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Cardiac Death Occurring Suddenly in Young Adults: Present Review on Assessment, Screening and Preventive Measures

Anand Anand, Aryan Rakwal, Ashish Yadav, Dr. Nakul Gupta, Sheetal Soni*

IIMT College of Pharmacy, Knowledge Park 3, Greater Noida, Gautam Budha Nagar-201310, U.P., India

ABSTRACT:

The Sudden Cardiac Death (SCD) can occur at any stage of life, even in young people. While it happens less often in those under 35, each case is alarming because the causes are varied and sometimes remain unclear. In older adults, Coronary artery disease is the leading factor, but in younger individuals, problems such as Arrhythmias and Cardiomyopathies are more common triggers. Early detection of sudden cardiac death in young is very important as it occurs suddenly and without any warning signs. Various approaches such as Electrocardiography and Echocardiography can help to access potential risk of sudden cardiac death. It is very important that future research is conducted so as to reduce the risk of SCD and to establish preventive measures by early detection of signs.

Keywords: Fatal, Clinical Feature, Inherent, Frequency, Burden, Investigation.

1. INTRODUCTION:

The Sudden Death (SD) is characterized as a fatal outcome that occurs within one hour of symptom onset, within 24 hours of the last confirmed contact in cases without witnesses, or in individuals who initially survive cardiac arrest but later die during subsequent care. Health subjects that are asymptomatic at first show SD as first clinical feature and the cause can only be discovered by autopsy. Sudden cardiac death (SCD) can be characterized as a sudden, inherent life threatening event that arises within one hour after the beginning of symptoms, in patients who previously seemed well or whose disease was not thought to carry an immediate risk of death[1]. Among genetically determined cardiac diseases, hypertrophic cardiomyopathy (HCM) is the most prevalent and is strongly associated with sudden cardiac death (SCD) in young individuals. The Implantation of Cardioverter-Defibrillators (ICDs) remains the standard and only effective strategy for protecting against malignant arrhythmias[2]. Each year, sudden cardiac death causes between 300,000 and 400,000 deaths in the U.S. In developed nations such as the United States, nearly half of all deaths from cardiovascular disease are due to sudden cardiac death, which frequently appears as the first sign of underlying coronary artery disease. Conversely, in low- and middle-income countries, the frequency of sudden cardiac death tends to reflect the overall burden of ischemic heart disease and is therefore considerably lower. Multiple population-level investigations have reported a 15%–19% reduction in sudden cardiac death incidence linked to coronary heart disease since the early 1980s [3].

2. EPIDEMIOLOGY:

Cardiac arrest leading to sudden cardiac death (SCD) is recognized as a critical worldwide public health issue, accounting for approximately 15%–20% of overall mortality. Despite progressive advances in resuscitation practices across many regions, survival following an episode of sudden cardiac arrest remains low. In most situations, SCD is observed in older adults with acquired structural abnormalities of the heart, whereas in younger individuals it is less common and usually linked to inherited cardiac disorders. Most cases of sudden cardiac death occur in adults, while fewer than 1% are reported in individuals younger than 35 years. These demographic patterns may help account for the slower decline in SCD and OHCA incidence among women compared with men in recent decades [4]. Evidence from other global regions is limited. However, it can be inferred that the proportion of SCDs linked to Coronary Artery Disease (CAD) generally follows the overall burden of CAD mortality, as observed in Western nations. For example, Japan demonstrates low CAD incidence and mortality, which corresponds with reduced SCD rates. Conversely, pronounced geographic differences exist, with higher rates of CAD-associated SCD suspected in Central Asia, Oceania, and Eastern Europe [5]. the sudden cardiac cases percentage in different countries is shown in graphical representation in **fig.1**

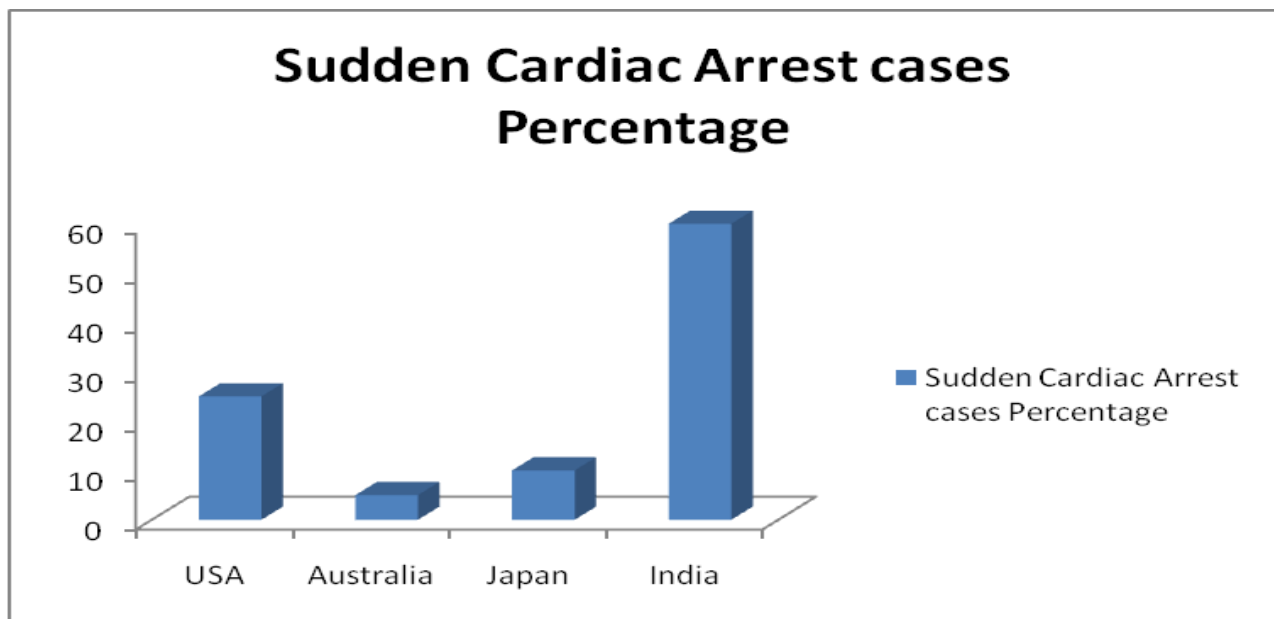


Fig.1: Sudden Cardiac Cases Percentage in Different Countries

Since sudden and unanticipated fatalities, particularly in younger individuals, often necessitate forensic autopsy, rare pathologies are occasionally uncovered. These include, for instance, previously unrecognized acquired valvular abnormalities most notably aortic valve stenosis which are associated with an elevated risk of SCD. In addition, vasculitic processes involving the coronary arteries or markedly stenotic fibromuscular dysplasia of the Atrio Ventricular (AV) nodal artery may also be detected. However, the pathological significance of AV nodal artery dysplasia remains under discussion, as emerging evidence suggests a broader prevalence than initially assumed. Furthermore, sudden cardiac deaths linked to previously undiagnosed cardiac amyloidosis, characterized by extensive myocardial amyloid deposition, are exceptionally uncommon [6].

3. REGIONAL PREVALANCE:

i. Patterns in Occurrence, Cardiac Rhythm, and Outcomes: Available evidence suggests a decline in sudden cardiac death (SCD) rates in past decades, though recent data indicate a possible resurgence in incidence.

ii. Age, Sex and Ethnicity: Utmost cases of unforeseen cardiac death (SCD) do in grown-ups, with prevalence adding steadily with age. Among those youngish than 35 times, the topmost threat is seen in early nonage (0 – 5 times). Men are estimated to face a three- to fourfold advanced liability of SCD compared with women, though recent substantiation indicates this gap may be narrowing. It's also honored that individualities of African-American origin carry a disproportionately advanced threat. It is also recognized that individuals of African-American origin carry a disproportionately higher risk [7].

iii. India: Hypertension is regarded as the leading chronic risk factor in India. Recent population-based investigations indicate that its occurrence is rising, particularly among younger individuals and those living in rural areas. Findings from large-scale national surveys, such as NFHS-5 and ICMR-INDIAB, reveal marked regional differences in the burden of hypertension, with higher rates observed in relatively advanced states and districts. Notably, elevated levels of early-onset hypertension are reported in the less economically developed regions [8].

iv. Europe: Within the 42 countries of the European Society of Cardiology (ESC), the median prevalence of heart failure (HF) is about 1.7%. In the 42 countries that are part of the European Society of Cardiology (ESC), about 1.7% of people have heart failure (HF). Estonia reports some of the highest rates older adults, nearly twice as high as in Poland and Serbia.

Hospital admissions for HF also vary a lot across these countries. Serbia has the lowest number of hospitalizations, while Romania has the highest, with several times more cases. The time people spend in the hospital is different too—on average less than a week in Poland, but close to two weeks in Croatia [9].

4. AETIOLOGY

1. Ischemic Heart Diseases (IHD)

Regardless of major medical progress in recent dicker, sudden cardiac death (SCD) continues to be one of the main causes of death in people with ischemic heart disease. At present, patients with structural heart disease and a left ventricular ejection fraction (LVEF) below 35% are considered for implantable cardioverter-defibrillator (ICD) therapy as a primary strategy to prevent SCD. Yet, more than 80% of individuals who experience SCD have an LVEF above 35%, while only a small proportion of those fitted with an ICD actually require lifesaving shocks [10].

2. Stroke (Cerebrovascular Diseases)

Sudden death is significant yet often fail to observe outcome of stroke. An acute stroke can disorder central autonomic regulation, leading to heart muscle damage, electrocardiographic changes, cardiac rhythm disturbances, and eventually sudden death. Both clinical and experimental studies indicate that autonomic imbalance is more common following atrophy affecting the insular cortex, a key region responsible for regulating sympathetic and parasympathetic functions. The presence of cardiovascular comorbidities further raises the likelihood of cardiac complications and mortality after stroke. Therefore, many sudden deaths and severe non-fatal cardiac events post-stroke are likely the result of combined cardiovascular and neurological factors. The precise pathways that cause sudden death remain only partly understood. Ongoing research is essential to clarify the autonomic effects of acute stroke and to confess patients most vulnerable to sudden death [11].

3. Hypertensive heart diseases

Pulmonary Arterial Hypertension (PAH) is a controlling disorder characterized by marked illness and high mortality due to pulmonary vascular disease and right ventricular (RV) impairment. Although modern PAH treatments have increase survival and clinical outcomes, patients still meet serious complications, including a considerable risk of SCD. A high number of dangerous heart meter problems, along with structural issues similar as contraction of the left main coronary roadway, pulmonary roadway analysis or rupture, and severe bleeding in the lungs (massive hemoptysis), can greatly increase the threat of unforeseen cardiac death (SCD). Regular monitoring and thorough testing are essential for spotting these pitfalls beforehand and taking timely action to help unseasonable deaths. This review highlights the crucial threat factors and focuses on strategies to ameliorate issues through early discovery, forestallment, and effective treatment [12].

4. Atrial flutter

Atrial fibrillation (AF) is a chronic condition linked to significant risks of cardiovascular illness and death. This secondary analysis of the RACE II trial sought to set on factors connected with cardiovascular complications and mortality in patients with early permanent AF [13].

5. RISKS FACTOR:

1. Behavior Factor

Smoking is a well- established threat factor for unforeseen cardiac death (SCD) in the general population. Still, its part in individualities with Acute Coronary Pattern (ACS), a condition that

formerly increases the liability of SCD, remains uncertain [14].

2. Biological Factor

Several studies have demonstrated a close connection between SCD and pulmonary disorders, including Chronic Obstructive Pulmonary Disease (COPD). This study aims to evaluate whether individuals who died from SCD show more significant cardiopulmonary histopathological alterations compared to those who died from violent causes, with both groups matched for demographic features such as age and sex [15].

3. Environmental Factor

The planet warms, the air thickens with particles and water carries PFAS plus metals - these forces act on the heart; they keep arteries in a low flame, raise oxidants along with scar vessel walls. The result is a wider toll of cardiovascular disease across every region. Each pollutant harms in its own way. The small particles labeled PM2.5 slip into tissue and switch on inflammatory signals - they also jam normal metabolism. Ozone but also carbon monoxide pours oxidants into the bloodstream and fray the endothelial surface. Nitrogen dioxide alters left ventricular shape as well as precedes sudden arrhythmic death. Sulfur dioxide and metals such as cadmium or arsenic strip electrons from membranes plus rupture cells. Pesticide residues and fragments of micro- but also nanoplastic drift into circulation - both correlate with higher cardiac event rates and with earlier death.[16].

6. CLINICAL PRESENTATION & WARNING SIGN:

1. Symptoms & Sign

The World Health Organization (WHO) defines unforeseen cardiac death (SCD) as an unanticipated fatal event being either within one hour of symptom onset when witnessed, or within 24 hours of being last seen alive without symptoms. unforeseen cardiac arrest remains a leading cause of death worldwide, with survival rates to sanitarium discharge reported at only 9.3 for out- of- sanitarium cases and 21.2 for in- sanitarium cases. These numbers emphasize the critical need for accurate vaticination and effective forestallment strategies [17].

2. Diagnosis

Emerging approaches such as vibrational spectroscopy particularly Fourier transform infrared (FTIR) and Raman spectroscopy are gaining attention as promising techniques. This study therefore explores

the potential and effectiveness of vibrational spectroscopic methods in identifying SCD [18].

3. Patient Experience

Cases with a left ventricular ejection bit (LVEF) of ≤ 35 face a heightened threat of unforeseen cardiac death (SCD) during the original months following a Myocardial Infarction (MI). The Wearable Cardioverter Defibrillator (WCD) is an honored, safe, and effective device that offers protection against SCD during this high- threat period. This study aimed to assess the cost- effectiveness of WCD in combination with guideline- directed medical remedy (GDMT) compared with GDMT alone for post-MI cases within the English National Health Service (NHS) [19].

4. Treatment Guidance

Unforeseen cardiac death conditions are inheritable in nature; the part of genetics is central in both diagnosing and managing SCD- associated conditions. Traditionally, inheritable testing has been applied to confirm judgments and descry at- threat cousins; still, advancing knowledge of the inheritable base of SCD offers openings for individualized treatment, early threat assessment, and a shift toward genetically guided curatives. This review highlights the changing inheritable geography of SCD- related diseases, the progress in gene- grounded curatives and treatment strategies, and the eventuality of prophetic genetics to identify individualities susceptible to SCD [20].

7. MAJOR DISEASES IN SUDDEN CARDIAC DEATH:

Different diseases contributing to sudden cardiac death

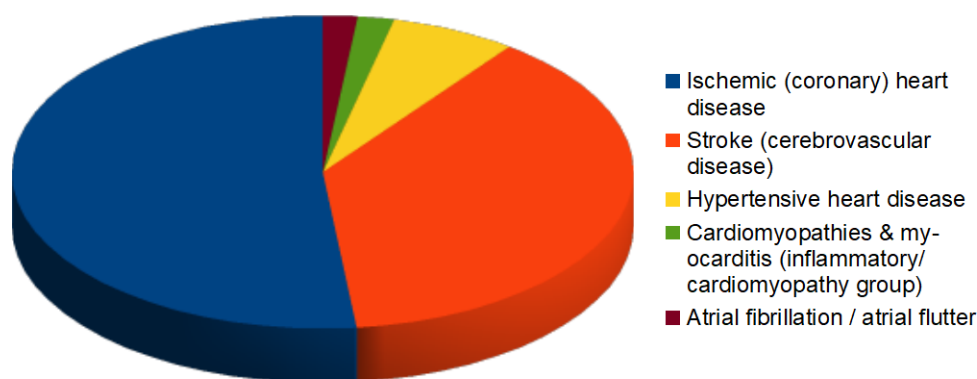


Fig 2: No of deaths by major disease in each cause per 100 deaths

1. Ischemic heart disease

Myocardial ischemia refers to a mismatch between the oxygen conditions of the heart muscle and the available force. In individualities with coronary roadway complaint, the circumstance of ischemia plays a pivotal part in prognosticating issues. colorful individual approaches are employed in clinical practice to identify myocardial ischemia, because vascular resistance is largely regulated at the microcirculatory position, particularly in cases who have angiographically normal coronary highways, a decline in coronary inflow reserve is considered an index of coronary microvascular dysfunction [21].

- Prognosis in ischemic heart syndromes has traditionally been linked to the extent and severity of coronary atherosclerosis.
- Recent studies challenge this view, suggesting other mechanisms also play a role.
- Findings from the Danish Ischemic Heart Disease Registry:
- Patients with angina and normal coronary arteries showed:
- 85% higher risk of major adverse cardiovascular events (MACE), including:

a. Cardiovascular death

b. Hospitalization for myocardial infarction

c. Heart failure

d. Stroke

- 52% higher risk of all-cause mortality.
- The increased risks were similar in both men and women [22].

2 Stroke (Cerebrovascular Disease):

Stroke ranks as the second most common cause of death globally and is a significant source of long-term disability. The condition is particularly current in developing nations, with ischemic stroke being the predominant form [23]. Stroke-Heart Pattern (SHS) results from multiple pathophysiological mechanisms and is inclusively nominated “Stroke Convinced Heart Injury (SIHI).” exploration indicates a significant part for Cardiac Autonomic Nervous System (CAN) dysfunction, activation of the Hypothalamic Pituitary Adrenal (HPA) axis, and seditious processes in SHS. Hospitalization mortality for cases with Acute Ischemic Stroke (AIS) complicated by ischemic heart complaint is approaching 30.

- Complex cardiovascular disease contributes to around 20% of post-stroke deaths, making it the second most common cause after neurological complications.
- Cardiac mortality is highest within the first month after stroke, particularly during the second week.
- About 4% of AIS patients die due to cardiac causes, while up to 19% experience at least one major adverse cardiovascular event (MACE) [24].

3 Hypertensive heart disease:

Hypertension is a major and current threat factor contributing to the development of Heart Failure (HF) across all ranges of left ventricular ejection bit. Substantial substantiation indicates that effective Blood Pressure (BP) operation can lower the threat of cardiovascular events, including the onset of HF [25]. Pulmonary arterial hypertension (PAH) is a serious and potentially fatal complication in individualities with systemic Connective Towel Conditions (CTD). This review focuses on the frequency, clinical significance, individual approaches, and operation strategies for PAH in CTD, pressing the significance of early discovery and timely, effective treatment. opinion of PAH in CTD cases is grueling and requires comprehensive assessment.

Key evaluations include:

- a. Cardiological symptoms
- b. Echocardiography
- c. Electrocardiogram (ECG)
- d. Serum biomarkers
- e. Right heart catheterization is considered the gold standard for confirming PAH.
- f. Recognizing the high prevalence of PAH in CTD and implementing systematic screening can facilitate early detection.
- g. Early diagnosis allows for timely initiation of appropriate treatment, potentially improving patient survival [26].

4 Cardiomyopathies & myocarditis (inflammatory/cardiomyopathy group):

Inflammation of the cardiac muscle, known as acute myocarditis, usually engages the body’s innate and antigen-specific immune defenses. People who previously experienced myocarditis, have systemic autoimmune disorders like lupus, or are treated with checkpoint inhibitors are more susceptible to this condition [27].

In one study, the average age of death due to myocarditis was 47 years. Patients with severe acute myocarditis—characterized by hemodynamic instability, left ventricular ejection fraction below 50%, or persistent ventricular arrhythmias—carry a 10.4% risk of death or requiring a heart transplant within 30 days, which increases to 14.7% over five years [28].

5 Atrial fibrillation / atrial flutter:

Atrial fibrillation (AF) is the most constantly being supraventricular arrhythmia, impacting roughly 1 of the overall population. Its circumstance rises sprucely with advancing age, reaching nearly 10 among aged grown-ups [29]. Atrial fibrillation (AF) is a complex arrhythmia characterized by rapid-fire and irregular atrial exertion. It infrequently presents as a primary electrical complaint and is generally the end result of colorful underpinning cardiac conditions. The liability of developing AF increases with certain threat factors, particularly advancing age, while comorbidities similar as diabetes, hypertension, rotundity, heart failure, and coronary roadway complaint also contribute significantly to its onset and progression [30]. In 2017, the global database recorded 3.046 million new cases of atrial fibrillation (AF). The estimated incidence rate in 2017 was 403 per million people, representing a 31% increase compared to 1997. The global prevalence of AF reached 37.574 million cases (0.51% of the world population), rising by 33% over the past two decades. Countries with high socio-demographic index exhibit the highest AF burden, whereas middle socio-demographic index countries experienced the largest recent increase. Projections indicate that the total AF burden could rise by over 60% by 2050 [31].

8. DIAGNOSTIC EVALUATION:

1. Cardiopulmonary Exercise Testing

The cardiopulmonary exercise evaluation was conducted using a progressive treadmill stress test based on the modified Bruce protocol. Throughout the procedure, blood pressure and a 12 lead ECG were continuously recorded. Exercise performance and cardiorespiratory capacity were measured by identifying the anaerobic threshold and maximal oxygen uptake through expired gas analysis (OXYCON ALFA-JAEGER, Wuerzburg, Germany). The anaerobic threshold was established following the method described by Wasserman et al [32].

2. Diagnostic Evaluation

The gold-standard disquisition for diastolic congestive heart failure (D- CHF) is cardiac catheterization, which reveals elevated ventricular stuffing pressures while systolic performance remains complete and ventricular chamber sizes appear normal. Hemodynamic pressures in the cardiac chambers upstream of the disabled ventricle are also raised; for illustration, advanced left atrial pressure and pulmonary capillary wedge pressure in cases of left ventricular diastolic dysfunction. When micromanometer catheters are employed, two precious pointers of abnormal LV diastolic relaxation include peak negative dp/dt and τ (the time constant of LV relaxation) [33].

3. Echocardiography

Echocardiography is the primary disquisition of choice in individualities with suspected heart failure (HF) and serves as a fluently accessible bedside fashion. It evaluates both right and left ventricular performance, identifies structural blights in cardiac chambers and faucets, and facilitates the discovery of localized wall stir abnormalities. nonetheless, in cases of pronounced rotundity, gestation, or mechanical ventilation, acquiring satisfactory aural windows maybe difficult. For similar cases, Transesophageal Echocardiography (TEE) provides a suitable volition. In individualities with tachyarrhythmias, applicable control of heart rate is essential to gain optimal echocardiographic imaging [34].

4. Chest X-ray

Typical observations include a cardiothoracic ratio exceeding 50%, redistribution of pulmonary blood flow toward the upper lung fields, the presence of Kerley B-type interstitial lines, and fluid accumulation within the pleural spaces [35].

5. Catheterization

Protocol Participants were evaluated while continuing their usual medications, in a fasting state, under light sedation, and positioned supine, as outlined previously. Right heart catheterization was conducted using a 9-Fr introducer sheath via the right internal jugular vein. Hemodynamic pressures in the right atrium, pulmonary artery, and Pulmonary Capillary Wedge Position (PCWP) were recorded at end-expiration, averaged over at least three cardiac cycles. After initial hemodynamic measurements, patients underwent invasive exercise testing to maximal tolerance. The protocol began with a workload of 20 W maintained for 5 minutes, followed by progressive 20 W increments every 3 minutes until self-reported fatigue [36].

9. NON-PHARMACOLOGICAL TREATMENT:

1. Lifestyle Interventions: According to the 2021 ESC guidelines for diagnosing and managing heart failure (HF), effective case tone- operation is essential for optimizing HF issues, as it greatly improves Quality of Life (QoL), reduces sanitarium readmissions, and lowers mortality rates among affected individualities. Educating cases about the underpinning mechanisms of heart failure and the life variations that may prove salutary is vital in strengthening tone- care practices. furnishing customized education grounded on scientific data or expert agreement is considered abecedarian. Common strategies for patient education involve delivering information in multiple formats to suit varying knowledge and educational backgrounds, exercising styles similar as the ‘ask – tell – ask’ approach, ‘educate- back’ fashion, or motivational canvassing, while also prostrating implicit communication walls

2. Resynchronization Therapy / Physiological Pacing: Cardiac Resynchronization Therapy (CRT) represents the leading device-based intervention for patients with moderate to severe heart failure, with its efficacy demonstrated in multiple landmark clinical trials. Furthermore, CRT may occasionally be considered as an upgrade for individuals with existing pacemakers or implantable cardioverter-defibrillators (ICDs) who develop worsening HFrEF due to a high burden of ventricular pacing [37].

3. Weight Management: Rotundity contributes to heart failure both directly, through its impact on the myocardium, and laterally, via rotundity-related comorbidities. redundant body weight induces hemodynamic differences, similar as elevated blood volume and cardiac affair, incompletely intermediated by activation of the Renin-Angiotensin Aldosterone System (RAAS). Beyond promoting hypertension, rotundity also raises the liability of diabetes and dyslipidemia, all of which are established threat factors for the onset of heart failure [38].

10. DRUGS CLASSIFICATION FOR SUDDEN CARDIAC DEATH:**1. Monotherapy**

S.NO	Hypertension	ACE inhibitors	Enalapril, Lisinopril, Ramipril
1.		ARBs	Losartan, Valsartan, Telmisartan
2.		Beta-blockers	Atenolol, Metoprolol, Bisoprolol
3.		Calciumchannel blockers	Amlodipine, Diltiazem, Verapamil
4.		Thiazide diuretics	Hydrochlorothiazide, Indapamide, Chlorthalidone
5.	Coronary Artery Disease / Post-PCI	Antiplatelet agents	Aspirin, Clopidogrel, Ticagrelor, Prasugrel
6.	Heart Failure	ACE inhibitors / ARBs	Enalapril, Valsartan
7.		ARNI	Sacubitril/valsartan
8.		Beta-blockers	Carvedilol, Metoprolol succinate, Bisoprolol
9.		MRAs	Spironolactone, Eplerenone
10.	Arrhythmias (e.g., AF)	Rate control	Beta-blockers, Diltiazem, Verapamil
11.		Rhythm control	Amiodarone, Flecainide
12.		Anticoagulants	Warfarin, Apixaban
13.	Dyslipidemia	Statins	Atorvastatin, Rosuvastatin
14.		Ezetimibe	Ezetimibe
15.		PCSK9 inhibitors	Alirocumab, Evolocumab

[39]

Aspirin and its anti-thromobolitic effect in cardiovascular diseases:

- **Established role:** Aspirin's blood-thinning properties have long been central in the prevention of cardiovascular disease, especially for secondary prevention.
- **Changing outlook:** With the development of newer antiplatelet drugs and rising awareness of aspirin's bleeding risks, its value across the full range of CVD prevention is now being reconsidered.
- **Recent research shift:** Modern trials are exploring strategies that exclude aspirin in secondary prevention.
- **Evidence from trials:** A recent meta-analysis comparing P2Y12 inhibitor monotherapy with extended dual antiplatelet therapy (which includes aspirin) [40].

Enalaprilat: The Renin–Angiotensin–Aldosterone System (RAAS) is essential for maintaining cardiovascular and kidney balance and is now also recognized for its wide-ranging effects on immune regulation. Blocking the RAAS with drugs such as Angiotensin-Converting Enzyme Inhibitors (ACEIs) and Angiotensin Receptor Blockers (ARBs) has shown benefits not only in controlling high blood pressure and treating heart failure but also in conditions like autoimmune diseases, infections, cancers, and neurodegenerative disorders [41].

2. Dual Therapy:

	Drug Combination	Examples	Main Use
1.	ACE Inhibitor + Beta-blocker	Enalapril + Metoprolol	Heart failure, post-MI
2.	ACE Inhibitor + Diuretic	Ramipril + Hydrochlorothiazide	Hypertension
3.	ACE Inhibitor + Calcium Channel Blocker	Perindopril + Amlodipine	Hypertension, CAD
4.	ARB + Diuretic	Losartan + Hydrochlorothiazide	Hypertension

	Drug Combination	Examples	Main Use
5.	ARB + Calcium Channel Blocker	Telmisartan + Amlodipine	Hypertension, CAD
6.	Beta-blocker + Diuretic	Atenolol + Chlorthalidone	Hypertension
7.	Beta-blocker + CCB (DHP)	Bisoprolol + Amlodipine	Hypertension, angina
8.	Aspirin + P2Y ₁₂ Inhibitor	Aspirin + Clopidogrel/Ticagrelor	ACS, post-PCI
9.	Statin + Antiplatelet	Atorvastatin + Aspirin	Secondary prevention
10.	Anticoagulant + Antiplatelet	Rivaroxaban + Aspirin	CAD, PAD

Statins with Ace Inhibitors: For cases witnessing carotid revascularization, the combination of statins and ACE impediments or ARBs during the perioperative phase offers better protection than statin remedy alone. Cases witnessing this operation are advised to continue taking ACEIs ARBs, especially if they also have concurrent hypertension. To validate the fresh advantage of ACEI/ ARB remedy in this environment, more prospective exploration is necessary [42].

The combined use of beta-blockers and ACE inhibitors in individuals with hypertension and elevated heart rate is supported by strong clinical evidence.

- CAD, or Coronary Artery Disease
- AF, or Atrial Fibrillation
- Failure of the heart
- They work in tandem through complimentary mechanisms:

ACE inhibitors produce vasodilation, lower vascular resistance, and provide vascular protection; beta-blockers decrease heart rate and cardiac output. Extensive research has confirmed the following benefits of the bisoprolol + perindopril combination:

- Long-term effectiveness
- Due to their lengthy half-lives, both medications can be taken once daily and still have a therapeutic impact for 24 hours [43].

3. Trio therapy:

S.NO	Condition	Typical Triple Therapy Combination	Rationale / Benefits
1.	Hypertension (Resistant)	ACE Inhibitor/ARB + Calcium Channel Blocker + Thiazide/Thiazide-like Diuretic	Provides vasodilation, volume reduction, and smooth muscle relaxation for optimal BP control.
2.	Coronary Artery Disease (Post-MI / Stable Angina)	Antiplatelet (Aspirin/Clopidogrel) + Beta-blocker + Statin	Prevents thrombosis, reduces cardiac workload, and improves lipid profile → lowers risk of reinfarction
3.	Heart Failure with Reduced EF (HFrEF)	ACE Inhibitor/ARB/ARNI + Beta-blocker + Mineralocorticoid Receptor Antagonist (Spironolactone/Eplerenone)	Improves survival, reduces remodeling, decreases hospitalization risk.
4.	Atrial Fibrillation with High Stroke Risk	Oral Anticoagulant + Beta-blocker/Rate control drug + ACE Inhibitor/ARB	Prevents stroke, controls ventricular rate, and reduces atrial remodeling.
5.	Pulmonary Arterial Hypertension (PAH)	Endothelin Receptor Antagonist + PDE-5 Inhibitor + Prostacyclin Analog	Targets multiple vasoconstrictor pathways for maximal pulmonary vasodilation and symptom relief.

A new fixed-dose Combination Small Pill Combinations (SPC) containing telmisartan, amlodipine, and indapamide has shown significant benefits in lowering blood pressure [44].

- The triple therapy was found to be more effective compared with the use of dual combinations.
- The regimen was generally well tolerated, with good safety outcomes.
- This combination therapy represents a novel treatment choice for managing hypertension.
- Its clinical application could lead to a marked improvement in blood pressure control in routine practice [45].

11. FUTURE OUTLOOK OF CARDIOVASCULAR DISEASES: EMERGING THERAPIES, PREVENTIVE STRATEGIES, AND EVOLVING CHALLENGES

1. Advancing Treatment of Atherosclerosis:

Lipoprotein A Presently, no clear physiological part of lipoprotein has been linked, and its attention is nearly entirely mandated by inheritable regulation through nonstop product in hepatocytes. Around 20 of the general population may parade elevated tube Lp(a) situations, and epidemiological data indicate that attention above 75 nmol/ L in primary care populations are linked with an advanced threat of Atherosclerotic Cardiovascular Complaint (ASCVD) events. nonetheless, being clinical guidelines do give formal recommendations for routine Lp(a) webbing [46].

2. 3d Printing:

Notably, progress in 3D printing has demonstrated its promise as a transformative technology, with potential applications in medicine, particularly within cardiovascular care. Chief among these is its ability to broaden access to medical services by overcoming geographical limitations and extending care to underserved or remote populations thereby minimizing delays and improving the efficiency of healthcare provision [47].

3. Estrogen Against Oxidative Stress:

The prevalence of cardiovascular complaint (CVD) is lower in premenopausal women compared to men of analogous age, but rises markedly after menopause. This pattern highlights the inarguable cardioprotective part of estrogen. Oxidative stress is a crucial contributor to the development of CVD, and this composition emphasizes the defensive influence of estrogen against cardiovascular complaint through its modulation of OS. In postmenopausal women, estrogen remedy should be considered only after a thorough evaluation of individual factors similar as clinical symptoms, cardiovascular threat, and bone cancer vulnerability [48].

4. The Corolla Device:

The CORolla device is an innovative implant specifically engineered for placement within the left ventricle (LV). Its mechanical design enables it to exert an outward radial force on the LV endocardium, thereby storing potential energy during systolic contraction and releasing it during diastolic recoil [49].

5. Estrogen Related Receptor [Err}Agonist Ameliorate:

Both SLU-PP-332 and SLU-PP-915 helped the heart pump blood more effectively (improved ejection fraction), reduced scar tissue formation (fibrosis), and increased survival in heart failure caused by pressure overload. Importantly, they did this without making the heart muscle abnormally thick (cardiac hypertrophy). These drugs, called ERR agonists, also switched on many metabolic genes, especially those that control how the heart uses fats for energy and how the mitochondria (the cell's "powerhouses") function.

ERR agonists help the heart keep using oxygen efficiently for energy, which protects it from heart failure caused by pressure overload in living systems [50].

6. Nanoparticles {Np}In Treatment:

Nanomedicines give a new approach to treating hemorrhagic stroke. still, their clinical use is still at an early stage, and well- designed clinical trials on nano-grounded interventions are urgently needed. Preclinical beast models should be precisely matched to translational exploration pretensions to insure meaningful results. farther disquisition is also necessary to address the safety profile of nanomedicines. Promising unborn strategies include biomimetic nanoparticles, inflammation- targeted nanoparticles, theranostic nanomaterials, and nanoparticles with precise delivery systems for hemorrhagic stroke remedy [51].

7. Extracellular Vesicles Derived from Stem Cells:

- Extracellular vesicles (EVs) from stem cells may help protect the brain after injury.
- In the early or acute stage, they can act quickly to limit damage.
- They also contribute to tissue healing and repair.
- Over time, EVs have been shown to support better neurological recovery.
- This makes them a promising option for treating brain injury after cardiopulmonary resuscitation.

vi. Researchers suggest that altering stem cells through induction or genetic editing could:

- boost the amount of EVs produced,
- improve their biological makeup, and
- make them more precise in targeting damaged tissues [52].

12. CONCLUSION:

Sudden cardiac death in young people is uncommon, but its impact is devastating when it happens. Recognizing those at risk through careful medical evaluation, family history, and in some cases genetic testing, can make a real difference. Prevention depends on a mix of approaches—promoting healthy lifestyles, running focused screening programs, providing timely treatment, and making life-saving tools like automated defibrillators more widely available. Raising awareness among doctors, families, and communities is just as important as ongoing research, so that more lives can be protected and fewer families face such sudden loss.

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