Diabetes and Sudden Cardiac Death

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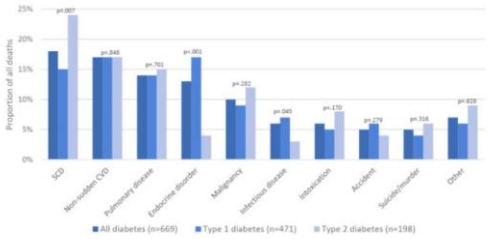
I. INTRODUCTION

The global burden of type 2 diabetes (T2DM) is set to escalate dramatically, with projections indicating over 380 million individuals living with the condition by 2025. This alarming trend is particularly evident in countries like India, where cardiovascular disease (CVD) mortality is expected to rise sharply, from 2.26 million deaths in 1990 to a staggering 4.77 million deaths by 2020. Diabetes, particularly type 2 diabetes, is a multifaceted condition that not only affects daily lifestyle but also significantly heightens the risk of sudden cardiac death (SCD). Individuals with diabetes face approximately twice the risk of SCD compared to those without the condition, primarily due to the complex interplay of metabolic abnormalities. Hypertension, hyperlipidaemia, and obesity, which are prevalent in diabetic patients, exacerbate cardiovascular risk by accelerating the development of coronary heart disease (CHD)—a leading cause of SCD. The pathophysiology of this association involves autonomic dysfunction, electrophysiological abnormalities, and structural changes in the heart, including diabetic cardiomyopathy, all of which contribute to the increased likelihood of arrhythmias and fatal outcomes. The epidemiological data confirm that diabetic individuals are at significantly higher risk for sudden cardiac events, underscoring the urgent need for effective management strategies. Tight glycaemic control, blood pressure regulation, lipid management, and weight reduction are critical in reducing cardiovascular complications. Moreover, newer pharmacological agents such as SGLT2 inhibitors and GLP-1 receptor agonists are proving beneficial in not only managing diabetes but also in reducing cardiovascular mortality. With the increasing prevalence of diabetes and its devastating cardiovascular consequences, focused research and innovation in prevention, early detection, and personalized care will be key to combating this growing public health crisis.

II. EPIDEMIOLOGY OF SUDDEN CARDIAC DEATH IN DIABETES

Risk stratification for sudden cardiac death (SCD) varies significantly across age groups, with monogenetic and polygenetic causes predominating in younger individuals, while chronic structural diseases associated with acquired conditions, such as coronary artery disease (CAD), valvular heart diseases, and heart failure, are more prevalent in older populations. In individuals under 50 years of age, studies estimate that up to 70% of all SCD cases may be attributed to inherited causes. Diabetes mellitus (DM) has been consistently identified as a strong predictor of SCD. Notably, the Paris Prospective Study, which tracked approximately 6000 middle-aged male civil servants for over 23 years, revealed that DM independently increased the relative risk (RR) of SCD. Furthermore, diabetes management plays a critical role in reducing both macrovascular and microvascular complications, potentially lowering the risk of SCD in diabetic patients.

In patients with cardiovascular implantable electronic devices (CIEDs), cardiac magnetic resonance (CMR) imaging has proven valuable in risk stratification, as visual assessment of myocardial fibrosis can exclude those at risk for SCD.



III. MATH

MECHANISMS LINKING DIABETES TO SCD

Cardiovascular autonomic neuropathy (CAN) represents a severely debilitating yet frequently underdiagnosed complication in individuals with diabetes, characterized by progressive damage to the autonomic nerve fibres that innervate the heart and blood vessels. This neuropathy disrupts the delicate balance of autonomic control over cardiovascular function, leading to profound alterations in heart

rate regulation and vascular dynamics. CAN has wide-ranging clinical manifestations, including orthostatic hypotension, resting tachycardia, exercise intolerance, and silent myocardial infarction, the latter often going unnoticed due to the lack of typical pain sensations. In its later stages, the condition exacerbates cardiovascular risk, contributing to intraoperative cardiovascular instability and increased mortality. The pathophysiology of CAN mirrors that of other diabetic neuropathies, with damage to autonomic fibres occurring in a length-dependent fashion. Initially, the Vagus nerve, the body's longest parasympathetic nerve responsible for much of the parasympathetic control of the heart, is most affected. This results in a marked reduction in parasympathetic tone and contributes to resting tachycardia. Over time, sympathetic denervation progresses, starting from the apex of the heart and extending to the base, compounding the imbalance between sympathetic and parasympathetic regulation. These autonomic dysfunctions not only predispose patients to sudden cardiac death (SCD) and myocardial ischemia, but they also significantly complicate the management of other diabetic complications, such as congestive heart failure (CHF) and diabetic neuropathy. As CAN impairs the heart's ability to appropriately respond to stress and increases the vulnerability to fatal arrhythmias, it emerges as a critical factor in reducing survival and quality of life for patients with diabetes. The early recognition and targeted management of CAN are essential for improving outcomes and mitigating its devastating cardiovascular consequences.

IV. ELECTROPHYSIOLOGICAL ABNORMALITIES

Electrophysiological abnormalities play a critical role in the heightened risk of sudden cardiac death (SCD) in individuals with diabetes, with emerging evidence indicating that diabetic neuropathy and autonomic dysfunction significantly contribute to arrhythmic events. In diabetes, autonomic imbalance, particularly the impairment of vagal tone, leads to an increased sympathetic drive and a subsequent reduction in parasympathetic control of the heart, fostering an environment conducive to ventricular arrhythmias (Hernández et al., 2018). The prolonged QT interval, commonly observed in diabetic patients, is another hallmark electrophysiological abnormality, reflecting altered cardiac repolarization and enhancing the risk of ventricular tachycardia (VT) and ventricular fibrillation (VF), both of which are closely linked to SCD. Furthermore, the presence of myocardial fibrosis in diabetic cardiomyopathy, as detected through advanced imaging techniques like cardiac magnetic resonance imaging (CMR), can lead to heterogeneous conduction and reentry circuits, further predisposing individuals to fatal arrhythmias. As diabetic heart disease progresses, electrophysiological remodeling exacerbates these abnormalities, increasing the likelihood of lethal arrhythmic events. These findings underscore the complex interplay between metabolic derangements, structural changes, and electrophysiological disturbances in diabetes, highlighting the urgent need for early detection and tailored interventions to mitigate the risk of SCD in this high-risk population. Early electrocardiographic screening and implantable cardioverter defibrillators (ICDs) are critical in reducing mortality by addressing these electrophysiological abnormalities and preventing sudden arrhythmic events in diabetic patients.

V. RISK FACTORS

The risk factors linking diabetes to sudden cardiac death (SCD) are multifaceted, involving a complex interplay of metabolic, vascular, and electrophysiological disturbances that significantly elevate the risk of fatal arrhythmias. Hyperglycemia, a hallmark of diabetes, contributes to vascular endothelial dysfunction, promoting the formation of atherosclerotic plaques and coronary artery disease (CAD), both of which are key precursors to SCD. Additionally, insulin resistance and obesity, frequently coexisting with diabetes, exacerbate the risk of cardiovascular events by increasing the burden of hypertension, dyslipidemia, and systemic inflammation. The resulting autonomic dysfunction, characterized by an imbalance between sympathetic and parasympathetic nervous system activity, is a significant contributor to arrhythmogenesis in diabetic patients. Reduced vagal tone and increased sympathetic drive lead to ventricular arrhythmias, while QT interval prolongation, commonly observed in diabetes, further predisposes individuals to ventricular tachycardia (VT) and ventricular fibrillation (VF), both of which are leading causes of SCD. Moreover, the presence of diabetic cardiomyopathy, characterized by myocardial fibrosis and impaired cardiac remodeling, heightens the risk of SCD by promoting electrical heterogeneity and reentry circuits in the heart.

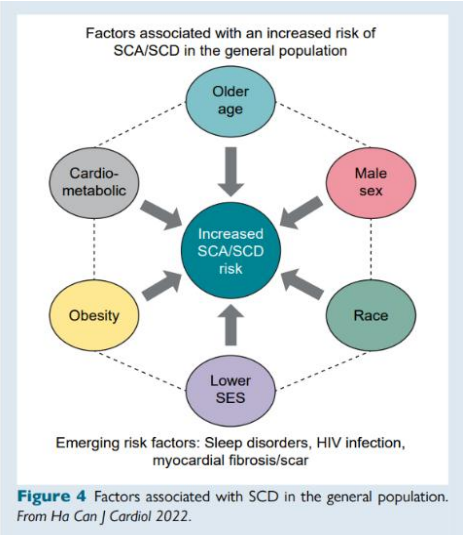
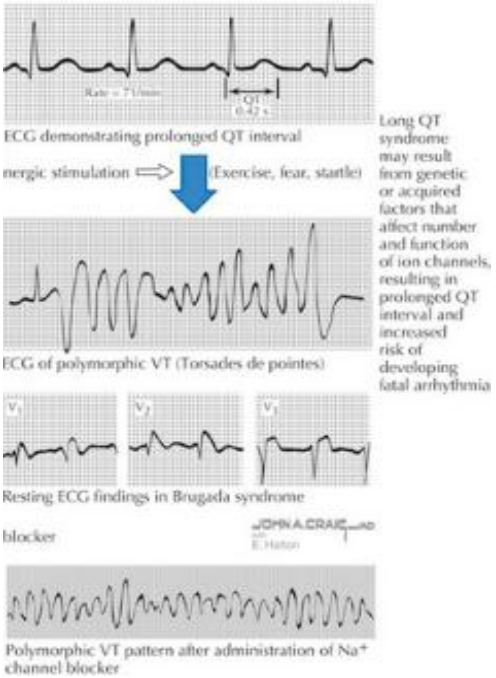


Figure 4 Factors associated with SCD in the general population. *From Ha Can J Cardiol 2022.*

VI. RISK FACTORS

Electrocardiographic (ECG) abnormalities serve as key clinical indicators in assessing the risk of sudden cardiac death (SCD) in individuals with diabetes, with distinctive findings that reflect the underlying electrophysiological disturbances associated with the condition. One of the most significant electrocardiographic manifestations in diabetic patients is QT interval prolongation, which has been linked to an increased susceptibility to ventricular arrhythmias, including ventricular tachycardia (VT) and ventricular fibrillation (VF), both critical precursors to SCD. Prolonged QT intervals in diabetic individuals are thought to result from altered cardiac repolarization due to autonomic dysfunction, where the reduced parasympathetic tone and heightened sympathetic activity contribute to electrical instability within the heart Additionally, ST-segment depression and T-wave inversions are often observed, indicative of myocardial ischemia and electrical remodelling associated with diabetic cardiomyopathy. These electrocardiographic markers, in conjunction with clinical findings such as resting tachycardia, exercise intolerance, and orthostatic hypotension, provide valuable insight into the autonomic imbalance and cardiac structural changes that elevate the risk of SCD in diabetic patients. Furthermore, the presence of silent myocardial infarction, often undetected due to the loss of typical pain sensations in diabetic individuals, further complicates the clinical picture, as it may lead to unnoticed ischemic events that trigger fatal arrhythmias. As such, the integration of ECG screening in diabetic patients, particularly those with cardiovascular risk factors, is critical for early detection of arrhythmic potential and for guiding therapeutic interventions aimed at preventing sudden cardiac death.



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