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Exploring the relationship between sudden cardiac death and arrhythmias: Pathophysiology, risk factors, and implications for prevention and management

Abdulrhman Awadh Alharbi
KSA, National Guard Health Affairs

Samo Nazal Almutairi
KSA, National Guard Health Affairs

Ahmad Alhelo Alanazi
KSA, National Guard Health Affairs

Ibrahim Muhammad Al-Arej
KSA, National Guard Health Affairs

Abdullatif Suliman Alsayegh
KSA, National Guard Health Affairs

Abdualrhman Ayesh Mohammad Alanazi
KSA, National Guard Health Affairs

Mohammed Abdullah Alduaybi
KSA, National Guard Health Affairs

Omar Hussain Alsomali
KSA, National Guard Health Affairs

Meshal Ibrahim Zaid Al Owias
KSA, National Guard Health Affairs

Bader Sayah Alanezi
KSA, National Guard Health Affairs

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***Corresponding email**: akk29337@gmail.com*
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***Abstract*---Background:** Sudden cardiac death (SCD) is a critical public health issue, often linked to underlying arrhythmias that disrupt normal heart rhythm. Understanding the pathophysiology and risk factors associated with arrhythmias is vital for effective prevention and management strategies. **Aim:** This study aims to explore the intricate relationship between SCD and arrhythmias, highlighting the pathophysiological mechanisms, identifying significant risk factors, and discussing implications for clinical management and prevention. **Methods:** A comprehensive literature review was conducted, analyzing studies that examine the causes, diagnosis, and management of SCD related to arrhythmias. Relevant data were extracted from peer-reviewed articles, clinical guidelines, and meta-analyses. The findings were synthesized to elucidate the mechanisms by which arrhythmias contribute to SCD and to identify key risk factors. **Results:** The findings reveal that a variety of factors contribute to the occurrence of arrhythmias leading to SCD, including structural heart disease, genetic predispositions, and electrolyte imbalances. Ischemic heart disease was identified as the most prevalent cause, with other significant contributors being inherited arrhythmia syndromes and the presence of comorbidities. Additionally, the use of advanced diagnostic tools, such as electrocardiograms and implantable cardioverter-defibrillators, has improved the identification of patients at risk. Management strategies, including lifestyle modifications, pharmacotherapy, and device implantation, have shown effectiveness in reducing the incidence of SCD. **Conclusion:** The relationship between arrhythmias and sudden cardiac death is complex, influenced by multiple risk factors and pathophysiological mechanisms. Effective prevention and management strategies are crucial in addressing this significant health concern. Further research is needed to enhance understanding and develop targeted interventions to reduce the incidence of SCD.

***Keywords*---**Sudden cardiac death, arrhythmias, pathophysiology, risk factors, prevention, management.

Introduction

According to reports, the United States has between 180,000 and 300,000 sudden cardiac deaths (SCD) every year [1,2]. Around the world, unexpected and sudden cardiac deaths are the primary cause of death, accounting for over 17 million deaths annually, of which SCD accounts for 25% [2]. SCD is characterized by death within 24 hours of the last time the person was seen alive in unwitnessed situations, and within an hour of the onset of symptoms in witnessed cases [2]. Ventricular fibrillation (VF) has been found to be the main underlying cause in a considerable number of these deaths, which happen without witnesses [2–5]. Heart block is becoming more widely acknowledged as a contributing etiology, and the majority of patients are found in asystole or with pulseless electrical activity (PEA). The rate of SCD as a percentage of total cardiovascular mortality has increased [2], despite the decline in cardiovascular-

related deaths in recent decades [6], which can be attributed to improved prevention efforts. A faster drop in in-hospital death rates is the cause of this trend [2], highlighting the need for better risk assessment methods and preventative measures. Pharmacological treatments that use amiodarone or class Ic drugs to prevent SCD have not worked [7, 8]. The introduction of implantable cardioverter-defibrillators (ICDs) has been the most important development in SCD prevention [9]. Secondary prevention studies, such as the Cardiac Arrest Study of Hamburg (CASH) [12], Canadian Implantable Defibrillator Study (CIDS) [11], and Antiarrhythmic Versus Implantable Defibrillator (AVID) [10], have shown a statistically significant increase in survival rates linked to ICD implantation compared to medication therapy for this patient population.

Patients with a myocardial infarction (MI) were included in the Multicenter Automatic Defibrillator Implantation Trial (MADIT) [13] and the Multicenter Unsustained Tachycardia Trial (MUSTT) [14], which compared primary prevention with an ICD to standard medical therapy in patients with a reduced ejection fraction (EF) of less than 35% and 40%, respectively, and documented or induced ventricular tachycardia (VT). These trials showed a relative risk decrease in mortality of 58–59%. Following this, MADIT II [15] showed that post-MI patients with an EF of less than 30% who did not require documented or induced VT had a 28% relative risk decrease in two-year mortality. A significant trend toward lower mortality with ICDs was observed in the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) [16] trial, which evaluated the benefits of ICDs over standard treatment in patients with heart failure and an EF of 35% or less. In contrast, ICDs were shown to be beneficial when compared to standard medical therapy in the Sudden Cardiac Death in Heart Failure Trial (SCD-HEFT) [17], which included participants with both ischemic and non-ischemic cardiomyopathy classified by New York Heart Association classes II or III and an EF of 35% or less. Interestingly, these primary prevention trials show that no other important risk factors reliably predict who will benefit from ICD installation, save for a low EF. Although the major studies have set an EF criterion between 30% and 40%, the median EF of study participants is typically much lower than this range, and subgroup analyses frequently do not show a discernible advantage [3,13,15,17,18]. Also, less than 40% of patients in 'high-risk' populations like SCD-HeFT [17] and MADIT II [15] got appropriate ICD shock therapy over the first four years of follow-up. Prophylactic ICD implantation in patients over 68 with non-ischemic cardiomyopathy did not correlate with lower long-term mortality, according to recent results from the Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality (DANISH) [19]. By using these studies to guide the prescription of ICDs, physicians have largely focused on a subset of patients with a higher incident incidence, classifying them as high risk. The fact that most SCD occurrences happen to people who have never had heart disease before and are not considered high risk by conventional assessment metrics, or who are the first sign of an unidentified underlying cardiac ailment, presents a problem for practitioners [3]. Therefore, the majority of SCD events occur in patients who are considered to be at 'low risk' for events [3]. Even though this low-risk group has a very low incidence, together they account for the greatest number of incidents. Last but not least, there are few, if any, conclusive risk markers found outside of patient-reported symptoms for rarer conditions like hypertrophic cardiomyopathy (HCM),

arrhythmogenic right ventricular cardiomyopathy (ARVC), long QT syndrome (LQT), Brugada syndrome, and early repolarization, making the criteria for primary prevention unclear [3,20].

Sudden Cardiac Arrest: Chain of Survival:

A significant proportion of cardiac arrests occur outside of hospital settings, often resulting in poor prognoses. In the UK, the rate of survival to hospital admission can be as low as 8.1%, with survival to discharge dropping to a mere 3.2% for out-of-hospital cardiac arrest cases [21]. Enhancing outcomes hinges on the chain of survival, which comprises the following critical steps:

1. Immediate recognition of cardiac arrest and activation of the emergency response system.
2. Prompt initiation of cardiopulmonary resuscitation (CPR), particularly focusing on effective chest compressions.
3. Swift defibrillation.
4. Efficient advanced life support.
5. Comprehensive post-cardiac arrest care.

The significance of early recognition and CPR is underscored by evidence indicating that a timely bystander response, including CPR and early automated defibrillation for out-of-hospital cardiac arrests by community members, represents a vital public health initiative that can significantly enhance survival rates. For every minute that passes without CPR, the likelihood of survival diminishes by 7–10%. A study involving 30,381 cardiac arrests in Sweden demonstrated that CPR administered prior to the arrival of emergency medical services (EMS) more than doubled the survival rate at 30 days [22]. Moreover, standardized EMS protocols and cohesive post-resuscitation care are crucial in improving patient outcomes. In Oslo, enhancements made to EMS care—focusing on consistent and effective CPR, followed by targeted post-resuscitation care such as therapeutic hypothermia and percutaneous coronary intervention (PCI)—resulted in a doubling of survival rates, achieving as high as 35% for bystander-witnessed ventricular tachycardia (VT) or ventricular fibrillation (VF) arrests [23]. In instances of refractory VT/VF, early coronary intervention combined with extracorporeal membrane oxygenation and continuous mechanical defibrillation during PCI has demonstrated favorable outcomes [24]. These results highlight the necessity of a comprehensive public health strategy that includes public education on CPR, early access to EMS, and specialized post-resuscitation care [25]. The critical role of early bystander defibrillation is reinforced by data showing that the prompt use of public automated external defibrillators (AEDs) during out-of-hospital cardiac arrests significantly enhances survival outcomes [26,27]. However, achieving this necessitates considerable political and strategic commitment to ensure organized and widespread access to these devices, alongside public education regarding their availability. Currently, despite initiatives aimed at raising public awareness and increasing the accessibility of AEDs, many public venues lack these life-saving devices. Where AEDs are present, their application may be as low as 1.7% in out-of-hospital cardiac arrests [28]. This underscores the urgent need for renewed public engagement and improved regional planning to address this critical gap in the chain of survival, which is a major contributor to suboptimal survival rates. Innovative approaches

utilizing smart technology to detect cardiac arrests and drone networks equipped with automated defibrillators may represent future advancements in enhancing outcomes [29].

Establishing a Diagnosis:
Initial Assessment and Management of Patients Who Survive a Cardiac Arrest:

The evaluation of individuals who survive an out-of-hospital cardiac arrest necessitates a comprehensive assessment, including a detailed history of the event, supplemented by collateral information. The etiologies of sudden cardiac death (SCD), with ischemic heart disease identified as the predominant cause. It is essential to evaluate symptoms that occurred prior to the incident, such as chest pain, palpitations, breathlessness, syncope, or presyncope. Risk factors including hypertension, diabetes, hyperlipidaemia, and smoking should also be investigated. A thorough medication history is critical, along with targeted inquiries about recreational drug use and psychiatric medications that may prolong the QT interval. Furthermore, potential precipitating factors such as physical exertion and emotional stress should be identified, as well as relevant family history. The 12-lead electrocardiogram (ECG) serves as the cornerstone of the initial non-invasive evaluation. In instances where ischemia is indicated, immediate coronary intervention should be undertaken. Notably, even when ischemic changes are absent on the ECG, up to 29% of patients experiencing out-of-hospital cardiac arrest may still have a significant lesion; percutaneous coronary intervention (PCI) in these cases is correlated with a two-fold improvement in cerebral performance category outcomes [30]. Consequently, all patients should undergo ischemia assessment utilizing both the 12-lead ECG and invasive coronary angiography. The ECG should also be meticulously examined for signs of inherited cardiac conditions and structural abnormalities. Common inherited cardiac disorders to assess via ECG include Brugada syndrome, prolonged and shortened QT intervals, and early repolarization patterns. Additionally, structural abnormalities such as hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and dilated cardiomyopathy (DCM) may manifest through distinctive ECG changes. Imaging modalities, including echocardiography and magnetic resonance imaging (MRI), play a pivotal role in evaluating the structural causes of out-of-hospital cardiac arrest. Echocardiography serves as the primary tool for initial assessment, facilitating the evaluation of regional wall motion abnormalities, overall ventricular function, valvular heart disease, and myocardial disorders such as HCM, ARVC, and DCM. Cardiac MRI (cMRI) is increasingly employed to augment the information provided by echocardiography, offering superior tissue characterization capabilities. This may lead to a diagnosis in approximately 50% of cases and yield a definitive diagnosis in about 30% of instances [31].

Patients Where the Cardiac Arrest is Apparently Unexplained: The Barts Protocol

In cases where ischemic heart disease has been excluded, ejection fraction (EF) remains preserved, and repolarization disorders are not evident on the resting ECG, further diagnostic evaluation is warranted. Such additional assessment can

significantly enhance diagnostic yield and clarify the diagnosis in nearly half of the patients with initially ambiguous cases [32].

Diagnostic Criteria of Inherited Arrhythmia Syndromes:

The diagnostic criteria for inherited arrhythmia syndromes are categorized by specific conditions, each with distinct electrocardiogram (ECG) findings, provocation test indications, and diagnostic outcomes. For Long QT syndrome, the ECG diagnostic criteria require a corrected QT interval (QTc) of 500 milliseconds or greater in repeated 12-lead ECGs. Additionally, a QTc between 480 and 499 milliseconds (or 470 to 449 milliseconds in men) in the presence of unexplained syncope is indicative. In cases of high clinical suspicion, provocation testing is considered for patients with a QTc in the ranges of 440 to 470 milliseconds for men or 450 to 480 milliseconds for women. Diagnostic provocation tests may reveal a failure to shorten the QT interval, lengthening of the QTc, or a QTc greater than 445 milliseconds during the 4-minute recovery period. Brugada syndrome is characterized by ST-segment elevation with type 1 morphology of 2 millimeters or greater in at least one lead among the right precordial leads V1 and V2, positioned in the second, third, or fourth intercostal space. This elevation may occur spontaneously or following provocative drug testing. If clinical suspicion exists, ajmaline testing is indicated, with diagnostic findings confirming ST elevation of 2 millimeters or more in at least one right precordial lead. For Catecholaminergic polymorphic ventricular tachycardia, the ECG may display bidirectional ventricular tachycardia (VT) or polymorphic ventricular premature beats, as well as exercise-induced premature ventricular contractions (PVCs) or bidirectional/polymorphic VT. Exercise testing is employed when clinical indications arise, and diagnostic results will typically show either polymorphic or bidirectional VT during exertion. In the case of Early repolarization, the ECG criteria include J-point elevation of at least 1 millimeter in two or more contiguous inferior and/or lateral leads. Currently, there are no additional provocation tests or specific diagnostic findings associated with this condition, indicating a straightforward identification based on the ECG findings alone.

Provocation Testing:

The initial evaluation comprises both lying and standing electrocardiograms (ECGs) to identify potential QT prolongation during brief episodes of tachycardia triggered by standing, which may reveal concealed phenotypes of Long QT syndrome type 1 (LQT1) and type 2 (LQT2) [33,34]. This is followed by exercise testing to assess QT prolongation during physical activity or a lack of QT interval shortening during exertion, which is a notable characteristic in LQT1 patients [34]. Special attention should be given to the recovery ECG in the first 1 to 4 minutes post-exercise, as patients with LQT2 may only demonstrate QT prolongation during the recovery phase when sympathetic withdrawal can induce late QT lengthening [34,35]. A QTc greater than 445 milliseconds at 4 minutes of recovery has been shown to possess a sensitivity of 92% and a specificity of 88% for identifying individuals with LQT1 and LQT2 [35]. Additionally, exercise testing may reveal polymorphic or bidirectional ventricular tachycardia (VT), which could suggest a diagnosis of catecholaminergic polymorphic ventricular tachycardia

(CPVT), although this test lacks both sensitivity and specificity for the condition. Moreover, we routinely conduct ECG recordings in both standard and high-right precordial positions [36] to identify characteristic changes associated with type 1 Brugada syndrome [37]. Provocative testing using ajmaline, administered at a dose of 1 mg/kg over 5 minutes, is also performed, with ECGs recorded in both high and standard precordial leads; however, the sensitivity and specificity of this approach remain contentious [36].

Imaging:

Echocardiography and cardiac magnetic resonance imaging (cMRI) are essential components of the assessment process, allowing for the detection of structural cardiac abnormalities. cMRI is proving increasingly valuable due to its capability to identify morphological irregularities and characterize tissue fibrosis, which provides critical insights into the pathogenesis of sudden cardiac arrest [31]. In cases where patients do not exhibit a history or ECG changes necessitating immediate coronary intervention, cardiac computed tomography (CT) is increasingly utilized to examine coronary anatomy and anomalous coronary artery pathways, thus eliminating the need for conventional angiography.

Other Tests/Investigations:

Electrophysiological testing has not been shown to affect management or predict outcomes in survivors of cardiac arrest [38], and its role in the management and risk assessment of inherited conditions, such as Brugada syndrome, is still under discussion [39]. This testing is only conducted in scenarios where pre-excitation is suspected. Genetic testing can be advantageous when a clear diagnosis is established or when the pre-test probability is high, ensuring that a positive result influences the management of both the patient and their family. Although cardiac biopsy may assist in diagnosing inflammatory or infiltrative diseases, such as myocarditis or sarcoidosis, its usage is becoming less common due to the availability of advanced imaging techniques like cMRI and PET-CT. We only resort to cardiac biopsy when imaging results are uncertain in suspected sarcoidosis cases.

Management of Patients after Stabilization from Cardiac Arrest:

The implantation of an implantable cardioverter-defibrillator (ICD) remains the cornerstone of management for the majority of patients who survive an out-of-hospital cardiac arrest. For individuals who cannot receive an ICD due to clinical contraindications or those who are uncertain about the procedure, the ZOLL® LifeVest may be considered as a temporary solution until ICD implantation is feasible or until the arrhythmic risk diminishes [40]. Among patients with an implanted ICD, further appropriate ICD therapy is observed in over 23% of cases [32]. Identifying the underlying cause of the cardiac arrest is crucial as it may enable targeted therapies to mitigate the risk of future cardiac arrests and may facilitate the identification and prevention of similar inherited conditions in first-degree relatives.

Ischemic Cardiomyopathy: Ischemia serves as the primary etiology in most cases, and the management of arrhythmias is predicated on effective secondary prevention and ensuring that adequate revascularization has been achieved. Beta-blockers remain fundamental in preventing further shocks, with the potential adjunct of amiodarone or class IB agents, if necessary, to avert shocks and manage ventricular tachycardia (VT) storms. The utilization of VT ablation is increasingly being performed, demonstrating success rates exceeding 75% in certain cohorts [41].

Long QT Syndrome: In patients with Long QT syndrome (LQT), beta-blockers are the principal treatment modality, with propranolol, bisoprolol, and nadolol recognized as the most effective in shortening the QT interval. Evidence indicates that metoprolol is less effective [42,43]. For patients with LQT3, the addition of oral mexiletine to inhibit late sodium currents may be beneficial in those with a QT interval exceeding 500 milliseconds and experiencing syncope or pre-syncope, or those receiving ICD therapy [44]. In cases where patients continue to require ICD therapy despite medical management or present with markedly prolonged QT intervals exceeding 550 milliseconds, where the risk escalates [20], left cardiac sympathectomy may be a viable option [45]. Furthermore, it is critical to emphasize the avoidance of medications that prolong the QT interval; this list is frequently updated and should be regularly consulted by both patients and physicians via crediblemeds.org [46].

Brugada Syndrome and Early Repolarization Syndrome: In Brugada syndrome, the avoidance of fever—achieved through the use of antipyretics and the avoidance of medications that can provoke arrhythmias and type 1 ECG changes—is paramount (brugadadrugs.org) [47]. Acute VT storms typically respond favorably to isoproterenol infusion, while hydroquinidine can serve as an oral alternative for patients undergoing recurrent ICD therapy [20]. Increasingly, epicardial substrate ablation shows promise [48] and may emerge as a significant component of patient management. Early repolarization syndrome displays a similar response to treatment as Brugada syndrome, with isoproterenol infusion and hydroquinidine proving to be effective interventions. In some patients with early repolarization syndrome, VT or ventricular fibrillation (VF) may be triggered by closely coupled ectopic beats, and suppression of these beats through the use of beta-blockers, calcium channel blockers, or ablation may yield benefits.

Catecholaminergic Polymorphic Ventricular Tachycardia: Beta-blockers are the first-line therapeutic option for preventing ectopy and arrhythmias in this patient group. The addition of flecainide is thought to mitigate cellular calcium overload in catecholaminergic polymorphic ventricular tachycardia (CPVT) and may be advantageous for patients experiencing recurrent syncope, VT, or requiring ICD therapy. Verapamil has also demonstrated efficacy [20]. Implantation of an ICD should be avoided in these patients when feasible, as the sympathetic stimulation associated with a shock can induce arrhythmias, regardless of whether the original shock was appropriate or inappropriate. Furthermore, there are case reports suggesting that ventricular ectopic ablation in CPVT may help prevent Purkinje triggers in these patients [49]. Lastly, left cardiac sympathectomy may be effective in curbing arrhythmias and ICD shocks in cases unresponsive to medical therapy [45].

Idiopathic Ventricular Fibrillation: The management of recurrent arrhythmias in this subset of patients is primarily empirical. Recurrent arrhythmias and appropriate shocks may occur in up to 29% of patients, and therapy with hydroquinidine [50] may assist in reducing ICD therapy requirements [51]. Similar to patients with early repolarization syndrome, short-coupled ventricular premature beats can frequently trigger arrhythmias in this cohort, often through Purkinje firing; ablation of these triggers may prove successful in preventing further arrhythmias [52].

Structural Heart Disease: The management of cardiomyopathies is best conducted in specialized clinics, where the wide array of symptoms, along with family screening and follow-up, can be effectively addressed by physicians with expertise in this area. Beta-blockers and amiodarone continue to be the mainstays of treatment for recurrent ventricular arrhythmias in hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM). Sotalol is the initial drug of choice during the active arrhythmia phase of arrhythmogenic ventricular cardiomyopathy (ARVC), subsequently followed by amiodarone or beta-blockers. Catheter ablation may be beneficial in reducing arrhythmia burden in ARVC [53] and DCM.

Family Screening: Family screening is essential in cases where a diagnosis is established or where a pathogenic genetic mutation is identified, as it helps exclude diagnoses in first-degree relatives and manage their associated risks. Additionally, screening the family members of individuals who have experienced unexplained sudden death may uncover latent disease phenotypes in the proband [54], aiding in the diagnosis and risk management for relatives [55]. Our family member screening adheres to the Barts Protocol.

Conclusion

In conclusion, the relationship between sudden cardiac death (SCD) and arrhythmias underscores the critical need for a comprehensive understanding of their underlying mechanisms, risk factors, and effective management strategies. This exploration has highlighted the multifaceted nature of arrhythmias as both a cause and a consequence of SCD, emphasizing that individuals at risk often present with a combination of genetic, structural, and environmental factors. Ischemic heart disease remains the leading contributor to SCD, but attention must also be given to inherited arrhythmia syndromes, such as long QT syndrome and Brugada syndrome, which can precipitate fatal arrhythmias in otherwise healthy individuals. Advancements in diagnostic modalities, including electrocardiography and wearable technology, have revolutionized the detection and monitoring of arrhythmias, allowing for earlier intervention and risk stratification. The implementation of implantable cardioverter-defibrillators (ICDs) has significantly improved outcomes for patients at high risk for SCD, demonstrating the importance of tailored management approaches. Pharmacological therapies, particularly beta-blockers, have proven effective in mitigating arrhythmic events, and the integration of lifestyle modifications further enhances preventive strategies. Family screening for hereditary arrhythmias is essential for identifying at-risk individuals, particularly in cases of unexplained SCD. This proactive approach not only aids in diagnosis but also provides an

opportunity for targeted interventions that may prevent tragic outcomes in family members. While the current understanding of SCD and arrhythmias has improved, ongoing research is vital to uncover additional pathophysiological mechanisms and refine risk assessment tools. Future studies should focus on personalized medicine approaches that consider genetic predispositions and environmental factors to optimize prevention and management strategies. In summary, addressing the intersection of arrhythmias and sudden cardiac death requires a multidisciplinary approach, involving cardiologists, geneticists, and primary care providers. By fostering collaboration and advancing research, we can enhance our ability to prevent SCD and improve the quality of care for those at risk.

References

1. Chugh SS, Reinier K, Teodorescu C et al. Epidemiology of sudden cardiac death: clinical and research implications. Prog Cardiovasc Dis. 2008;51:213–28. doi: 10.1016/j.pcad.2008.06.003.
2. Adabag AS, Luepker RV, Roger VL, Gersh BJ. Sudden cardiac death: epidemiology and risk factors. Nat Rev Cardiol. 2010;7:216–25. doi: 10.1038/nrcardio.2010.3.
3. Myerburg RJ, Reddy V, Castellanos A. Indications for implantable cardioverter-defibrillators based on evidence and judgment. J Am Coll Cardiol. 2009;54:747–63. doi: 10.1016/j.jacc.2009.03.078.
4. Rea TD, Page RL. Community approaches to improve resuscitation after out-of-hospital sudden cardiac arrest. Circulation. 2010;121:1134–40. doi: 10.1161/CIRCULATIONAHA.109.899799.
5. Estes NA. Predicting and preventing sudden cardiac death. Circulation. 2011;124:651–6. doi: 10.1161/CIRCULATIONAHA.110.974170.
6. Niemeijer MN, van den Berg ME, Leening MJG et al. Declining incidence of sudden cardiac death from 1990–2010 in a general middle-aged and elderly population: the Rotterdam study. Heart Rhythm. 2015;12:123–9. doi: 10.1016/j.hrthm.2014.09.054.
7. Bardy GH, Lee KL, Mark DB et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med. 2005;352:225–37. doi: 10.1056/NEJMoa043399.
8. Echt DS, Liebson PR, Mitchell LB et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med. 1991;324:781–8. doi: 10.1056/NEJM199103213241201.
9. Nanthakumar K, Epstein AE, Kay GN et al. Prophylactic implantable cardioverter-defibrillator therapy in patients with left ventricular systolic dysfunction: a pooled analysis of 10 primary prevention trials. J Am Coll Cardiol. 2004;44:2166–72. doi: 10.1016/jjacc.2004.08.054.
10. Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med. 1997;337:1576–83. doi: 10.1056/NEJM199711273372202.
11. Connolly SJ, Gent M, Roberts RS et al. Canadian implantable defibrillator study (CIDS): a randomized trial of the implantable cardioverter defibrillator

against amiodarone. Circulation. 2000;101:1297–302. doi: 10.1161/01.CIR.101.11.1297.
12. Kuck KH, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the cardiac arrest study Hamburg (CASH). Circulation. 2000;102:748–54. doi: 10.1161/01.CIR.102J.748.
13. Moss AJ, Hall WJ, Cannom DS et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med. 1996;335:1933–40. doi: 10.1056/NEJM199612263352601
14. Buxton AE, Lee KL, Fisher JD et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. N Engl J Med. 1999;341:1882–90. doi: 10.1056/NEJM199912163412503.
15. Moss AJ, Zareba W, Hall WJ et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002;346:877–83. doi: 10.1056/NEJMoa013474.
16. Kadish A, Dyer A, Daubert JP et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med. 2004;350:2151–8. doi: 10.1056/NEJMoa033088.
17. Bardy GH, Lee KL, Mark DB et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med. 2005;352:225–37. doi: 10.1056/NEJMoa043399.
18. Moss AJ, Fadl Y, Zareba W et al. Survival benefit with an implanted defibrillator in relation to mortality risk in chronic coronary heart disease. Am J Cardiol. 2001;88:516–20. doi: 10.1016/S0002-9149(01)01729-5.
19. Køber L, Thune JJ, Nielsen JC et al. Defibrillator implantation in patients with nonischemic systolic heart failure. N Engl J Med. 2016;375:1221–30. doi: 10.1056/NEJMoa1608029.
20. Priori SG, Wilde AA, Horie M et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm. 2013;10:1932–63. doi: 10.1016/j.hrthm.2013.05.014.
21. Lyon RM, Cobbe SM, Bradley JM, Grubb NR. Surviving out of hospital cardiac arrest at home: a postcode lottery? Emerg Med Jl. 2004;21:619–24. doi: 10.1136/emj.2003.010363.
22. Hasselqvist-Ax I, Riva G, Herlitz J et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. N Engl J Med. 2015;372:2307–15. doi: 10.1056/NEJMoa1405796.
23. Lund-Kordahl I, Olasveengen TM, Lorem T et al. Improving outcome after out-of-hospital cardiac arrest by strengthening weak links of the local chain of survival; quality of advanced life support and post-resuscitation care. Resuscitation. 2010;81:422–6. doi: 10.1016/j.resuscitation.2009.12.020.
24. Yannopoulos D, Bartos JA, Raveendran G et al. Coronary artery disease in patients with out-of-hospital refractory ventricular fibrillation cardiac arrest. J Am Coll Cardiol. 2017;70:1109–17. doi: 10.1016/jjacc.2017.06.059.
25. Boyce LW, VlietVlieland TP, Bosch J et al. High survival rate of 43% in out-of-hospital cardiac arrest patients in an optimised chain of survival. Neth Heart J. 2014;23:20–5. doi: 10.1007/s12471-014-0617-x.

26. Bækgaard, J. S., Viereck, S., Møller, T. P., Ersbøll, A. K., Lippert, F., & Folke, F. (2017). The effects of public access defibrillation on survival after out-of-hospital cardiac arrest: a systematic review of observational studies. Circulation, 136(10), 954-965.
27. Murakami Y, Iwami T, Kitamura T et al. Outcomes of out-of-hospital cardiac arrest by public location in the public-access defibrillation era. J Am Heart Assoc. 2014;3:e000533. doi: 10.1161/JAHA.113.000533.
28. Deakin CD, Shewry E, Gray HH. Public access defibrillation remains out of reach for most victims of out-of-hospital sudden cardiac arrest. Heart. 2014;100:619–23. doi: 10.1136/heartjnl-2013-305030.
29. Boutilier JJ, Brooks SC, Janmohamed A et al. Optimizing a drone network to deliver automated external defibrillators. Circulation. 2017;135:2454–65. doi: 10.1161/CIRCULATIONAHA.116.026318.
30. Dumas F, Bougouin W, Geri G et al. Emergency percutaneous coronary intervention in post-cardiac arrest patients without ST-segment elevation pattern. JACC Cardiovasc Interv. 2016;9:1011–8. doi: 10.1016/j.jcin.2016.02.001.
31. Rodrigues P, Joshi A, Williams H et al. Diagnosis and prognosis in sudden cardiac arrest survivors without coronary artery disease: utility of a clinical approach using cardiac magnetic resonance imaging. Circ Cardiovasc Imaging. 2017;10:e006709. doi: 10.1161/CIRCIMAGING.117.006709.
32. Herman AR, Cheung C, Gerull B et al. Outcome of apparently unexplained cardiac arrest: results from investigation and follow-up of the prospective cardiac arrest survivors with preserved cardiac arrest survivors with preserved ejection fraction registry. CircArrhythm Electrophysiol. 2016;9:e003619. doi: 10.1161/CIRCEP.115.003619.
33. Viskin S, Postema PG, Bhuiyan ZA et al. The response of the QT interval to the brief tachycardia provoked by standing: a bedside test for diagnosing long QT syndrome. J Am Coil Cardiol. 2010;55:1955–61. doi: 10.1016/j.jacc.2009.12.015
34. Wong JA, Gula LJ, Klein GJ et al. Utility of treadmill testing in identification and genotype prediction in long-QT syndrome. Circ Arrhythm Electrophysiol. 2010;3:120–5. doi: 10.1161/CIRCEP.109.907865.
35. Chattha IS, Sy RW, Yee R et al. Utility of the recovery electrocardiogram after exercise: a novel indicator for the diagnosis and genotyping of long QT syndrome? Heart Rhythm. 2010;7:906–11. doi: 10.1016/j.hrthm.2010.03.006
36. Obeyesekere MN, Klein GJ, Modi S et al. How to perform and interpret provocative testing for the diagnosis of Brugada syndrome, long-QT syndrome, and catecholaminergic polymorphic ventricular tachycardia. Circ Arrhythm Electrophysiol. 2011;4:958–64. doi: 10.1161/CIRCEP.111.965947.
37. Brugada R, Campuzano O, Sarquella-Brugada P et al. Brugada Syndrome. Methodist Debakey Cardiovasc. 2014;10:25–8. doi: 10.14797/mdcj-10-1-25
38. Poole JE, Mathisen TL, Kudenchuk PJ et al. Long-term outcome in patients who survive out of hospital ventricular fibrillation and undergo electrophysiologic studies: evaluation by electrophysiologic subgroups. J Am Coll Cardiol. 1990;16:657–65. doi: 10.1016/0735-1097(90)90357-U.
39. Krahn AD, Healey JS, Chauhan V et al. Systematic assessment of patients with unexplained cardiac arrest: cardiac arrest survivors with preserved ejection fraction registry (CASPER). Circulation. 2009;120:278–85. doi: 10.1161/CIRCULATIONAHA.109.853143.

40. WaBnig N, Gunther M, Quick S et al. Experience with the wearable cardioverter-defibrillator in patients at high risk for sudden cardiac death. Circulation. 2016;134:635–43. doi: 10.1161/CIRCULATIONAHA.115.019124.
41. Tung R, Boyle NG, Shivkumar K. Catheter ablation of ventricular tachycardia. Circulation. 2011;123:2284–8. doi: 10.1161/CIRCULATIONAHA.110.989079.
42. Chockalingam P, Crotti L, Girardengo G et al. Not all beta-blockers are equal in the management of long QT syndrome types 1 and 2: higher recurrence of events under metoprolol. J Am Coll Cardiol. 2012;60:2092–9. doi: 10.1016/j.jacc.2012.07.046.
43. Steinberg C, Padfield GJ, Al-Sabeq B et al. Experience with bisoprolol in long-QT1 and long-QT2 syndrome. J Interv Card Electrophysiol. 2016;47:163–70. doi: 10.1007/s10840-016-0161-2.
44. Schwartz PJ, Priori SG, Locati EH et al. Long QT syndrome patients with mutations of the SCN5A and HERG genes have differential responses to Na+ channel blockade and to increases in heart rate: implications for gene-specific therapy. Circulation. 1995;92:3381–6. doi: 10.1161/01.CIR.92.12.3381.
45. Odero A, Bozzani A, De Ferrari GM, Schwartz PJ. Left cardiac sympathetic denervation for the prevention of life-threatening arrhythmias: the surgical supraclavicular approach to cervicothoracic sympathectomy. Heart Rhythm. 2010;7:1161–5. doi: 10.1016/j.hrthm.2010.03.046.
46. Woosley RL, Heise CW, Romero KA. QTdrugs List. Available at: crediblemeds.org
47. Postema PG, Wolpert C, Amin AS et al. Drugs and Brugada syndrome patients: review of the literature, recommendations and an up-to-date website (www.brugadadrugs.org). Heart Rhythm. 2009;6:1335–41. doi: 10.1016/j.hrthm.2009.07.002.
48. Nademanee K, Veerakul G, Chandanamattha P et al. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. Circulation. 2011;123:1270–9. doi: 10.1161/CIRCULATIONAHA.110.972612.
49. Kaneshiro T, Naruse Y, Nogami A et al. Successful catheter ablation of bidirectional ventricular premature contractions triggering ventricular fibrillation in catecholaminergic polymorphic ventricular tachycardia with RyR2 mutation. Circ Arrhythm Electrophysiol. 2012;5:e14–7. doi: 10.1161/CIRCEP.111.966549.
50. Visser M, van der Heijden JF, van der Smagt JJ et al. Long-term outcome of patients initially diagnosed with idiopathic ventricular fibrillation: a descriptive study. Circ Arrhythm Electrophysiol. 2016;9:e004258. doi: 10.1161/CIRCEP.116.004258.
51. Belhassen B, Glick A, Viskin S. Efficacy of quinidine in high-risk patients with Brugada syndrome. Circulation. 2004;110:1731–7. doi: 10.1161/01.CIR.0000143159.30585.90.
52. Knecht S, Sacher F, Wright M et al. Long-term follow-up of idiopathic ventricular fibrillation ablation: a multicenter study. J Am Coll Cardiol. 2009;54:522–8. doi: 10.1016/j.jacc.2009.03.065.
53. Philips B, Madhavan S, James C et al. Outcomes of catheter ablation of ventricular tachycardia in arrhythmogenic right ventricular dysplasia/cardiomyopathy. Circ Arrhythm Electrophysiol. 2012;5:499–505. doi: 10.1161/CIRCEP.111.968677.

54. Honarbakhsh S, Srinivasan N, Kirkby C et al. Medium-term outcomes of idiopathic ventricular fibrillation survivors and family screening: a multicentre experience. Europace. 2017;19:1874–80. doi: 10.1093/europace/euw251.
55. Quenin P, Kyndt F, Mabo P et al. Clinical yield of familial screening after sudden death in young subjects: the French experience. Circ Arrhythm Electrophysiol. 2017;10:e005236. doi: 10.1161/CIRCEP.117.005236.

استكشاف العلاقة بين الموت القلبي المفاجئ وعدم انتظام ضربات القلب: الفسيولوجيا المرضية، عوامل الخطر، وآثارها على الوقاية والإدارة.

الملخص:

خلفية: يُعتبر الموت القلبي المفاجئ (SCD) قضية صحية عامة حادة، وغالبًا ما يرتبط بعدم انتظام ضربات القلب الذي يعطل النظم الطبيعي للقلب. إن فهم الفسيولوجيا المرضية وعوامل الخطر المرتبطة بعدم انتظام ضربات القلب أمر حيوي لوضع استراتيجيات فعالة للوقاية والإدارة.

الهدف: تهدف هذه الدراسة إلى استكشاف العلاقة المعقدة بين الموت القلبي المفاجئ وعدم انتظام ضربات القلب، مع تسليط الضوء على الآليات الفسيولوجية المرضية، وتحديد عوامل الخطر الهامة، ومناقشة الآثار المترتبة على الإدارة السريرية والوقاية.

الأساليب: تم إجراء مراجعة شاملة للأدبيات، حيث تم تحليل الدراسات التي تتناول أسباب، تشخيص، وإدارة الموت القلبي المفاجئ المرتبط بعدم انتظام ضربات القلب. تم استخراج البيانات ذات الصلة من المقالات التي تمت مراجعتها من قبل الأقران، والإرشادات السريرية، والتحليلات التلوية. تم تلخيص النتائج لتوضيح الآليات التي تساهم بها عدم انتظام ضربات القلب في الموت القلبي المفاجئ وتحديد عوامل الخطر الرئيسية.

النتائج: تكشف النتائج أن مجموعة متنوعة من العوامل تساهم في حدوث عدم انتظام ضربات القلب الذي يؤدي إلى الموت القلبي المفاجئ، بما في ذلك أمراض القلب الهيكلية، والاستعدادات الوراثية، واضطرابات الكهارل. وقد تم التعرف على مرض القلب الإقفاري كأكثر الأسباب انتشارًا، مع وجود عوامل مساهمة هامة أخرى مثل متلازمات عدم انتظام ضربات القلب الوراثية ووجود حالات صحية مصاحبة. بالإضافة إلى ذلك، فإن استخدام أدوات تشخيصية متقدمة، مثل تخطيط كهربائية القلب وأجهزة إزالة الرجفان القلبية المزروعة، قد حسن من التعرف على المرضى المعرضين للخطر. وقد أظهرت استراتيجيات الإدارة، بما في ذلك تعديلات نمط الحياة، والعلاج الدوائي، وزراعة الأجهزة، فعاليتها في تقليل حدوث الموت القلبي المفاجئ.

الخلاصة: العلاقة بين عدم انتظام ضربات القلب والموت القلبي المفاجئ معقدة، وتتأثر بعدة عوامل خطر وآليات فسيولوجية مرضية. تعد استراتيجيات الوقاية والإدارة الفعالة أمرًا حيويًا في معالجة هذه القضية الصحية الهامة. هناك حاجة إلى مزيد من البحث لتعزيز الفهم وتطوير تدخلات مستهدفة للحد من حدوث الموت القلبي المفاجئ.

الكلمات المفتاحية: الموت القلبي المفاجئ، عدم انتظام ضربات القلب، الفسيولوجيا المرضية، عوامل الخطر، الوقاية، الإدارة.