State-of-the-art analysis of electrocardiogram findings in sudden cardiac death

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ABSTRACT

Sudden cardiac death (SCD) is a significant public health issue, and efforts to prevent it have involved the analysis of various modalities, including echocardiography, cardiac CT, cardiac MRI, genetic testing and ECG. The ECG, invented >100 years ago, is the oldest diagnostic tool among these examinations. Left ventricular hypertrophy and QT prolongation were first identified as risk markers for SCD in the 1960s and 1970s. However, since the beginning of the 21st century, advances in digitalised ECG data have unveiled various additional important findings. In vitro experimental studies have also contributed to the discovery of these new markers. Newly proposed markers include the fragmented QRS complex, the interval between the peak and the end of the T wave and J waves. Many studies have validated the clinical significance of these new ECG markers in predicting SCD risk. Recently, artificial intelligence (AI) has been employed to analyse ECG data to identify the high-risk populations. While the results of AI studies are not yet sufficient for routine clinical practice, ongoing advancements are expected to improve their accuracy in the near future.

INTRODUCTION

Sudden cardiac death (SCD) is a significant public health issue and a leading cause of mortality. In a large proportion of patients, SCD is the first manifestation of underlying cardiac disease.[1] At present, the severely reduced left ventricular ejection fraction (LVEF) is widely used to identify candidates for primary prevention therapy with implantable cardioverter-defibrillators (ICDs) based on randomised clinical trials,[2] but this approach has significant and well-recognised limitations. Importantly, most cardiac arrests occur among subjects with preserved or only moderately reduced LVEF. The standard 12-lead ECGs are widely used as a screening tool and have received much interest in improving long-term SCD risk stratification. The ECG is useful for screening of myocardial diseases or hereditary arrhythmias and estimating the risk of arrhythmia during follow-up. The abnormalities in ECG waves can be divided into two parts: (1) the depolarisation (QRS complex) abnormality and (2) the repolarisation (QT-T wave) abnormality.

ECG abnormalities known as markers for SCD are categorised in table 1. Not all of these ECG abnormalities arise from specific pathological conditions, and some cases of cardiomyopathy do not present with specific ECG abnormalities. However, despite these limitations, ECG remains a valuable tool for diagnosing and monitoring heart disease by considering the possible underlying conditions suggested by the above ECG abnormalities. Here, we will describe the potential underlying conditions and heart diseases associated with individual ECG abnormalities.

Indices of depolarisation abnormalities

Left ventricular hypertrophy

Long-term left ventricular pressure or volume overload develops increased R-wave amplitude and changes in T wave, known as the left ventricular hypertrophy (LVH) pattern.[3] Additionally, an elevated left ventricular end-diastolic pressure leads to a left atrial overload, which is reflected in changes to the P wave. These changes increase the risk of heart failure (HF), SCD and atrial fibrillation (AF). LVH has been reported as a powerful risk factor for SCD since the 1970s,[4] and some genetic variants can be associated with LVH and SCD.[5]

Amyloidosis

Amyloidosis is a rare disorder of protein conformation and metabolism characterised by the deposition of insoluble fibrils in tissues. The condition is known as cardiac amyloidosis when it accumulates in the heart. In contrast to the significant hypertrophy observed on echocardiography, *low voltage QRS* is a common finding and a hallmark of amyloid cardiomyopathy. Low voltage QRS reflects the deposition of insoluble fibrils in the myocardium and is a predictor of SCD.[6]

QRS prolongation

Prolongation of the QRS interval, caused by delayed ventricular depolarisation, is associated with various pathological conditions: (a) bundle branch block (BBB) (eg, from fibrosis or inflammation), (b) ventricular hypertrophy or cardiomyopathy, (c) myocardial ischaemia leading to damage or fibrosis and (d) effects of antiarrhythmic or other medications. The MADIT II trial identified a wide QRS complex as a predictor of SCD in patients with HF.[7] Moreover, various studies have demonstrated that prolonged QRS interval increases mortality in patients with various aetiologies, even in the general population. Left ventricular conduction abnormalities (eg, left BBB, frequent premature ventricular complexes (PVCs), right ventricular pacing, Wolff-Parkinson-White (WPW) syndrome) can lead to systolic dysfunction, HF and ventricular tachyarrhythmias, collectively termed as conduction-induced cardiomyopathy. Therapy for each underlying condition is required to improve this condition.[8]

Fragmented QRS and epsilon wave

Fragmented QRS (fQRS) is defined by multiple spikes within the QRS complex with various

Table 1 ECG abnormalities known as markers for sudden cardiac death

Category	Indices
Depolarisation abnormalities	► Left ventricular hypertrophy ► QRS prolongation ► Fragmented QRS complex and epsilon wave ► Abnormal Q wave, poor R wave progression and delayed QRS transition
Repolarisation abnormalities	► Long and short QTc ► Prolonged T_{peak}-to-T_{end} interval ► ST-T wave abnormalities ► J wave (early repolarisation)
Combination of depolarisation and repolarisation abnormalities	Wide frontal QRS-T angle
Arrhythmias	► Atrial fibrillation ► Premature ventricular complex
Artificial intelligence	Black box indices

morphologies of the QRS wave. fQRS includes the presence of an additional R wave (R') or notching in the nadir of the R wave or the S wave, or the presence of >1 R' (fragmentation) in two contiguous leads, corresponding with the coronary artery territory, on the ECG with QRS <120 ms. Later, the definition of fQRS was extended in the presence of wide QRS complexes (>120 ms), such as BBB, PVCs and paced QRS complexes. To define fQRS in wide QRS complexes, the criteria was included >2 notches in the R or the S wave. Electrophysiologically, fQRS probably represents changes in the wavefront direction of the ventricular activation due to ventricular structures or myocardial scar. Therefore, fQRS is not very disease specific. fQRS also depends on the ECG recording techniques, such as the low-pass filter setting generally used at 100 or 150 Hz because the lower setting of the filter might abolish the small spikes. fQRS has been identified as a risk for ventricular tachyarrhythmias and SCD in many diseases, such as coronary artery disease, HF, hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC),[9] dilated cardiomyopathy, cardiac sarcoidosis,[10] congenital heart disease[11] and in many types of channelopathies, such as Brugada syndrome[12] and long QT syndrome (LQTS).[13] In Brugada syndrome, fQRS frequently appears in the right precordial leads that represent conduction abnormalities in the right ventricular outflow tract (RVOT) and is associated with the occurrence of ventricular fibrillation (VF) (figure 1).

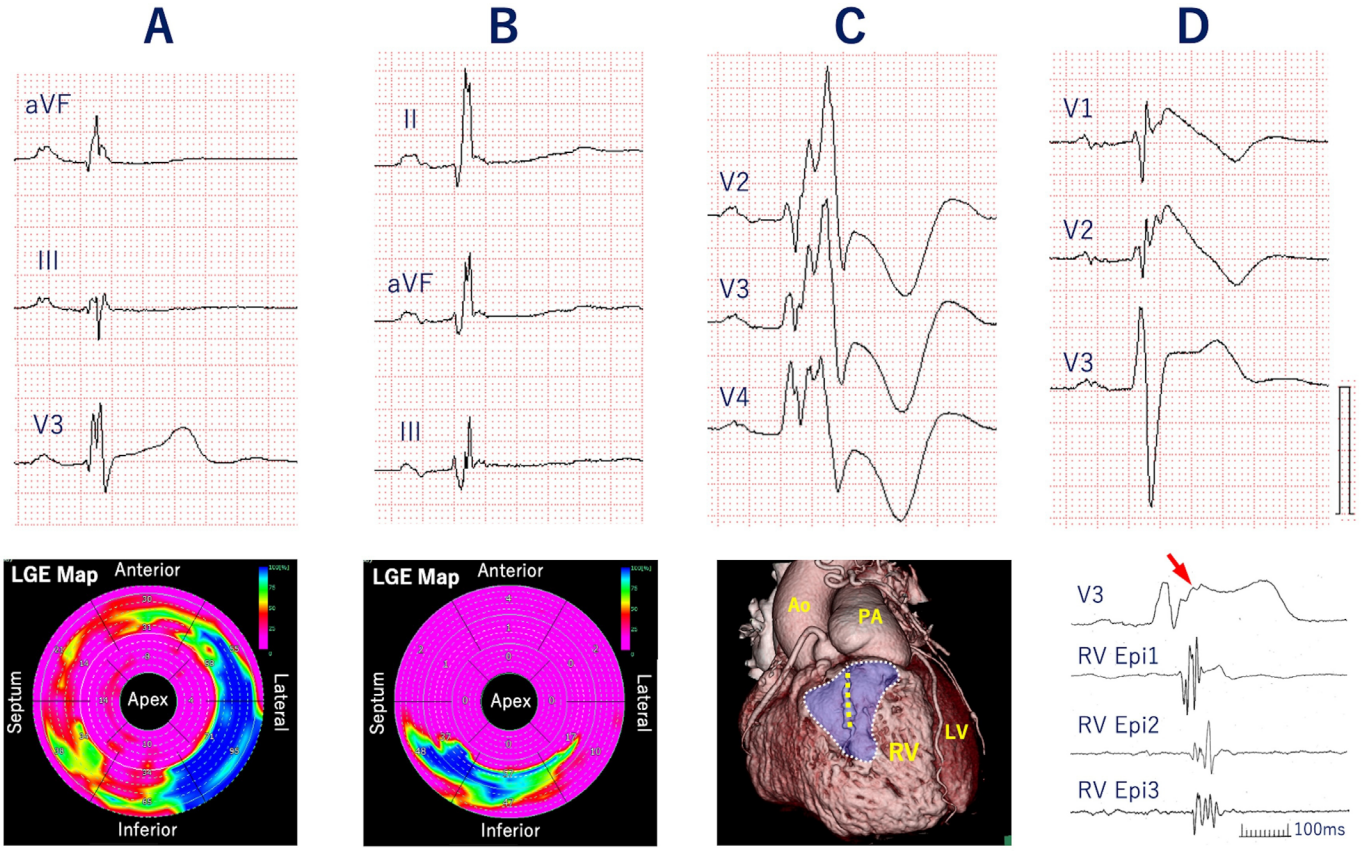

Figure 1 Cases with fragmented QRS (fQRS) in electrocardiograms. These panels show fQRS complexes in various diseases. Multiple spikes could be observed within the major QRS complex. Panels A and B show a patient with dilated cardiomyopathy and a patient with cardiac sarcoidosis, respectively. The upper panels show the ECGs with fQRS, and the lower panels display the late gadolinium enhancement (LGE) images (the blue areas indicate fibrosis) in cardiac magnetic resonance (MR) for each patient. Notably, fQRS is observed in leads corresponding to the areas of fibrosis (blue, green and yellow areas). Panel C shows a patient after surgery for tetralogy of Fallot. The lower panel displays the three-dimensional image obtained from CT. Blue area shows scar and suture lines and is an origin of fQRS. Ao, aorta; LV, left ventricle; PA, pulmonary artery; RV, right ventricle. Panel D shows a patient with Brugada syndrome who experienced ventricular fibrillation. The upper panel shows type 1 ECG with fQRS. The lower panel shows the local electrocardiograms obtained from the right ventricular outflow tract epicardium (RV epi), revealing localised fractionated potentials corresponding to fQRS observed in the 12-lead ECG. A red arrow shows fQRS at the end of the QRS complex.

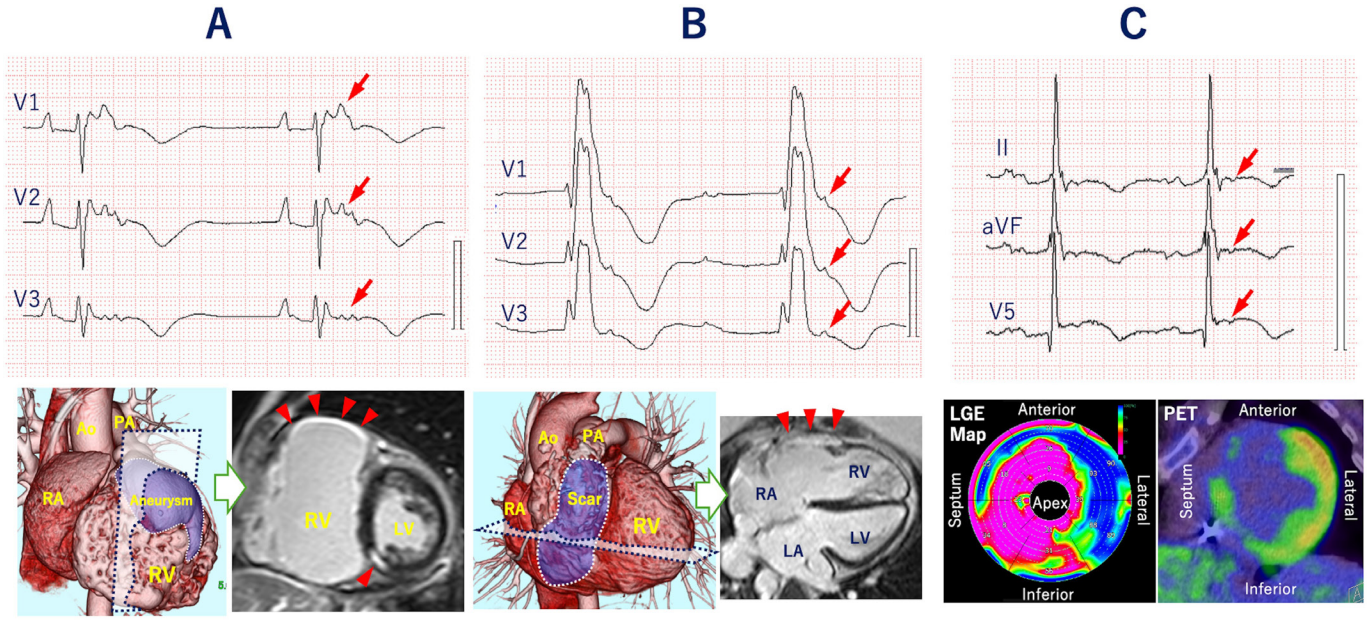

Figure 2 Cases with epsilon wave. Panels A and B show the ECGs (upper panel), the three-dimensional CT image (lower panel left) and the late gadolinium enhancement (LGE, arrow heads) in cardiac MRI (lower panel right) of arrhythmogenic right ventricular cardiomyopathy and postoperative tetralogy of Fallot, respectively. Both patients have extensive ventricular aneurysms or scars in the right ventricle, which are evident on MRI with LGE. Epsilon waves are observed in the V1–V3 leads (arrows), reflecting late potentials after major QRS complexes caused by the extensive ventricular aneurysms or scars. Panel C shows the ECG, the LGE map obtained by cardiac MRI (lower panel left) and positron emission tomography (PET)-CT of cardiac sarcoidosis. The LGE map (the blue area indicates fibrosis) and PET reveal extensive fibrosis and inflammation in the left ventricular lateral areas. Epsilon waves are observed in the leads corresponding to these areas (arrows).

The *epsilon wave*, first identified in patients with ARVC, appears as small deflections at the end of the QRS complex and reflects delayed conduction in the myocardium surrounded by inexcitable scar tissue, contributing to re-entrant circuits. It is also observed in cardiac sarcoidosis[14] and congenital heart diseases[11] and can predict ventricular tachyarrhythmias or SCD (figure 2).

Abnormal Q waves, poor R-wave progression and delayed QRS transition

Abnormal Q waves in myocardial infarction or cardiomyopathies indicate myocardial injury or scarring and are linked to SCD. Poor R-wave progression (PRWP) in precordial leads, another sign of myocardial scarring, occurs in 5.6% of the general population and is associated with all-cause mortality and SCD.[15] In coronary artery disease, PRWP increases the risk of SCD (HR 2.62).[16] Furthermore, precordial QRS transition, influenced by myocardial scarring, rotation, LV hypertrophy/dilation or conduction disturbances, increases the SCD risk by 2.14-fold.[17] These QRS abnormalities may promote lethal ventricular arrhythmias.

ECG indices associated with the repolarisation abnormality

Long and short QTc intervals

The QT interval is an indicator of cardiac repolarisation. Available population studies suggest that normal QTc values are between 350 and 450 ms in males and 360 and 460 ms in females.[18] A QTc cut-off value of 500 ms in congenital LQTS patients, at which the risk of arrhythmias is significantly increased, has been suggested (figure 3A–3C). It seems reasonable to also use this threshold for patients with acquired LQTS (figure 3D). Still, especially those patients with extremely short or prolonged QT intervals will be at the highest risk for arrhythmias. For short QT syndrome, this value would be <330 ms[18] (figure 3E and F).

Cardiac repolarisation is determined by the interplay between persistent inward sodium current (I_{Na}), slow inward calcium current ($I_{Ca\text{-}L}$) and outward potassium currents (I_{to}, I_{Kr}, I_{Ks}, I_{K1}). When these channels are subject to gain-of-function or loss-of-function influences (eg, due to drugs, mutations or changes in electrolyte levels), it can lead to delayed repolarisation or early repolarisation (ER), resulting in a longer action potential with a prolonged QT interval or a shorter action potential with a short QT interval. In prolonged QT interval, the prolonged duration of the plateau phase of the action potential allows for the reactivation of inward calcium channels, which can lead to early afterdepolarisations (EAD) and potentially result in arrhythmias such as torsades de pointes (TdP). T-wave alternans (TWA), a macroscopic alternative change of T-wave polarity in patients with LQTS, is a precursor of the TdP (figure 3G). The transmural action potential change or appearance of EAD might cause TWA.[19] In short QT interval, phase II re-entry associated with heterogeneous repolarisation or late phase III EADs triggers VF in ventricles with short refractory periods.[20]

QTc and JTc intervals

The QT interval consists of both depolarisation (QRS complex) and repolarisation (JT interval) components. Tikkanen *et al* reported that prolonged QRS durations and QTc intervals are associated with an increased SCD risk; however, the repolarisation component (JTc) appears to have no independent prognostic value.[21] Further research is required to confirm whether QTc prolongation reflects pure repolarisation abnormalities.

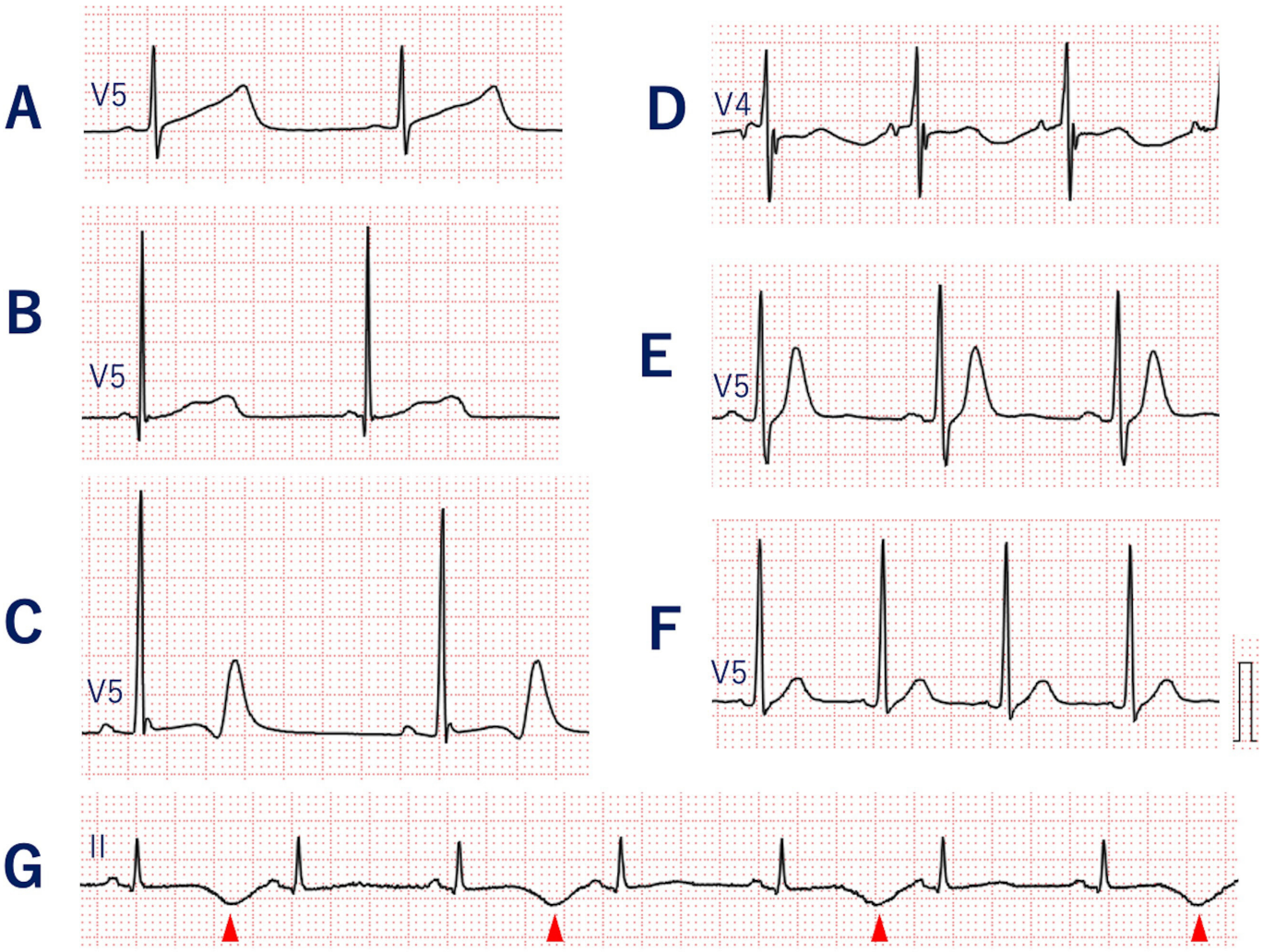

Figure 3 Cases with QT interval abnormalities. Panels A, B and C show the ECGs of congenital long QT syndrome type 1 (LQT1), LQT2 and LQT3, respectively. Each is characterised by distinct T-wave features: broad-based T waves for LQT1, low-amplitude and notched T waves for LQT2 and late-appearing T waves with a prolonged isoelectric ST segment for LQT3. Panels D and F show the ECGs of acquired long QT syndrome (ALQTS) and short QT syndrome, caused by hypokalaemia and hypercalcaemia, respectively. Panel E shows the ECG of congenital short QT syndrome. Panel G shows the ECG of ALQTS, caused by amiodarone. Notably, the ECG is characterised by alternative changes of T-wave polarity (T-wave alternans). Red arrows show deep negative T waves.

Prolonged T_{peak}-to-T_{end} interval

T_{peak}-T_{end} refers to the interval between the peak and the end of the T wave and is considered an indicator of transmural dispersion of repolarisation (TDR). It has been reported that the mean cut-off value was 103.3 ms for predicting arrhythmic or mortality outcomes.[22] Yan and Antzelevitch first proposed this in 1998, based on studies using arterially perfused canine ventricular wedge preparations. In this experimental model, the repolarisation of the epicardium that contains the shortest action potential coincides with the peak of the T wave, while the repolarisation of subendocardial M cells that have the longest action potentials coincides with the end of the T wave, thus making T_{peak}-T_{end} a measure of TDR[23] (figure 4). However, unlike isolated wedge preparations, the whole heart in vivo is more complex. While there is consensus that T_{peak}-T_{end} reflects a local dispersion of ventricular repolarisation, debate continues regarding whether the dispersion is transmural, global or a combination of both. The precordial leads measure the electrical field across the ventricular wall, leading to the belief that T_{peak}-T_{end} most represents TDR in these leads. T_{peak}-T_{end} and T_{peak}-T_{end} dispersion have been identified as indices prognostic of arrhythmic risk under many pathophysiological conditions, including general population,[24] inherited channelopathies (Brugada syndrome[25] and LQTS[26]), ischaemic heart disease,[22] HF[27] and resynchronisation therapy, cardiac sarcoidosis,[28] and HCM (figure 5).

Early repolarisation (J wave)

ER is classically recognised as an innocent ST elevation that usually appears in the precordial leads, and J waves frequently follow it. The definition of ER has been reconsidered as the presence of J waves themselves,[29] since the report of idiopathic VF by Haïssaguerre *et al*.[30] Now, classical ST elevation is not necessary for the diagnosis of ER. Two types of J waves have been recognised: notched and slur types (figure 6A and B). J waves exist at the end of the QRS complex and reflect an early repolarisation at phase I of action potential,[31] but delayed ventricular activation could also result in J waves.[32] Recently, idiopathic VF associated with J waves (ER) is called ER syndrome or J-wave syndrome,[31] and it is a relatively rare disease. However, the

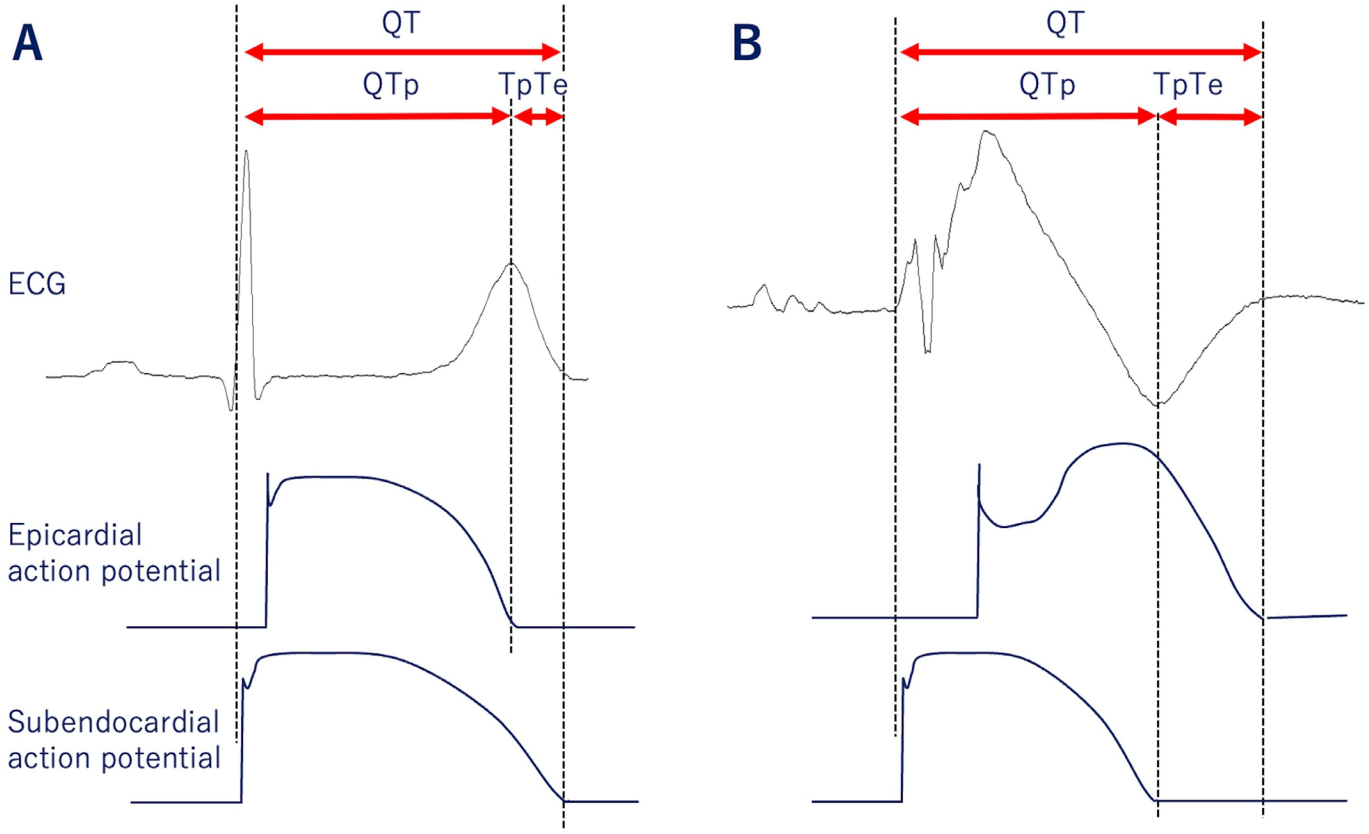

Figure 4 Measurement of T_{peak} to T_{end} (TpTe) interval on ECG and action potentials. Panel A shows a case of congenital long QT syndrome (LQT8). The TpTe interval is measured by the difference between QT interval and QT peak interval. TpTe interval indicates the transmural dispersion of repolarisation (TDR). Experimentally, the peak of the T wave represents the end of epicardial action potentials and the end of the T wave is coincident with subendocardial action potentials. Panel B shows a case of Brugada syndrome. The epicardial depolarisation is delayed, and the reduction in inward sodium current leads to a delayed phase II dome of action potential in the epicardium. Whereas changes in endocardial action potential are not significant. Then, the peak (bottom) of the negative T wave is coincident with the end of subendocardial action potential and the end of the T wave is the same as the timing of termination of the epicardial action potential. As a result, the TDR reverses and increases, and the Tpe interval is extended.

existence of J waves is associated with lethal arrhythmic events or SCD in the general population, and the relative risk in individuals with ER patterns is 1.7 for SCD.[31] It might include victims with ER syndrome, but most of the events could be caused by various situations (figure 6E and F): patients who have J wave before or at the onset of acute myocardial infarction[33] frequently experience ventricular tachycardia (VT)/VF events. Incidence of VT/VF is also higher in patients with old myocardial infarction and J waves. J waves could be associated with cardiac events in other various conditions. Observations from the general population and patients with ER syndrome have suggested malignant types of J waves, which can cause VT/VF or SCD, such as notched-type J wave (figure 6B), J waves followed by horizontal or downsloping ST segment[34] (figure 6C), tall J waves ≥0.2 mV[34] (figure 6D) and wide J waves. In contrast, sufficient verification has not been conducted, and it is difficult to identify a person at risk of SCD in the general population.

ST-T abnormalities

Several benign and pathological conditions can induce changes in repolarisation, which can be detected as an alteration of the ST segment or T wave. T-wave amplitude is usually upright in all leads except aVR and V1, with the greatest amplitude in V2 and V3. Mild T-wave inversion in V2 and inferior leads may be normal in young adults and women. T-wave abnormalities are frequently observed in various cardiomyopathies, mineral abnormalities and inherited arrhythmias and may represent early signs of underlying pathology. *T-wave inversion* is a useful diagnostic marker and indicator of sudden death risk (threefold higher in the general population).[35] The characteristic ST-T changes in some cardiomyopathies and inherited arrhythmias are presented below.

Arrhythmogenic right ventricular cardiomyopathy

ARVC typically involves the right ventricle, where normal myocardium is replaced by fatty infiltration and fibrosis, often causing SCD in young individuals and athletes. Inverted T waves in leads V1–V3 are the most important ECG abnormality and are thought to indicate repolarisation abnormalities in the RVOT.[36]

Brugada syndrome is an inherited channelopathy that can cause SCD. The high-risk type 1 ECG is characterised by ST elevation (>2 mm) followed by a negative T wave in the right precordial leads, which serves as a diagnostic criterion. Influenced by the autonomic nervous system, both diurnal variations and day-to-day fluctuations are observed.[31]

Congenital LQTS

Congenital LQTS is also inherited channelopathy, where the genetic subtype can often be predicted by analysing T-wave

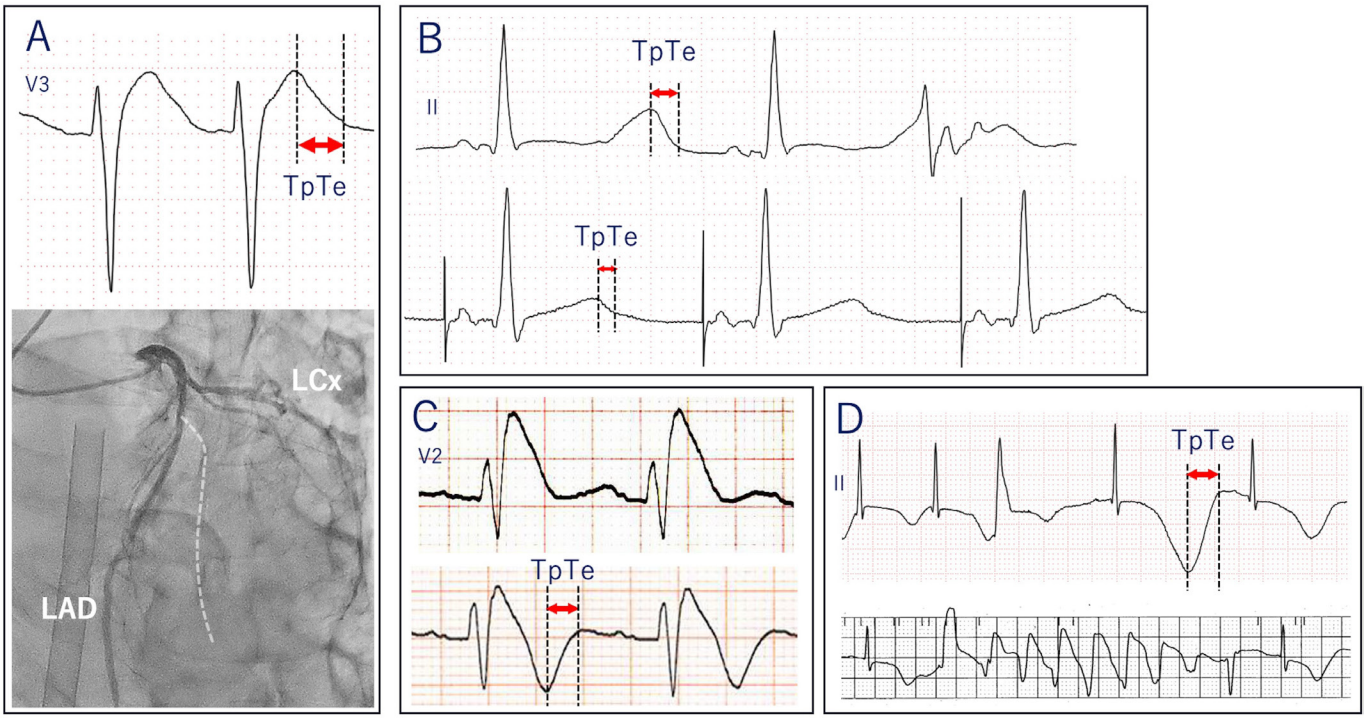

Figure 5 Extended T_{peak} to T_{end} (TpTe) intervals in the various diseases. (A) A patient with acute coronary syndrome with acute occlusion of a diagonal branch. This patient was resuscitated from ventricular fibrillation (VF). The ECG recorded in the emergency room shows a long TpTe interval (QT interval=313 ms, TpTe interval=188 ms). Lower panel shows occlusion of the first diagonal branch (white dot line). LAD, left anterior descending branch; LCx, left circumflex branch. (B) A patient with congenital long QT syndrome (LQT1). When the patient did not take beta-blockers, ECGs showed significant prolonged QT interval (711 ms) and TpTe interval (125 ms). After implantation of an implantable cardioverter-defibrillator and administration of a beta-blocker, QT and TpTe intervals are abbreviated (458 m and 69 ms, respectively). (C) A patient with Brugada syndrome. Upper panel shows an ECG recording immediately after the initial VF episodes. The negative T wave was eliminated, and the QT interval was abbreviated (315 ms), suggesting a marked abbreviation of epicardial action potentials. The lower panel shows an ECG recording of the next day. ECG demonstrates coved type ST elevation with negative T wave. QT interval was 473 ms and TpTe interval was 144 ms. (D) ECG recordings in a patient with Takotsubo cardiomyopathy. This patient had long-persistent atrial fibrillation. After the onset of the Takotsubo syndrome, maximum QT and TpTe interval were 877 ms and 244 ms, respectively (upper panel). This patient experienced polymorphic ventricular tachycardias during the acute phase (lower panel).

patterns: LQT1 is characterised by broad-based T waves, LQT2 by low-amplitude, notched T waves and LQT3 by late-appearing T waves with a prolonged isoelectric ST segment (figure 3A–3C).

The '*arrhythmic mitral valve*' has recently come into focus as a condition associated with SCD, regardless of the severity of mitral regurgitation. T-wave inversion and ST segment depression have been reported as high-risk ECG findings (figure 7). Specific mitral valve morphologies, such as mitral annular disjunction and redundant mitral leaflet, along with late gadolinium enhancement on cardiac MRI, or inflammatory changes observed on positron emission tomography-CT, have been identified as risk factors. For patients presenting with these features, Holter monitoring or, in some cases, continuous monitoring using an implantable loop recorder is recommended. In patients with rapid polymorphic ventricular tachycardia, implantable cardioverter-defibrillator implantation should be considered.[37 38]

ECG indices including both the repolarisation and depolarisation abnormalities

Wide frontal QRS-T angle

The spatial QRS-T angle is obtained by measuring the spatial angle between the major QRS and the T vectors. The QRS-T angle complements the ventricular gradient and can be effectively used to assess the abnormal depolarisation-repolarisation relationship (online supplemental figure 1A). In the Oregon Sudden Unexpected Death Study, which compared 666 SCD cases and 863 controls (average age 67 years), a frontal QRS-T angle >90° was linked to a 2.2-fold increased SCD risk, even after adjusting for multiple factors.[39] However, vectorcardiography is unfamiliar to even the cardiologist, and it might be challenging to use in daily clinical practice. QRS-T angle includes depolarisation and repolarisation information, which is usually recognised in the 12-lead ECG as a tall R wave followed by flat T waves or ST depression with negative T waves (online supplemental figure 1B).

Risk assessment for SCD using an ECG scoring model

The above ECG variables have been previously linked to an increased risk of SCD. However, the discriminative ability of individual ECG parameters is limited. To address this, an ECG risk score was established. It has been reported that individuals in the general population with four or more ECG abnormalities among six key indicators—heart rate, LVH, QRS transition zone, QRS-T angle, QTc and the T_{peak}-to-T_{end} interval—exhibit a significantly elevated risk of SCD, regardless of their LVEF. This approach is referred to as the six-variable ECG risk model.[40] Furthermore, monitoring dynamic changes in this risk model, especially concerning QTc and T_{peak}-to-T_{end} interval, may enhance the accuracy of SCD risk assessment.[41]

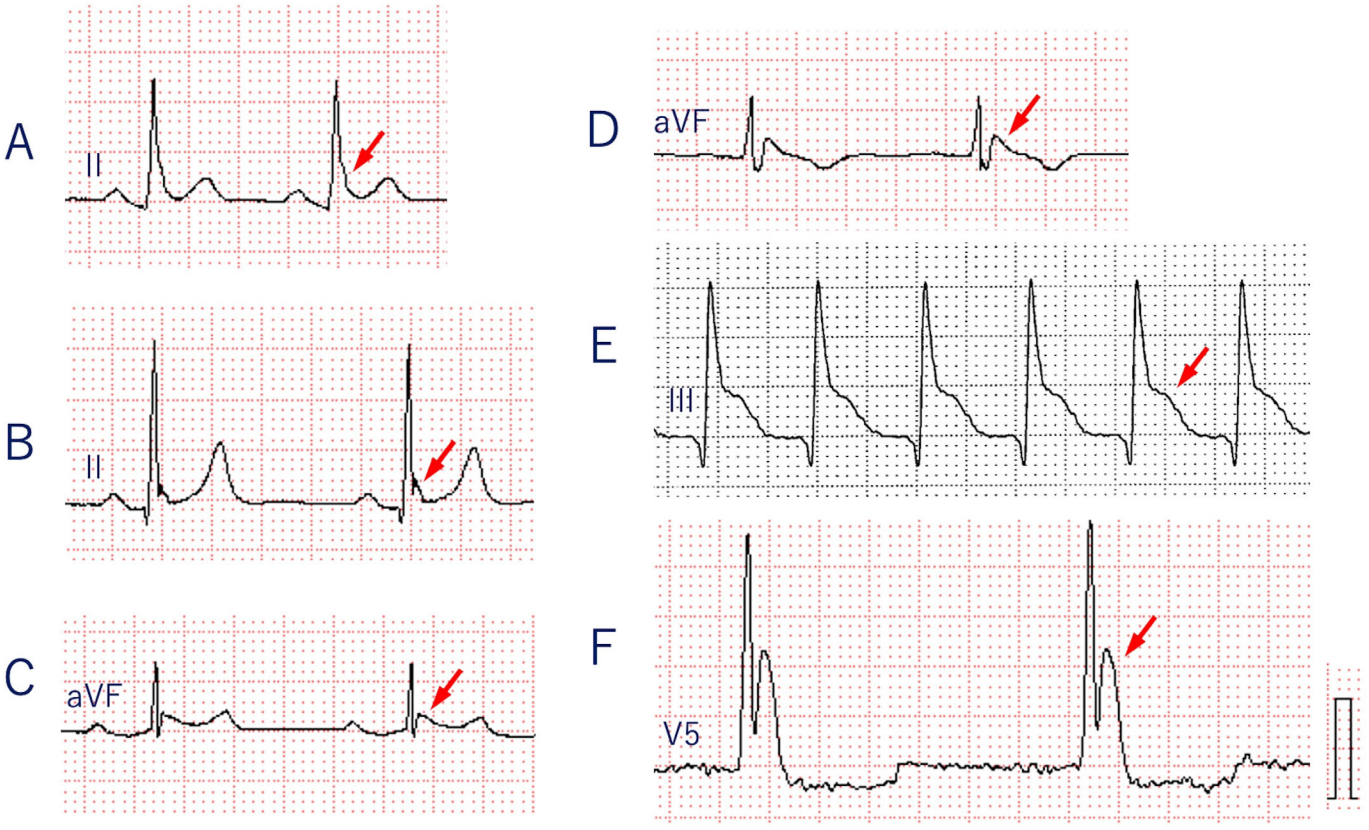

Figure 6 Cases with early repolarisation pattern (J waves). Panels A and B show the ECGs recorded in patients with early repolarisation syndrome (ERS). Panel A shows slur-type J wave and B shows notched-type J wave. Panel C shows an ECG recorded in a patient with Brugada syndrome who had a notched J wave and downsloping ST segment in the inferior leads. Panel D shows a young patient with ERS who has the type 1 Brugada ECG in the inferior leads but does not have the Brugada ECG in the precordial leads. Panel E is a resuscitated patient with acute coronary syndrome. Lambda wave or tombstone-like J-ST segment can be observed. Panel F shows a patient with severe accidental hypothermia with a body temperature of 24°C. Significant J wave, which is called the Osborn wave, is observed. Arrows show J waves in each patient.

Arrhythmias

Atrial fibrillation

It is reasonable that VT/VF is a precursor of SCD, but it is usually challenging to detect in people without any symptoms. On the contrary, AF is a common arrhythmia, especially in older people, with an increased risk of thromboembolism driving greater anticoagulant use over 10 years. Although thrombosis, bleeding, HF and cancer are leading causes of death in patients with AF, SCD is also significant, with a twofold to threefold higher risk compared with the general population.[42] The autonomic disturbance, cardiac channel variants, myocardial remodelling, myocardial infarction and pro-arrhythmic sequences by irregular rhythms could contribute to SCD in patients with AF.[43] In pre-excitation syndromes, such as WPW, the transition from AF to VF reportedly contributes to the risk of SCD (online supplemental figure 2A,B). Previously, an AF shortest R-R interval ≤250 ms and accessory pathway effective refractory period ≤270 ms were considered electrophysiological indicators for treatment. However, recent reports have suggested that SCD can occur in individuals without symptoms or with high-risk characteristics.[44]

Premature ventricular contractions

PVCs are generally benign in the absence of structural heart disease and can indicate an increased risk in affected patients. The Lown classification, primarily used for risk assessment after myocardial infarction, has also been applied to other cases. Polymorphic PVCs, runs of three or more, R-on-T-type PVCs and those with a short coupling interval have been associated with a higher risk. Recently, cases of VF induced by Purkinje-origin PVCs in patients without structural heart disease have been reported and have drawn increasing attention to the Purkinje system and microstructural abnormalities.[45]

Can artificial intelligence identify people who are at high risk?

ECG-based deep learning (DL) algorithms have been developed in recent years. ECG-based DL models have been successfully trained to detect various cardiac conditions, for example, LV dysfunction,[46] HCM[47] or to recognise patients at high risk for AF.[48] Unlike conventional ECG analysis, DL models do not require manual selecting and extracting of relevant features, enabling them to capture the entire ECG signal and achieve higher prediction accuracy.

An ECG-based DL algorithm has also been developed to assess the risk of SCD. While conventional ECG-based algorithms may contribute to SCD risk stratification, their predictive capabilities are generally moderate. The DL models developed using artificial intelligence (AI) are expected to improve predictive accuracy by using the entire digital signal. An ECG-AI model developed using data from community-based studies showed strong performance (area under the receiver operating characteristic curve (AUROC) 0.889) compared with the conventional six-variable ECG model (AUROC 0.712) for detecting SCD. In patients

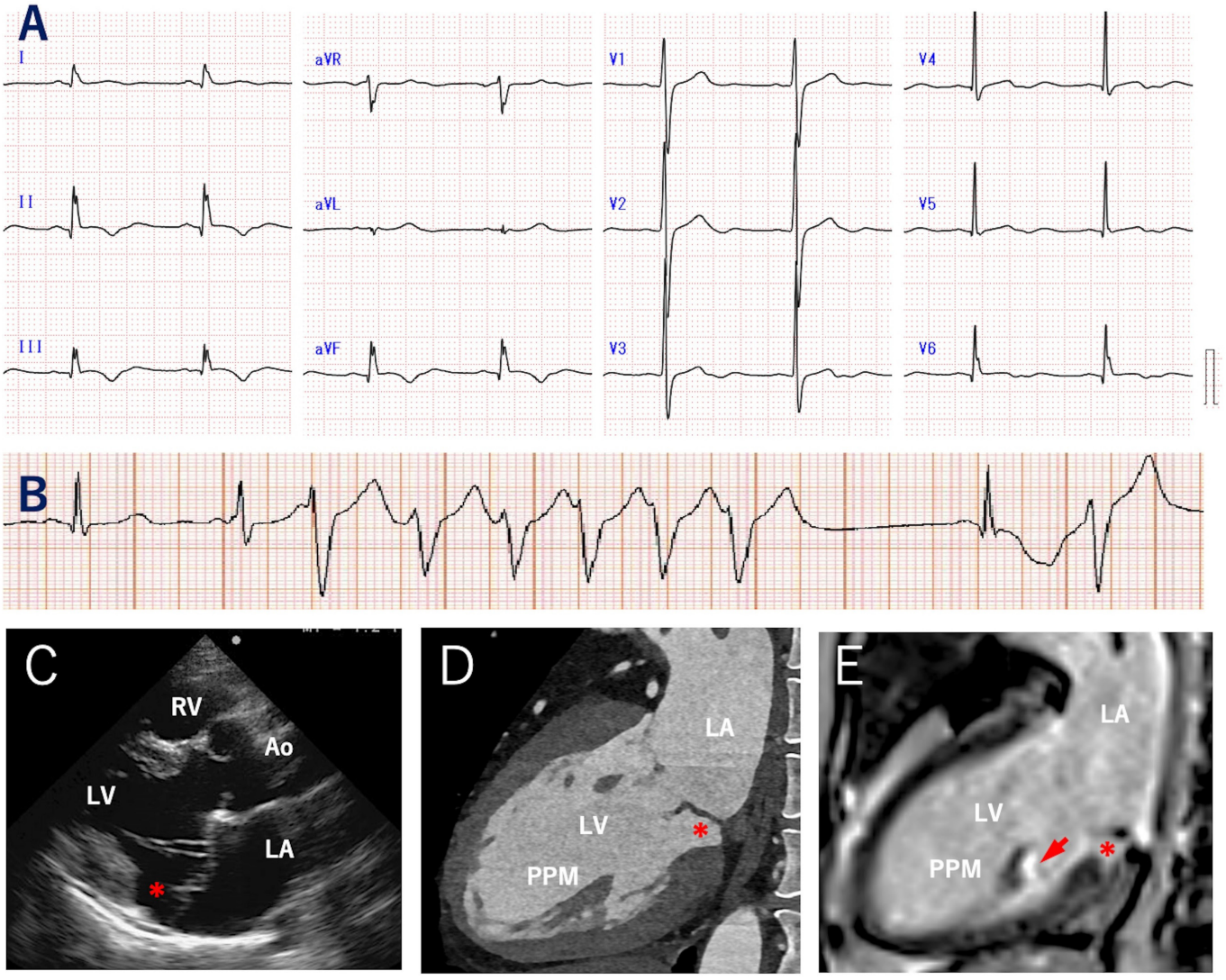

Figure 7 Mitral annular disjunction. (A) An ECG recorded in an adult patient with mitral annular disjunction (MAD) and mitral regurgitation. Negative T waves are observed in the inferior leads and V6. (B) An ambulatory ECG demonstrated non-sustained ventricular tachycardia in this patient. C–E show MAD in another patient with MAD. (C) Echocardiogram shows mitral valve prolapse with MAD (red star). (D) A cardiac CT also represents MAD. (E) Cardiac MRI shows late gadolinium enhancement was observed in the PPM (an arrow). Ao, aorta; LA, left atrium; LV, left ventricle; PPM, posterior papillary muscle; RV, right ventricle.

with HF, adding the ECG-AI index to classical guidelines also improved SCD discrimination.[49]

AI-ECG technology holds great promise but faces several challenges. Models are often trained on high-quality, curated databases, which limits their generalisability in routine clinical settings. External validation across diverse populations is needed, as factors like age, race and gender can influence results. Additionally, insufficient data can lead to overfitting, and large, diverse datasets are necessary for training and testing. AI-ECG also raises data privacy and security concerns, requiring robust measures to prevent cyberattacks. Moreover, even accurate predictions may not integrate well with basic patient information, reducing clinical value. A comprehensive evaluation of AI-ECG in clinical practice is essential.[50]

There are currently no large-scale interventional trials, such as the ECG AI-Guided Screening for Low Ejection Fraction (EAGLE) trial[46] for predicting low EF or the BEAGLE trial[48] for detecting AF, for DL models predicting SCD. Therefore, further evaluation is needed to determine their applicability in real-world clinical settings.

Implications of ECG findings in different populations

The performance of ECG in predicting SCD depends on the population at risk of SCD. Type 1 ECG (Brugada syndrome), significant QT prolongation (QT prolongation syndrome), low-voltage QRS (amyloidosis), negative T waves in extensive precordial leads (ARVC) or left BBB (cardiomyopathy) have relatively high disease specificity and require thorough investigation. Additionally, for patients with known high-risk diseases, close monitoring with attention to the appearance of high-risk findings is essential. ECG-AI models may improve the diagnostic accuracy of SCD risk in the future; however, further studies are needed to develop models that can be evaluated across races, sexes and ages, as well as determine how to combine them with clinical data.

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