide and dofetilide belong to this class, Particularly, amiodarone has demonstrated efficacy in treating various arrhythmias, including atrial and ventricular arrhythmias, although its long-term use may be limited by the risk of adverse effects **(14)**

4) Class 4 agents: These block the Ca channels and have a predominant effect on the sinus and AV node, these are primarily used for pulse control for AF and other tachyarrhythmias,. Verapamil, diltiazem belongs to this class. **(15)**.

5) Others:

Adenosine: It is an endogenous purigenic agent that increases K channel conductance and depresses inward Ca current resulting in transient AV block. It has wide therapeutic and diagnostic use in emergency room management of re-entry and automatic SVTs such as ectopic atrial tachycardia and some forms of adenosine sensitive VTs. IV dosing is 150-300 mcg/kg given rapidly because of its short half life (few seconds). Side effects include flushing, hypotension, chest pain (transient coronary spasm), bronchospasm and atrial fibrillation **(16)**.

Digoxin: This has several mechanisms of action. The direct effects include binding to Na-K ATPase complex and thus inhibiting Na channel. The inotropic response is due to Ca loading from higher intracellular Na concentration from the enhancement of Na-Ca pump. It also increases parasympathetic output and inhibits norepinephrine release. The drug is excreted in the urine unchanged and also crosses the placenta (hence its use as drug of choice in fetal arrhythmias). Oral dosing is 30-50 mcg/kg loading over 24 hrs in divided doses followed by 7-10 mcg/kg per day. IV dosing is two-thirds of oral dosing. Side effects include nausea, GI and visual disturbance. Cardiovascular effects of digoxin toxicity include bradycardia, AV block and ventricular arrhythmias. Electrolyte and renal abnormalities (especially hypokalemia and hypomagnesemia) potentiate digoxin toxicity **(17)**.

Medication type	How it can help with arrhythmias	Examples
Anticoagulants ("blood thinners")	Decrease the risk of developing blood clots that can lead to heart attacks and strokes; when the heart is not beating normally, blood can pool in the heart chamber and is more prone to clotting	warfarin, enoxaparin, apixaban, dabigatran, rivaroxaban
Beta-blockers	Used to treat high blood pressure and to slow a fast heart rate	metoprolol, atenolol, bisoprolol, sotalol
Calcium channel blockers	Used to slow a rapid heart rate or decrease the speed at which the electrical signals in the heart travel; typically, they are prescribed for atrial arrhythmias. Can also be used to lower blood pressure.	verapamil and diltiazem
Calcium channel blockers	Used to slow a rapid heart rate or decrease the speed at which the electrical signals in the heart travel; typically, they are prescribed for atrial arrhythmias. Can also be used to lower blood pressure.	verapamil and diltiazem
Digoxin	May slow a fast heart rate but can lead to other arrhythmias, so it must be used with caution and is not appropriate for everyone	N/A
Potassium channel blockers	Used to slow a fast heart rate by increasing the time it takes for heart cells to recover after contracting, making them unable to fire and squeeze as often.	amiodarone and ibutilide
Sodium channel blockers	Used to slow the heart rate by making cells less excitable.	flecainide, quinidine, procainamide, disopyramide, and lidocaine

table (1) Types of medication used in management of arrhythmia. (13)

3. Electrical Cardioversion or Defibrillation: In certain cases, electrical cardioversion may be required to restore a normal heart rhythm. This procedure is typically performed under sedation or general anesthesia. In certain arrhythmias, such as hemodynamically unstable supraventricular tachycardia (SVT) or ventricular tachycardia (VT), electrical cardioversion or defibrillation may be necessary. This involves delivering a synchronized electrical shock to the heart to restore normal rhythm. Appropriate energy levels and equipment should be used based on the patient's age and weight through paddles or electrodes placed on the chest. (13)

4. Catheter Ablation: Catheter ablation is a potential treatment option for specific types of arrhythmias that are resistant to medications or cause significant symptoms. It involves inserting catheters into the heart to identify and selectively destroy the abnormal electrical pathways or tissue causing the arrhythmia. (5)

5. Temporary Cardiac Pacing: In cases of bradyarrhythmias (slow heart rhythms), temporary cardiac pacing may be necessary. This involves placing temporary pacing wires or electrodes into the heart through a vein or artery to deliver electrical impulses and maintain an adequate heart rate. (18)

6. Surgical Interventions: In some cases, surgical interventions may be required to correct structural abnormalities that contribute to arrhythmias. This can involve procedures such as repair of congenital heart defects or implantation of devices like pacemakers or implantable cardioverter-defibrillators (ICDs). (19)

7. Management of Underlying Conditions: Pediatric arrhythmias can be associated with underlying medical conditions or electrolyte imbalances. Managing these underlying conditions is crucial to the overall management of arrhythmias. For example, treating infections, correcting electrolyte disturbances, or optimizing thyroid function may be necessary. (7)

8. Consultation with Pediatric Cardiology: Pediatric cardiologists should be involved in the management of pediatric arrhythmias in the PICU. They can provide expertise in the diagnosis, risk stratification, and treatment of arrhythmias. Consultation may include recommendations for further diagnostic tests, electrophysiological studies, or consideration of invasive procedures such as catheter ablation or device implantation. (4)

9. Continuous Cardiac Monitoring: Continuous cardiac monitoring, such as electrocardiography (ECG), is essential for ongoing assessment of the arrhythmia and response to treatment. Continuous monitoring allows for early detection of recurrence or new arrhythmias and facilitates timely intervention. (5)

10. Family Support: Stabilizing pediatric arrhythmias in the PICU can be an emotionally challenging time for the patient's family. Providing regular updates, clear communication, and emotional support to the family is crucial. Engaging the services of child life specialists, social workers, or psychologists can help address the psychological and emotional needs of the patient and their family. (19)

Long Term Management of cardiac arrhythmias

Long-term management and follow-up of pediatric arrhythmias are crucial for ensuring the ongoing well-being of the patient and optimizing their long-term outcomes. The specific approach to long-term management and follow-up may vary depending on the type of arrhythmia, the underlying cardiac condition, and the individual patient's needs (20)

Here are some key aspects of long-term management and follow-up for pediatric arrhythmias:

1. Pediatric Cardiology Follow-Up: Regular follow-up visits with a pediatric cardiologist are essential for monitoring the patient's cardiac health and evaluating the effectiveness of treatment. The frequency of follow-up visits will depend on the specific arrhythmia and the patient's clinical condition. During these visits, the cardiologist may perform a physical examination, review the patient's medical history, evaluate cardiac function through tests such as electrocardiography (ECG) or echocardiography, and adjust treatment as needed. (20)

2. Medication Management: If the patient is on antiarrhythmic medications, ongoing monitoring and management of the medication regimen are necessary. The cardiologist will assess the effectiveness and safety of the medications and make adjustments as required. Regular medication reviews and monitoring of potential side effects, drug levels, and therapeutic response are important. (13)

3. Lifestyle Modifications: In some cases, lifestyle modifications may be recommended to manage pediatric arrhythmias. This can include avoiding triggers or activities that may exacerbate arrhythmias, such as excessive physical exertion or certain medications. The cardiologist may provide guidance on appropriate physical activity, dietary modifications, and other lifestyle factors that can help support cardiac health. (20)

4. Genetic Counseling and Testing: For certain pediatric arrhythmias that have a known genetic basis or are associated with an underlying genetic condition, genetic counseling and testing may be recommended. This can help identify potential genetic abnormalities, provide information about the risk of recurrence in the family, and guide family planning decisions. (12)

5. Holter Monitoring and Event Recorders: Periodic monitoring with ambulatory ECG devices, such as Holter monitors or event recorders, may be necessary to capture arrhythmia episodes that occur intermittently. These devices can provide valuable information about the frequency, duration, and nature of arrhythmias and help guide treatment decisions. (6)

6. Electrophysiological Studies and Ablation: In some cases, electrophysiological studies (EPS) may be performed to further evaluate the underlying mechanisms of arrhythmias. EPS involves the insertion of catheters into the heart to assess electrical conduction and provoke arrhythmias for diagnostic purposes. If appropriate, catheter ablation procedures may be performed to selectively destroy the abnormal cardiac tissue responsible for the arrhythmia. (5)

7. Device Implantation: In certain cases, the placement of implantable devices may be required for long-term management of arrhythmias. This can include pacemakers for bradycardias or implantable cardioverter-defibrillators (ICDs) for high-risk ventricular arrhythmias. Regular follow-up visits with the device clinic are necessary to monitor device function, battery life, and make programming adjustments as needed. (18)

8. Education and Support: Providing education and support to the patient and their family is essential for managing pediatric arrhythmias. This can include information about the arrhythmia diagnosis, treatment options, lifestyle modifications, and recognizing signs of arrhythmia recurrence or complications. Ongoing

communication and access to resources, such as support groups or educational materials, can help empower the patient and their family to actively participate in their care. **(18)**

9. Psychological Support: Pediatric arrhythmias can have a significant impact on the emotional well-being of both the patient and their family. Psychosocial support, including access to psychologists, social workers, or other mental health professionals, can help address the psychological and emotional needs associated with living with a chronic condition. **(18)**

References:

1. DeWitt ES, Chandler SF, Hyland RJ, Beausejour Ladouceur V, Blume ED, VanderPluym C. (2019). Phenotypic Manifestations of Arrhythmogenic Cardiomyopathy in Children and Adolescents. *J Am Coll Cardiol.* Jul 23;74(3):346-358.
2. Dağlı, Hatice Yılmaz, Fatih Şap, Mehmet Burhan Oflaz, Beray Selver Ekioglu, Mehmet Emre Atabek, and Tamer Baysal. (2023). Evaluation Of Electrocardiographic Markers For The Risk Of Cardiac Arrhythmia In Children With Obesity." .
3. Elodie Surget , Krisai P, Cheniti G, Takagi T, Kamakura T , André C, Duchateau J, Pambrun T, Derval N, Sacher F, Jaïs P, Haissaguerre M, Hocini M. (2022). Sex differences in ventricular arrhythmia: epidemiology, pathophysiology and catheter ablation. *Rev Cardiovasc Med.* Jan 14;23(1):14
4. Kleinman ME, Chameides L, Schexnayder SM, Samson RA, Hazinski MF, Atkins DL, Berg MD, de Caen AR, (2010). . Part 14: pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* Nov 2;122(18 Suppl 3):S876-908.
5. Fabrizio Drago, Battipaglia I, Russo MS, Remoli R, Pazzano V, Grifoni G, Allegretti G, Silvetti MS. (2018). Voltage gradient mapping and electrophysiologically guided cryoablation in children with AVNRT. *Europace.* Apr 1;20(4):665-672.
6. Albakri A (2018). Restrictive cardiomyopathy: a review of literature on clinical status and meta-analysis of diagnosis and clinical management. *Pediatr Dimens.*;3(2):1-4.
7. Brian Olshansky, Richards M, Sharma AD, Jones PW, Wold N, Perschbacher D, Wilkoff BL. (2020) . Heart rate score predicts mortality independent of shocks in ICD and CRT-D patients. *J Interv Card Electrophysiol.* Jun;58(1):103-111
8. Dasgupta, Sharoda, et al. (2020) "Association between social vulnerability and a county's risk for becoming a COVID-19 hotspot—United States, June 1–July 25, Morbidity and Mortality Weekly Report 69.42 (2020): 1535
9. José L. Vázquez , de Pinho Favaro MT, Atienza-Garriga J, Martínez-Torró C, Parladé E, , Corchero JL, Ferrer-Miralles N, Villaverde A (2022). Recombinant vaccines in 2022: a perspective from the cell factory. *Microb Cell Fact.* Oct 5;21(1):203.
10. Blaufox, Andrew D., et al. (2011) "Transesophageal electrophysiological evaluation of children with a history of supraventricular tachycardia in infancy." *Pediatric cardiology* 32: 1110-1114.
11. Veillette, A , Li, B., Lu, Y., Zhong, M. C., Qian, J., Li, R., Davidson, D. et al (2022). Cis interactions between CD2 and its ligands on T cells are required for T cell activation. *Science immunology*, 7(74), eabn6373.
12. Dellefave-Castillo, L. M., Cirino, A. L., Callis, T. E., Esplin, E. D., Garcia, J., Hatchell, K. E., ... & McNally, E. M. (2022). Assessment of the diagnostic yield of combined cardiomyopathy and arrhythmia genetic testing. *JAMA cardiology*, 7(9), 966-974.
13. Brugada , Sieira, J., Dendramis, G. and, P., (2016) . Pathogenesis and management of Brugada syndrome. *Nature Reviews Cardiology*, 13(12), pp.744-756.
14. Almorad A, Del Monte A, Della Rocca DG, et al.: (2023) Outcomes of pulmonary vein isolation with radiofrequency balloon vs. cryoballoon ablation: a multi-centric study. *Europace.* 2023, 25:eua252. 10.1093/europace/eua252 Chaudhary et al. *Cureus* 15(9): e45958.
15. Andrade JG, Champagne J, Dubuc M, et al.: (2019) Cryoballoon or radiofrequency ablation for atrial fibrillation assessed by continuous monitoring: a randomized clinical trial. *Circulation.*, 140:1779-88.
16. Molina, C. E., Leroy, J., Richter, W., Xie, M., Scheitrum, C., Lee, I.O., Moack, C., Rucker-Martin, C., Donzeau-Gouge, P., Verde, I., Liach, A., Hove- Madsen, L., Conti, M., Vandecasteele, G. and Fischmeister, R. (2012): Cyclic adenosine monophosphate phosphodiesterase type 4 protects against atrial arrhythmias. *Journal of the American College of Cardiology*, 59 (24), 2182-2190.
17. Sanatani, S., Potts, J.E., Reed, J. H., Saul, J.P., Stephenson, E.A., Gibbs, K.A. and Kanter, R.J. (2012): The Study of Antiarrhythmic Medications in Infancy (SAMIS). A multicenter, randomized controlled trial comparing the efficacy and safety of digoxin versus propranolol for prophylaxis of supraventricular tachycardia in infants. *Circulation: Arrhythmia and Electrophysiology*, 5(5), 984-991.
18. Silvetti, M.S , Di Mambro, C., Russo, M.S., Righi, D., Placidi, S., Palmieri, R.,, Gimigliano, F., Prosperi, M. and Drago, F., (2015). Ventricular pre-excitation: symptomatic and asymptomatic children have the same potential risk of sudden cardiac death. *Ep Europace*, 17(4), pp.617-621.
19. Kimberly A Holst ., Sameh M. Said, Timothy J. Nelson, Bryan C. Cannon, and Joseph A. Dearani. (2017). "Current interventional and surgical management of congenital heart disease: specific focus on valvular disease and cardiac arrhythmias." *Circulation research* 120.6 1027-1044.

20. Moak, J. P., Leifer, E. S., Tripodi, D., Mohiddin, S. A., & Fananapazir, L. (2011). Long-term follow-up of children and adolescents diagnosed with hypertrophic cardiomyopathy: risk factors for adverse arrhythmic events. *Pediatric cardiology*, 32, 1096-1105.