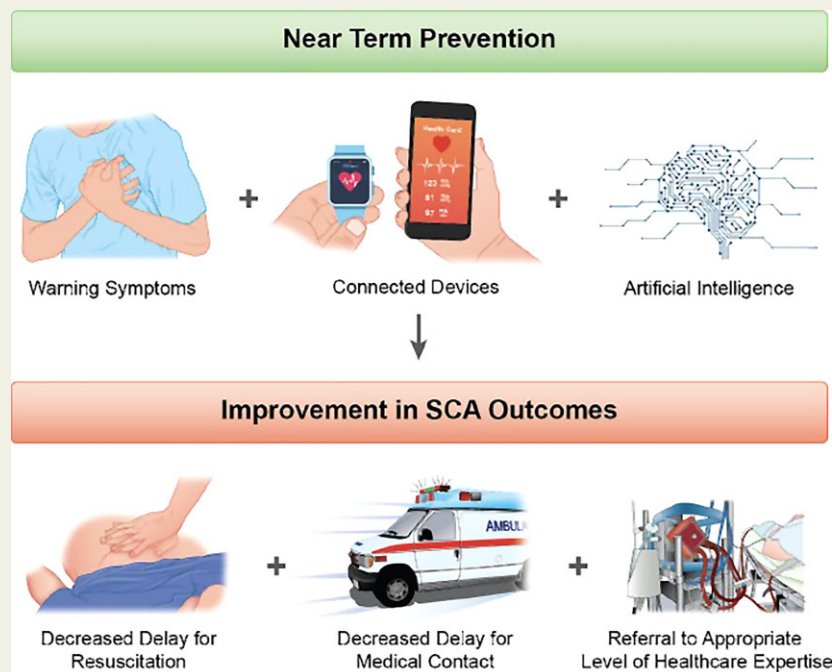


Fighting against sudden cardiac death: need for a paradigm shift—Adding near-term prevention and pre-emptive action to long-term prevention

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Graphical Abstract Envisioning near-term sudden cardiac death prevention. The combination of warning symptoms, connected devices and artificial intelligence will make near-term prevention effective in reducing sudden cardiac death (SCD) burden in a near future. This strategy will improve SCD prediction, reduce delay for resuscitation, decrease delay for medical contact and improve referral to the appropriate level of healthcare expertise.

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More than 40 years after the first implantable cardioverter-defibrillator (ICD) implantation, sudden cardiac death (SCD) still accounts for more than five million deaths worldwide every year. Huge efforts in the field notwithstanding, it is now increasingly evident that the current strategy of long-term prevention based on left ventricular ejection fraction as the key selection criterion is actually of very limited impact, also because the largest absolute numbers of SCD are encountered in the general population not known to be at risk. It has been recently reemphasized that SCD is often not so sudden, with almost half of the victims experiencing typical warning symptoms preceding the event. Importantly, heeded and prompt medical attention can dramatically improve survival. Essentially, such timely action increases the chances of the SCD event being witnessed by emergency medical services and provides the opportunity for early intervention. In addition, newer technologies incorporating digital data acquisition, transfer between interconnected devices, and artificial intelligence, should allow dynamic, real-time monitoring of diverse parameters and therefore better identification of subjects at short-term SCD risk. Along with warning symptoms, these developments allow a new approach of *near-term prevention* based on the hours and minutes preceding SCD. In the present review, we challenge the current paradigm of mid- and long-term prevention using ICD in patients at the highest risk of SCD, and introduce a complementary concept applicable to the entire population that would aim to pre-empt SCD by timely detection and intervention within the minutes or hours prior to the event.

Keywords Sudden cardiac death • Near-term prevention • Implantable cardioverter-defibrillator • Remote monitoring • Symptoms • Artificial intelligence

Introduction

Of all presentations of cardiovascular disease, sudden cardiac death (SCD) is the most challenging, accounting for millions of deaths worldwide every year.^{1,2} Despite major investments by the medical and research communities over the past decades, prognosis of out-of-hospital cardiac arrest remains poor with <10% survival.³ Sudden cardiac death poses a large financial burden for health care systems, and its dramatic nature has important psychological and societal impact.⁴

The problem with SCD is the suddenness of the event and the rapidity with which it is fatal, giving very limited opportunity to intervene once the event actually occurs. This is reflected in the poor survival rates despite commendable efforts in the field of resuscitative science. Therefore, almost universally, strategies for reducing SCD burden have focused on trying to identify well ahead of time, the individual likely to experience SCD. Two decades of experience have shown that this strategy of long-term prevention—mainly based on implantable cardioverter-defibrillator (ICD) insertion in the vulnerable subject—suffers from key limitations, including poor identification of high-risk subjects and an imperfect technology in the form of the ICD. Indeed, whilst a high proportion of primary prevention ICD recipients will never use their ICD, a significant number will experience complications. On the other hand, many subjects who eventually suffer SCD never receive an ICD based on current risk identification methods.

A lot has been said about improving long-term risk stratification, testing many novel markers. The goal, however, has proved elusive so far. In this review, we take the opportunity to challenge current thinking and explore an alternative approach,⁵ based on accumulating evidence that SCD is not always unheralded, that timely identification of high-risk subjects in the minutes, hours, or days preceding SCD can open up a new dimension of near-term prevention. We outline the limitations of existing preventive approaches for SCD and then present the case for the feasibility of this complementary strategy in the near future.

Limitations of the current therapeutic arsenal to reduce sudden cardiac death

Since the first human epicardial ICD implantation in 1980 by Dr Michel Mirowski and his team, with devices exceeding 150 cm³ and requiring open chest and abdominal surgery, technology has dramatically improved with the transvenous ICD now measuring <40 cm³. To circumvent ICD complications, mainly related to transvenous leads, the subcutaneous ICD has been developed in the last decade and progressively adopted widely.^{6–8} Additionally, the wearable cardioverter-defibrillator has emerged as a solution for transient high-risk situations in different scenarios,^{9–12} wherein permanent ICD implantation would not be desirable.¹³ In a complementary approach, catheter ablation aims to eliminate arrhythmia occurrence rather than treating it after its occurrence with pacing or shock as the ICD does. Ablation is being increasingly used, with expanding applications in both structural heart disease and in genetic arrhythmia syndromes.^{14–20} Ventricular tachycardia ablation has been shown to reduce the incidence of ventricular arrhythmias in randomized studies when carried out for secondary prevention, but very little data exist for mortality reduction in primary prevention settings, with no convincing demonstration of improvement in survival at mid- and long-term.^{21–23}

It needs to be acknowledged that the above therapies are limited by both modest efficacy and potential adverse effects. With the transvenous defibrillator, 10–20% lead failure has been documented within the decade following ICD implantation.^{24,25} There is also a substantial risk of device infection with serious consequences.^{24,26} Subcutaneous ICD, though avoiding some of these issues, suffers from a relatively high rate of oversensing leading to inappropriate shocks.²⁷ Lastly, wearable cardioverter-defibrillator is still controversial with regard to efficacy and compliance issues.²⁸

Taking a step back, it is important to recollect that ~80% of common SCD is related to coronary artery disease.^{29–35} Accordingly, we need to keep in mind that the most powerful tools to prevent SCD are likely not technological tools but measures to reduce coronary artery disease in the general population. The Tromsø study showed that reductions in cholesterol, blood pressure levels, and smoking accounted for 66% of the decline in coronary heart disease events which were mainly driven by SCD.³⁶ To a lesser extent, better coronary artery disease management and pharmacotherapy might also have played a role in SCD reduction.³⁷ The other important SCD substrate is heart failure, both coronary artery disease and non-coronary artery disease related. Whilst no novel advance in pharmacological therapy specific for ventricular arrhythmias has emerged in recent years, both the scope of and adherence to heart failure pharmacotherapy have improved, with consequent benefits for SCD reduction.³⁸ The incidence of SCD in heart failure with reduced ejection fraction has dramatically declined over the last 10–15 years.^{34,39} Heart failure medications induce favourable reverse remodelling and prevent the arrhythmogenesis responsible for SCD.^{40–43}

To summarize, despite impressive technological tools such as modern implantable devices and catheter therapy to fight against SCD, the most effective strategies to date remain primary prevention of coronary artery disease and heart failure pharmacotherapy. Finally, with the pivotal ICD trials being almost two decades old, the extent to which similar trials in the current era with optimally treated patients would show benefit, remains unknown, although recent findings from EU-CERT-ICD controlled multicentre cohort study have shown the benefit of primary prophylactic ICD

treatment with an almost 30% lower mortality in contemporary heart failure patients cohorts.⁴⁴

The challenge in identifying high-risk subjects

The history of long-term SCD primary prevention began with the identification of the association between low left ventricular ejection fraction (LVEF) and risk of SCD.⁴⁵ Subsequently, the MADIT II trial demonstrated a significant 31% reduction in mortality with ICD implantation amongst patients with a history of myocardial infarction (MI) and an LVEF \leq 30%,⁴⁶ thereby catapulting LVEF into centre stage for SCD risk stratification.

After the additional pivotal SCD-HeFT trial,⁴⁷ presently, long-term primary prevention of SCD mainly focuses on patients with known cardiomyopathy and is based on ICD implantation in patients with LVEF \leq 35%, whether it is due to coronary heart disease or non-ischemic cardiomyopathy.⁴⁸ Primary prevention in the vast majority of patients with structural heart diseases, is entirely based on LVEF, because randomized trials having considered LVEF as the sole risk criterion were positive. Thus, in a sense, LVEF 'bypassed' all the rigorous steps of evaluation which would have been usually employed to test whether it is a sufficiently discriminatory marker of SCD.⁴⁹ Firstly, LVEF is neither highly sensitive nor specific with regard to SCD prediction. This is reflected in the relatively high number of patients needed to be implanted with an ICD for saving one life, as well as the fact that more than two-thirds of SCD in the general population

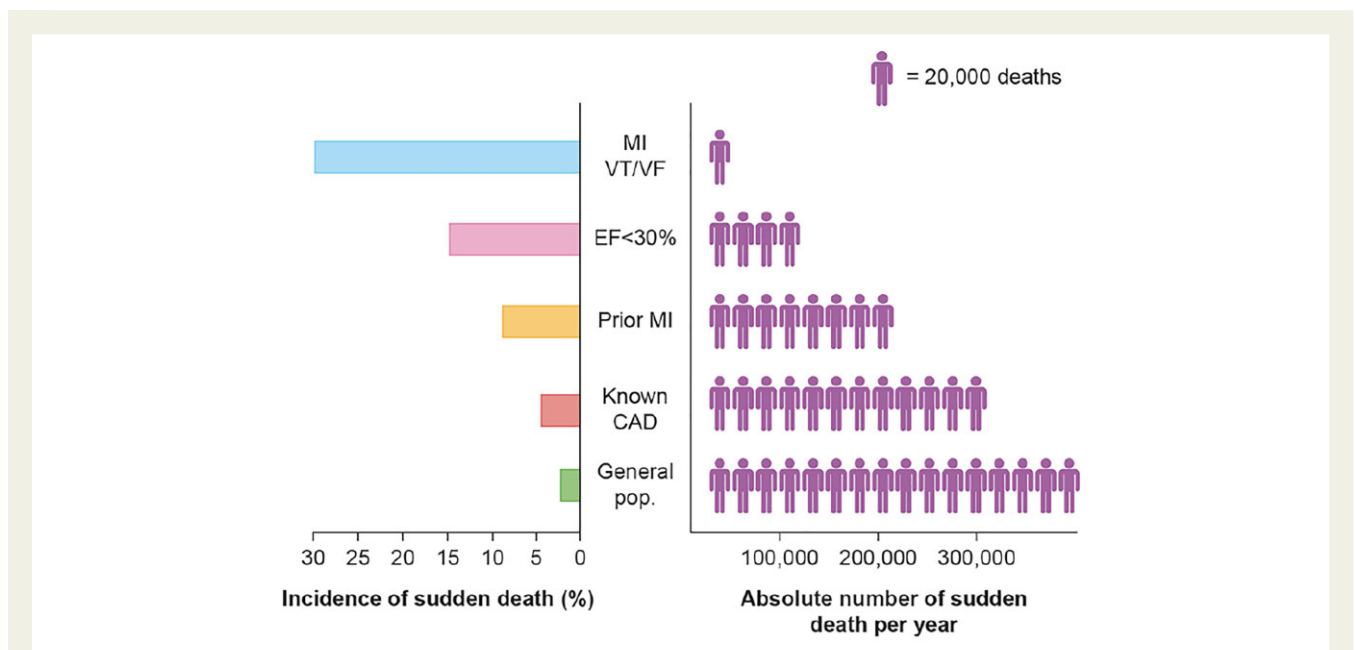


Figure 1 Relative and absolute numbers of sudden cardiac death. The incidence and corresponding absolute numbers of sudden cardiac death in the United States across different risk groups. The vast majority of sudden cardiac death occurs in the general population in whom incidence is the lowest. On the contrary, a minority of sudden cardiac death occurs in patients with known heart disease who have the highest incidence of sudden cardiac death. MI, myocardial infarction; VF, ventricular fibrillation; VT, ventricular tachycardia; EF, ejection fraction; CAD, coronary artery disease; and pop., population. Adapted from Noseworthy and Newton-Cheh⁵¹ and Myerburg *et al.*⁵²

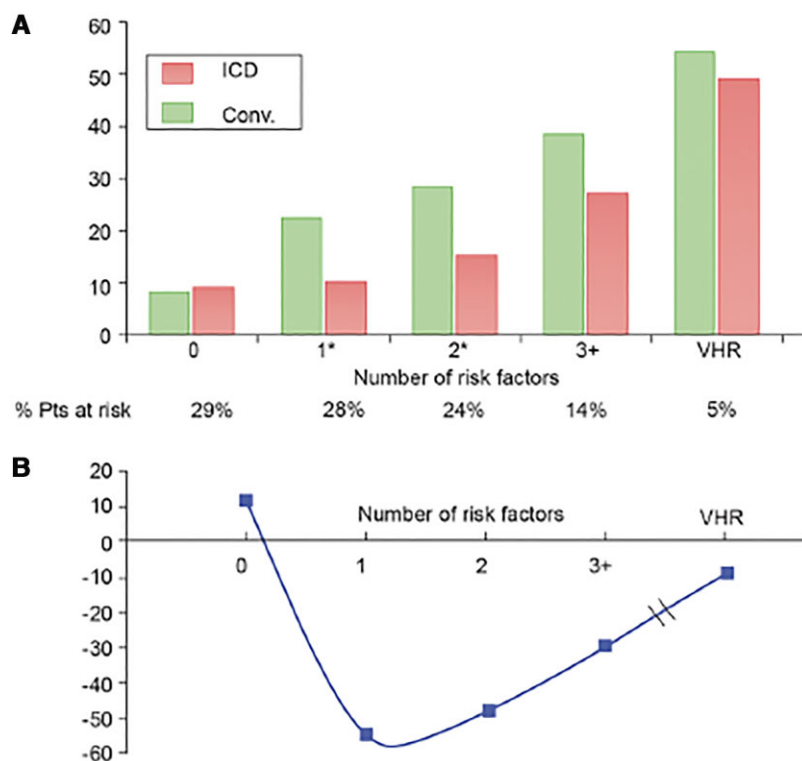


Figure 2 Competing risk in sudden cardiac death. The effectiveness of the implantable cardioverter-defibrillator in reducing mortality depends not only on sudden cardiac death risk, but also on the competing risk of non-sudden cardiac death. (A) Two-year mortality in the conventional therapy group and in the implantable cardioverter-defibrillator group by number of risk factors—based on a multivariate proportional hazards regression model, risk of all-cause mortality in the conventional therapy group were the following: New York Heart Association functional class > II, atrial fibrillation, QRS > 120 ms, age > 70 years, blood urea nitrogen > 26 mg/dL (and < 50 mg/dL). (B) Two-year mortality reduction by implantable cardioverter-defibrillator by number of risk factors. VHR, very high risk. Adapted from Goldenberg et al.⁷²

occur in patients with mildly reduced or normal LVEF (Figure 1).^{50–52} In addition, LVEF, especially when assessed with echocardiography (the modality most commonly used in clinical practice), might have limited reproducibility.^{53,54} Given these realities, new markers and strategies for risk stratification of SCD are urgently needed. Optimization of echocardiographic assessment of the left ventricle through a dynamic evaluation using speckle tracking (strain method) would be of incremental importance for the prediction of SCD or malignant ventricular arrhythmias in some patients, as this method correlates well with cardiovascular magnetic resonance and has a reduced inter-observer variation.^{55–57} Several approaches using newer imaging techniques such as magnetic resonance, autonomic nervous system activity are ongoing, but none has been sufficiently proven yet to be incorporated into guidelines.^{58,59} Electrophysiological study may also be helpful in identifying patients at higher risk of SCD. Beyond ejection fraction, post-MI patients with positive programmed ventricular stimulation associated with electrocardiographic non-invasive risk factors (premature ventricular complexes, non-sustained ventricular tachycardia, late potentials, prolonged QTc, increased T-wave alternans, reduced heart rate variability, abnormal deceleration capacity with abnormal turbulence) may benefit from ICD

implant at long-term.^{60–67} Lastly, since LVEF represents a continuum of risk, it is time to move from a dichotomous to a continuous risk stratification approach, whilst also considering the competing risk of non-SCD.

The second issue is competing risk. The present guidelines base their strategy only on the absolute risk of SCD without taking into account competing risk from other modes of death.^{68–71} Simply put, patients who will benefit from ICD therapy the most are not those with the highest absolute risk of SCD, but rather those with the highest SCD/non-SCD risk ratio (Figure 2).⁷² In other words, a good risk marker needs to discriminate between SCD vs. non-SCD mortality. This is of particular importance since the usual risk factors associated with SCD, for instance age, LVEF, New York Heart Association functional class, ECG QRS duration, and atrial fibrillation are also associated with non-sudden forms of death such as progressive heart failure. The importance of competing risk has been amply demonstrated in the setting of both coronary and non-coronary artery disease, showing that patients at very high risk of other modes of death will not have a net benefit from ICD therapy, especially in the long-term and in non-coronary artery disease.^{72–75} Routine ICD use in such subjects will therefore diminish the overall benefit of this therapy in the population.

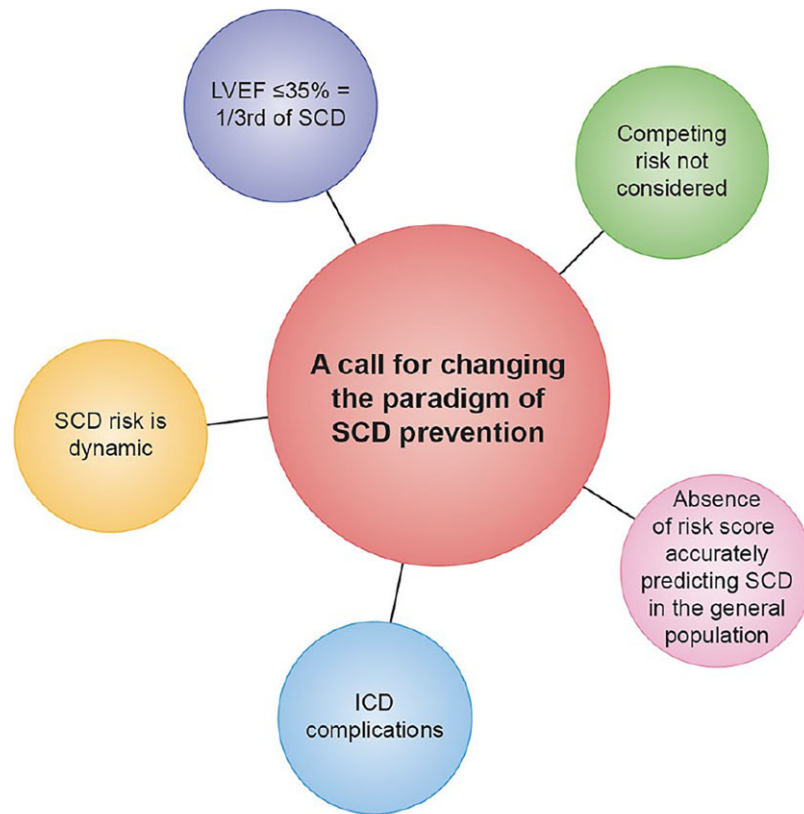


Figure 3 Limitations of current approach to sudden cardiac death risk stratification. The current strategy for sudden cardiac death prevention focuses only on patients with known heart disease, and does not take into account the dynamic nature of sudden cardiac death, as well as the competing risk of non-sudden cardiac death. Finally, implantable cardioverter-defibrillator therapy is associated with a significant complication rate. LVEF, left ventricular ejection fraction.

The early period after an MI presents another unique challenge, as SCD risk is relatively higher within the first month after MI, especially in patients with reduced LVEF (1–2% absolute SCD risk).^{76–78} However, controlled trials assessing ICD therapy in this early phase in patients with low ejection fraction failed to demonstrate a reduction in overall mortality with the ICD.^{79,80} The precise reasons behind this unexpected finding remain speculative, but could reflect a combination of factors including a potentially greater contribution from non-SCD and non-arrhythmic SCD during this period as well as recovery of LVEF with time in some patients.¹³ Furthermore, the VEST trial was the first and only randomized trial assessing the role of the wearable cardioverter-defibrillator in reducing mortality in the immediate post-MI period in patients with LVEF \leq 35%.²⁸ In this trial, the wearable cardioverter-defibrillator did not significantly reduce SCD risk, but it did reduce total mortality. The actual device wear time was very low and the majority of SCD in the wearable cardioverter-defibrillator group occurred whilst not wearing the vest.

The need to move towards a better and individualized risk prediction in both patients with and without severely reduced ejection fraction is being increasingly recognized and has spurred major new efforts such as the PROFID project or the CMR-SCD study.^{81,82} PROFID is a large European effort towards

personalized prediction and prevention of SCD after MI.^{81,83} The two phases of the PROFID programme are first the development of a clinical prediction model for the individual risk of SCD, based on a collection of existing highly phenotyped data with the largest number of post-MI patients ever in this regard (~1 000 000 patients), applying statistical modelling and machine learning methods. In the second phase, two parallel randomized clinical trials will validate the utility of use of the clinical prediction model for the decision making on ICD implantation, whilst health economic analyses will assess its economic impact on health care systems.⁸⁴ The PROFID-Reduced trial (NCT04540354) will randomize patients with LVEF \leq 35% but a low predicted individual risk for SCD to ICD vs. no-ICD in a non-inferiority design, whilst the PROFID-Preserved trial (NCT04540289) will randomize patients with LVEF $>$ 35% and a high predicted individual risk for SCD to ICD vs. no-ICD in a superiority design.

Whilst we have a laid-out prevention strategy (albeit imperfect), in patients with known heart disease, we do not have any in patients without. This is important, given that the majority of SCD occurs in subjects without known heart disease.^{85,86} Several studies have tried to identify simple markers allowing the recognition of high-risk subjects in the general population, using ECG parameters for instance.^{87–89} Using multiple markers

for a 'cumulative' risk approach has also been proposed. However, even high relative risks may not translate into large increments in absolute risk.

To summarize, the current strategy for SCD prevention focuses only on patients with known heart disease and does not take into account competing risk of non-SCD (Figure 3). Additionally, up till now, no high-risk group has been identified in the general population, where the largest absolute numbers of SCD are encountered. There is a need to move towards high yield, multiparametric scores to improve the accuracy of prediction. These will hopefully emerge through data collection encompassing the entire population of out-of-hospital cardiac arrest patients, not restricted to only those admitted to the hospital, and with the use of big data.^{81,90}

Warning symptoms prior to sudden cardiac death: opportunity for timely action!

Contrary to general belief, the majority of SCD patients is in contact with the healthcare system shortly before SCD.⁹¹ A fairly homogeneous body of literature has shown that SCD is actually preceded by symptoms in approximately half of the subjects.^{92–94} These symptoms are mainly chest pain, dyspnoea, and syncope, during the month prior to SCD, with symptom recurrence in >90% of these cases within the 24 h preceding SCD.⁹⁵

When not neglected and acted upon in a timely fashion, the presence of symptoms translates into a seven-fold increase in survival because it allows an upstream alert and subsequently shortens the delay to resuscitation.^{95,96} Stecker et al.⁹⁷ demonstrated that patients with previously known coronary artery disease had 50% higher odds of survival from resuscitated sudden cardiac arrest, one of the potential explanations for this improved outcome being a greater awareness of symptoms and a potentially earlier activation of emergency medical services (EMS). Patients' consideration of symptoms is largely impacted by their education level and prior history. Campaigns to improve awareness in this regard may lead to improved outcomes post-sudden cardiac arrest.⁹⁶

Taking a broader view, the presence of symptoms before SCD is an opportunity for a new type of prevention, which can be called *near-term prevention*, based upon prompt action in response to warning signs. However, a key concern that this strategy raises immediately is the issue of specificity of such symptoms, with attendant risks of overburdening EMS as well as unnecessary panic amongst patients. Therefore, amongst patients with symptoms, it is crucial to refine the approach, to identify those specifically at high risk of SCD.

How to move from symptoms to near-term prevention?

To improve the specificity of a near-term prevention strategy, a multi-pronged approach going beyond symptoms and clinical

features may be needed. The frequency of symptoms prior to SCD has opened the room for pre-emptive action but also raised the need for acute risk stratification for identifying those at highest risk of SCD. The utility of multiple clinical parameters has been assessed in patients with chest pain related to acute ST-elevation MI. In this setting, patients at high risk of SCD could be identified prior to hospital admission, using five simple parameters, all of which can be assessed over the phone (younger age, absence of obesity, absence of diabetes mellitus, shortness of breath, and a short delay between chest pain onset and call to EMS), with the identification of a subgroup of patients with an almost 30% risk to develop SCD prior hospital admission.⁹⁸ Whilst the efforts for better acute risk stratification have only been tested in the ST-elevation MI setting so far, the extension to the general population with symptoms still needs to be evaluated in further studies.⁹⁵

Beyond clinical variables and/or baseline ECG features known to be associated with a higher risk of SCD, the identification of electrical instability occurring in the hours or days before SCD,⁹⁹ through 'dynamic monitoring'^{65,66} is an exciting possibility. Few studies have been performed with interesting results. A study carried out in patients with an ICD demonstrated a significant increase in J-point amplitude recorded with the intracardiac far-field electrogram immediately before the onset of polymorphic ventricular tachycardia and ventricular fibrillation.¹⁰⁰ A second study showed that RR interval irregularity was increased just before ventricular fibrillation.¹⁰¹ Another one on the usefulness of trends in continuous ECG telemetry monitoring (at the hospital) noted changes in several ECG measures, including QRS duration, QTc, RR, and ST segment in the few hours preceding SCD.¹⁰² Furthermore, artificial intelligence, and particularly machine learning, has the potential to improve SCD prediction by integrating clinical, electrical, and other features. The role of machine learning has already been demonstrated in long-term prediction of SCD.^{103,104} Parameters compatible with near-term prevention should now be identified and integrated in future algorithms.

The idea behind near-term prevention is not to provide a continuous monitoring to the entire population, but to target the largest possible population, on a short period, triggered by the patient upon the occurrence of symptoms. Management of the data sent by the subjects/patients and the level of alertness should take into account their recent symptoms, their medical history, and in particular their history of coronary artery disease.

What will make the near-term prevention approach possible?: connected devices and artificial intelligence

Long-term monitoring (including the use of an implantable loop recorder) is currently offered for patients with known cardiac disease. However, it does not apply to patients without known cardiac disease who account for a large proportion of SCD victims. By opposition, immediate but time-limited assessment in patients who develop symptoms might allow a broader

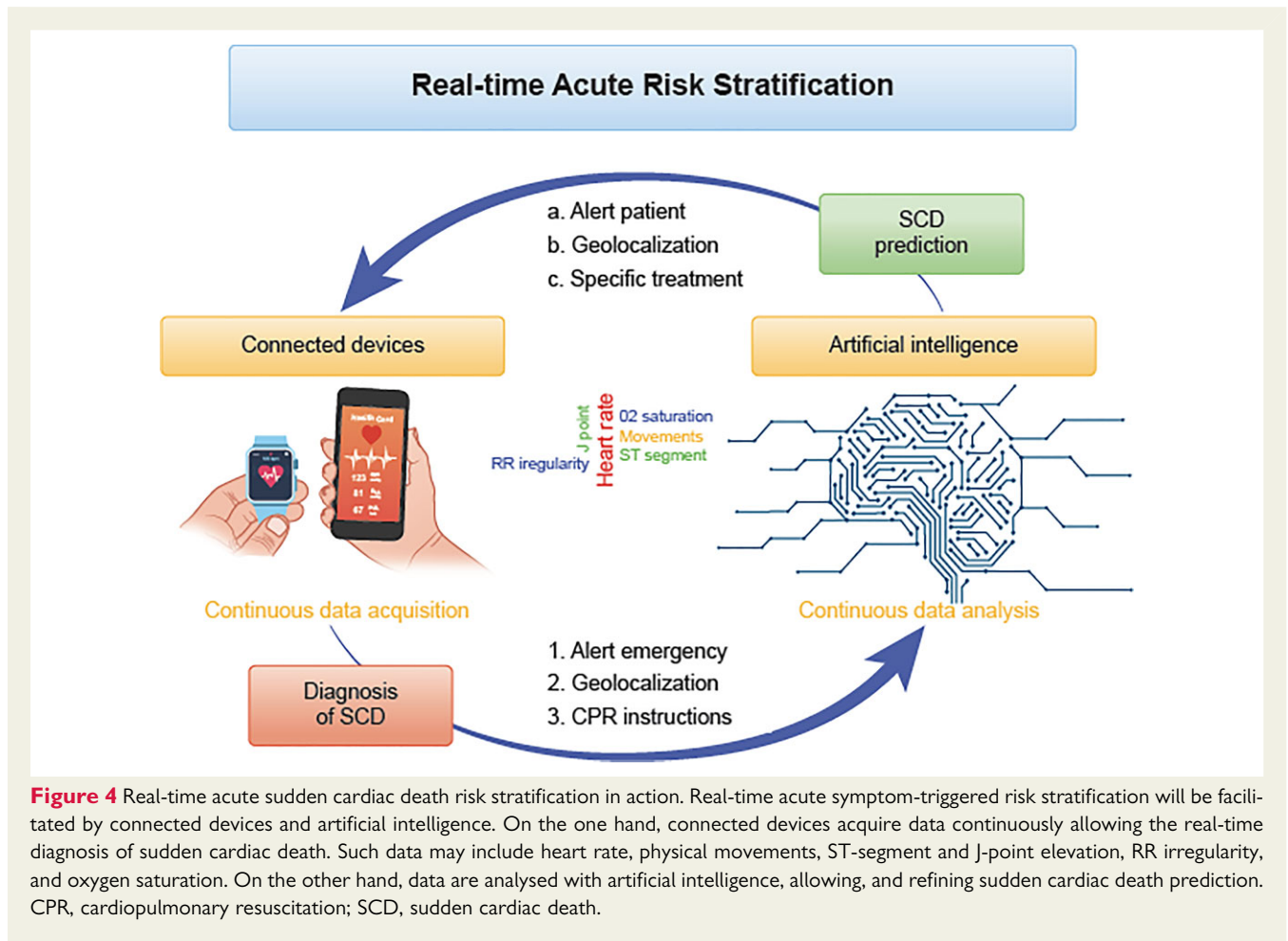


Figure 4 Real-time acute sudden cardiac death risk stratification in action. Real-time acute symptom-triggered risk stratification will be facilitated by connected devices and artificial intelligence. On the one hand, connected devices acquire data continuously allowing the real-time diagnosis of sudden cardiac death. Such data may include heart rate, physical movements, ST-segment and J-point elevation, RR irregularity, and oxygen saturation. On the other hand, data are analysed with artificial intelligence, allowing, and refining sudden cardiac death prediction. CPR, cardiopulmonary resuscitation; SCD, sudden cardiac death.

coverage of the population, including individuals without previous cardiac history.

As previously mentioned, prediction of SCD with the 'static' ECG, which reflects a one-time electrical status, has been disappointing, and dynamic monitoring holds promise in this regard. Sudden cardiac death prediction will likely be improved with a greater use of digitized ECG tracings, which permit better precision in measurements and possibly automation of interpretation.¹⁰⁵ Despite this limitation and the fact that the feasibility of its use in near-term prevention strategies is unlikely, static ECG might still offer the opportunity to predict SCD at long-term, especially if specific SCD prediction criteria are identified.

Signal acquisition is becoming easier with the recent development of a wide range of connected devices.¹⁰⁶ Patch ECG monitors offer a more convenient, less artefact-prone alternative to conventional Holter ECG.¹⁰⁷ Smartwatches are omnipresent and many incorporate technology to capture personalized health data.¹⁰⁸ Finally, the AliveCor Kardia 6L has the ability to record a six-lead ECG and has obtained Food and Drug Administration approval for QT monitoring.^{109,110} These devices offer portability and allow the patients to record their heart rhythm periodically and more importantly, at the time of symptoms.

With such connected devices, symptom-triggered data acquisition has the potential to become the cornerstone of near-term prevention, as sudden cardiac arrest risk is dynamic and modulated by a

variety of environmental factors, seasonal variations, and circadian rhythms.^{111,112} More novel developments may be around the corner. Recently, an implantable device designed to continuously monitor ST-segment changes, with alerts in case of significant ST deviation was studied in patients at high risk for MI and showed a reduction in detection to arrival time, although a reduction in hard outcomes was not demonstrated.¹¹³ However, invasive devices such as these will have limited applicability in the general population. Therefore, further innovation and efforts are needed to make continuous monitoring widespread in the community through the use of commonly available, non-invasive monitors. The way forward will involve miniaturization of sensors as well as their incorporation in routine mobile phone technology.¹¹⁴

For a strategy of dynamic monitoring to be successful at a community-wide scale, some automation of data analysis will also be crucial since the amount of information generated will be enormous. In this regard, artificial intelligence and machine learning have the potential to play an important role in arrhythmia diagnosis and prediction¹¹⁵ (*Graphical Abstract*). For example, Attia *et al.*¹¹⁶ demonstrated that artificial intelligence could predict atrial fibrillation from a sinus rhythm ECG. In the short term, it is quite possible that ventricular arrhythmia too may be predicted from a sinus rhythm ECG, with the ability of artificial intelligence to discern patterns beyond traditional ECG measurements performed by the human brain. Two studies from South Korea have directly

assessed the relevance of artificial intelligence to SCD prediction. In one study, using machine learning, in-hospital sudden cardiac arrest could be predicted in >50% of patients several hours before the event.¹¹⁷ Likewise, Lee *et al.* built a model using artificial neural networks based on heart rate and respiratory variability, that could predict ventricular tachycardia 1 h before the event with good accuracy.^{104,118,119}

Each step of the practical implementation of near-term prevention in the general population should be handled with caution to avoid medical and ethical flaws. Undoubtedly, target population selection, as well as data overload and confidentiality are significant issues to consider. Data acquisition and analysis will require the use of connected devices, machine learning and artificial intelligence processing, and the reliability of these technologies should be optimized and verified, with cost-effectiveness analysis.^{84,87,88} Besides, the ethical aspects of data collection and conservation should be addressed, most likely by extrapolating the current protocols established for remote medical monitoring.

Near-term prevention: a vision for the future

A 'near-term' implementation is possible using the currently available technologies, including a patient-triggered assessment by EMS, preferably, using the currently available smartphones and smartwatches to allow an ECG recording upon the development of symptoms. If this initial assessment shows a high-risk profile, pre-emptive actions can be undertaken such as asking the patient to try to get a witness present whilst awaiting the arrival of EMS. Emergency medical services can also be activated, offering the patient the chance to have EMS on site or on their way if the SCD actually occurs. According to their initial assessment, the patient can be oriented to the appropriate department that could be an emergency or intensive care unit for a temporary admission or a catheterization laboratory in case of acute MI.

In the near future, one can imagine that connected devices, such as smartwatches, will continuously monitor the at-risk patient and automatically detect SCD by utilizing key parameters such as heart rate and oxygen saturation, and by detecting the absence of physical movement. Sudden cardiac death will also be confirmed through the absence of response to audible messages and device vibrations (Figure 4). Immediately after SCD detection, an alert will be automatically transmitted to the closest emergency centre and to potential first responders in the vicinity, reducing response time. Connected devices will also assist bystander cardiopulmonary resuscitation, giving oral or video instructions for resuscitation.¹²⁰ Sudden cardiac death victims will be precisely located thanks to geolocalization, and automated external defibrillators, or other medical devices will be efficiently delivered by drones, overcoming potential traffic, and terrain obstacles.¹²¹ The utility of drone assistance has been confirmed in a randomized study and these devices might reduce automated external defibrillators arrival time by up to 6 min.^{122–124} Such delay reductions would be expected to be even more prominent in developing regions of the world with less-organized roadways and traffic systems. Therefore, non-human rapid assistance through drones has the

potential to overcome geographical problems of automated external defibrillator distribution, reduce disparities in their utilization, and majorly improve resuscitation outcomes.

It remains important not to consider the near-term prevention in opposition with the traditional risk stratification and mid-/long-term prevention. These strategies are complementary and target different populations on different time courses. Whereas mid- and long-term strategies aim to prevent SCD on the long run amongst patients with known heart disease, near-term prevention aims to target the overall population, including the vast majority of subjects without any cardiovascular condition, but on a shorter period.

Conclusion

Beyond primordial prevention of coronary heart disease and heart failure pharmacology, long-term SCD prevention over the last 20 years has been disappointing, both due to limitations of the tools used (ICD, catheter ablation, antiarrhythmic pharmacology), as well as the difficulty in accurately identifying subjects at high risk of SCD. Near-term prevention using warning symptoms and dynamic monitoring is a promising complementary strategy, which could be applied not only to high-risk subjects with known heart disease, but potentially to the overall population. Integrating signal monitoring through connected devices into the clinical risk profile and using newer tools such as artificial intelligence will refine identification of patients at risk, improve SCD prevention, and rapidly rescue stricken patients.

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