**The Electrocardiogram in the Diagnosis and Management of Patients with Dilated Cardiomyopathy**

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**Abstract**

The term dilated cardiomyopathy (DCM) defines an heterogenous series of cardiac disorders which are characterized by left ventricular (LV) or biventricular dilatation and systolic dysfunction in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. In approximately one third of the cases, DCM is familial with a genetic pathogenesis and various patterns of inheritance. Although the ECG has been considered traditionally non-specific in DCM, the recently acquired knowledge of the genotype-phenotype correlations provides novel opportunities to identify patterns and abnormalities that may point toward specific DCM subtypes. A learned ECG interpretation in combination with an appropriate use of other ECG-based techniques such as ambulatory ECG monitoring and exercise tolerance test and imaging modalities, such as echocardiography and cardiovascular magnetic resonance, may allow the early identification of specific genetic or acquired forms of DCM. Furthermore, ECG abnormalities may reflect the progression of disease and provide a useful tool in risk stratification and management. In the present review, we discuss the current role of the ECG in the diagnosis and management of DCM. We describe various clinical settings where the appropriate use and interpretation of the ECG can provide invaluable clues, contributing to the important role of this basic tool as cardiovascular medicine evolves.

**Keywords:** Electrocardiogram; Dilated cardiomyopathy; Diagnosis; Management

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**INTRODUCTION**

Dilated cardiomyopathy (DCM) is currently defined by the presence of left ventricular (LV) or biventricular dilatation and systolic dysfunction in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment1. Dilated cardiomyopathy is an umbrella definition that encompasses multiple disorders where the myocardial abnormality is not related to coronary or valvular or congenital heart disease and cannot be explained by abnormal haemodynamic conditions. Besides being very generic, the term DCM may be downright inaccurate, as chamber dilatation is often absent: indeed, the term “dilated” has been recently questioned. This nosographic complexity builds on a significant genetic heterogeneity with mutations found to be linked to the disease in at least 50 different individual genes and a polymorphic clinical presentation with arrhythmias and heart failure being the most common manifestation1.

Recent technological advances in cardiovascular imaging and particularly the increasingly widespread use of cardiovascular magnetic resonance (CMR) offer an opportunity for deep phenotypic and aetiological definition through tissue characterization, allowing the identification of among others oedema, fibrosis or infiltration. Yet, in this complex landscape full of rapidly developing diagnostic technologies, the ECG retains an extremely powerful role in the assessment of patients with DCM, which can provide diagnostic red flags useful to orient the following phases of the diagnostic work-up, prognostic stratification criteria and information that can direct appropriate decision making.

In this review, we will discuss the several reasons why the ECG is still a paramount piece of the puzzle in diagnosis, risk stratification and management of DCM. Following an overview of abnormalities involving each segment of the ECG, individual diseases characterized by specific patterns are discussed in detail.

**METHODS**

The authors approached the topic formulating the research question: what is the role of ECG in diagnosis and management of DCM? Therefore a systematic search through the web-based engine Pubmed was conducted in order to identify all studies meeting the eligibility criteria. Most relevant studies answering the main research question were selected. Finally, results were presented systematically taking in account the complexity of the disease and the various aetiologic backgrounds.

**Systematic approach in ECG interpretation**

Electrocardiographic abnormalities characterize the majority of patients with DCM, with abnormal ECG features reported in more than 80% of the cases ((**Table 1**)2,3. Despite the traditional opinion that ECG abnormalities in DCM are non-specific, in contrast with other cardiomyopathies, such as hypertrophic cardiomyopathy (HCM) or arrhythmogenic right ventricular cardiomyopathy (ARVC), recent advances in the understanding of genotype-phenotype correlations provide the opportunity to recognize specific ECG patterns that are typical of certain genetic or acquired forms2. As the ECG is rarely normal in DCM, ECG abnormalities should trigger the initiation of a diagnostic work-up. However, when interpreting the ECG of patients with cardiomyopathies, the approach should be “cardiomyopathy-oriented”, i.e. abandoning classical concepts derived from the world of ischemic and hypertensive heart disease, and focus on specific “red flags” (**Table 2**) that should be carefully integrated in the broader clinical and familial context.

P wave

Atria are often dilated in DCM, reflecting raised filling pressures and/or associated valvular abnormalities. This may be reflected on the ECG with P wave changes suggestive of left and/or atrial enlargement4. While isolated right atrial enlargement is uncommon2,3,5, left atrial enlargement is seen in a variable proportion of patients and is often a considered a marker of long-standing disease2,3,5,6. Atrial fibrillation (AF) is part of the final common pathway for all forms of DCM following progression to heart failure. Early onset of AF in young individuals, however, may suggest specific DCM aetiologies, mainly of genetic origin7 (**Table 2**).

PR interval

First-degree and/or advanced atrio-ventricular (AV)-blocks can be found in patients with DCM1; conduction abnormalities , especially in young patients, suggest a specific genetic background often associated with neuromuscular diseases, laminopathy or ion channel disorder. Conduction abnormalities are also relatively common in acquired conditions such as cardiac sarcoidosis and Chagas disease8.

The QRS complex

Loss of vital myocardium and diffuse LV fibrosis may both lead to reduced QRS amplitude, especially in the precordial leads2,5,9. Low QRS voltages may also reflect fat infiltration, such as in arrhythmogenic cardiomyopathy due to desmosomal gene mutations, with involvement of the left as well as of the right ventricle8,10. When left ventricular hypertrophy (LVH) voltage criteria (either Sokolow-Lyon or Cornell) are met in patients with DCM, a hypertensive aetiology should be excluded 2,5,11.

Left bundle branch block (LBBB) is found in roughly one third of patients with DCM12, sometimes preceding the structural phenotype, and carries an adverse prognostic value; LBBB can be the result of a discrete lesion within the his bundle, as suggested by Narula et al.13, explaining why pacing at the distal His bundle can improve electrical end echocardiographic desynchronization in patients with LBBB14. Many patients with a diagnosis of LBBB have a combination of left ventricular hypertrophy and left anterior fascicular block rather than true LBBB15. True LBBB should be diagnosed if QRS duration is ≥140 ms (130 ms in women), there is a QS or rS pattern in V1-V2 and mid-QRS notching or slurring in ≥2 of leads V1, V2, V5, V6, I, aVL. After cardiac resynchronization therapy, this morphology is associated with a better echocardiographic response and survival than other intraventricular delays16.

Right bundle branch block (RBBB) is generally uncommon in patients DCM (2-6%)2,3,5 but it is frequently found in patients with neuromuscular disease due to pathogenic variants in the dystrophin gene17.

Q waves

The lack of consensus regarding the definition of a pathological Q wave, with multiple proposed diagnostic criteria, constitutes a source of confusion. Q wave duration ≥40 ms or an absolute depth of >3 mm are considered pathological criteria by some, whereas others recommend an amplitude ≥25% of the ensuing R wave4. Q waves may be observed in DCM in the absence of ischemic heart disease and are more common in the anterior and lateral leads2,3. As discussed below, cardiac involvement in muscular dystrophies is often characterized by posterior or inferior Q waves which reflect transmural myocardial fibrosis18.

ST segment/T wave abnormalities

Repolarization abnormalities are common in DCM, and generally reflect LV impairment. T wave inversion (TWI) especially in the lateral leads is a recognized feature of certain genetic forms (for example Filamin C or desmosomal disease)19. In contrast to hypertrophic cardiomyopathy, where striking repolarization abnormalities (such as deep TWI especially in the lateral leads) are common, the TWI in DCM is less deep and not associated with voltage criteria for LVH20,21.

The QT interval

The QTc interval is generally normal in DCM. A short QT interval has been associated with primary carnitine deficiency which may cause DCM22. QT variability at prolonged monitoring has been shown to be of potential use in sudden cardiac death (SCD) risk stratification in patients with DCM23.

Ventricular premature beats (VPBs)

Ventricular premature beats (VPBs) may be found in up to 40% of patients with DCM24. Frequent VPBs may promote LV systolic dysfunction and in some cases it may be challenging to establish whether VPBs are the main driving force of LV systolic dysfunction (tachycardiomyopathy), an arrhythmic manifestation of an underlying cardiomyopathy or an innocent by-stander. There is no consensus regarding the burden of VPBs considered to be sufficient to cause LV systolic dysfunction, however a high burden has been variably defined as ranging from >10 000 to 25 000 VPBs/day and as >10% to 24% of total heart-beats during the 24 hours25. The type and not only the burden of VPBs is relevant in the differential diagnosis between forms of DCM. Moreover, certain VPBs morphologies are commonly identified in athletes and are considered benign. These include infundibular and fascicular morphologies. On the contrary, other morphologies of VPBs such as LBBB/intermediate or superior axis or RBBB/intermediate or superior axis and wide QRS may be a sign of underlying myocardial disease26.

An “arrhythmogenic” subset of genetic DCM, epitomized by lamin A/C and desmosomal forms of DCM is characterized by complex and polymorphic ventricular arrhythmias (including frequent VPBs) early in the course of the disease, heralding increased risk of sudden cardiac death. The presence VPBs and/or of NSVT does not generally dictate the choice of protecting a patient with DCM-phenotype with an implantable cardioverter defibrillator (ICD) in primary prevention. However, the presence of frequent arrhythmias, especially if associated with pathogenic variants in desmosomal genes and/or myocardial fibrosis at cardiovascular magnetic resonance (CMR), may suggest a high risk of SCD and therefore an ICD should be considered in this setting.

The development of ventricular arrhythmias at the exercise tolerance test (ETT), including an increase in VBPs or development of NSVT during exercise may be a sign of an arrhythmogenic phenotype with underlying desmosomal pathogenic variants.

Supraventricular arrhythmias

The identification of AF through ambulatory monitoring is an important aspect of management of DCM and may dictate important choices as commencement of anticoagulation therapy for stroke prevention1. The detection of paroxysmal supraventricular arrhythmias in young patients with DCM should prompt investigation for familial LMNA cardiomyopathy7.

In summary, from a practical standpoint, when approaching a patient with unexplained LV dilatation and/or systolic dysfunction, a systematic analysis of the ECG from the beginning of the P wave to the end of the T wave may provide invaluable clues that may point toward the diagnosis of specific subtypes with implications for management and prognosis.

**The ECG in specific genetic forms of DCM**

Some ECG features are clues of specific genetic DCM subtypes, as certain disease-causing genes are associated with characteristic ECG abnormalities28 (**Table 2 and Figure 1**) which may have diagnostic as well as prognostic value for the patients and their relatives. For example, pathogenic variants in certain genes (Lamin A/C, Filamin C, desmosomal genes and Phospholamban) may express an arrhythmogenic phenotype, which should lead to early decisions on implantable cardioverter defibrillator (ICD) in primary prevention. In the following lines we describe ECG patterns in some of the most common DCM associated genotypes.

Titin (TTN)

Truncating variants in the gene for the sarcomeric protein titin (TTN) have been identified as the most common genetic cause of DCM and found in 10 to 20% of cases29. A typical ECG pattern of patients harbouring pathogenic variants in TTN has not been described. A recent study30 on one of the largest cohorts to date, showed that patients with TTN truncating variants had a higher prevalence of AF and ventricular arrhythmias than DCM patients with other aetiologies, while the prevalence of LBBB and conduction abnormalities was lower.

Lamin A/C (*LMNA*)

*LMNA* variants are found in up to 8% of DCM cases31. Early conduction disease, manifesting as sinus bradycardia, sinus node arrest, AV-blocks (first or second degree AV-block, later progressing to complete heart block) or LBBB are relatively common in this form of DCM1. Such findings often precede the development of an overt dilated phenotype **(Figure 1A)**. These patients exhibit a high prevalence of supraventricular arrhythmias, in particular AF (present in almost half of the patients at their first presentation), but also atrial flutter and atrial tachycardia32. Frequent VPBs and episodes of non-sustained ventricular tachycardia (NSVT) may also be found at the ECG or at ambulatory monitoring. Risk of sudden cardiac death and progression to refractory heart failure is consistently high is this genetic subset.

Similar to the *LMNA* variants, variants in the emerin gene (*EMD* or *STA*), responsible for Emery-Dreifuss muscular dystrophy, frequently lead to conduction disturbances33 and supraventricular arrhythmias34.

Filamin C (*FLNC*)

Filamin C is an intermediate filament that cross-links polymerized actin, contributing in anchoring cellular membrane proteins to the cytoskeleton. *FLNC* variants account for about 4% of DCM cases19,31,35. Repolarization abnormalities, especially TWI in the precordial or in the inferolateral leads are a common finding in patients with *FLNC* variants21. Approximately 25% of carriers show low voltages in the limb leads21 **(Figure 1B)** and frequent VPBs and NSVT are common21.

Dystrophin (*DMD*)

The Dystrophin gene is located on the short arm of the X chromosome and shows an X-linked pattern of inheritance. Cardiac involvement is present in approximately 90% of the cases of Duchenne’s muscular dystrophy and 70% of Becker’s muscular dystrophy1. The ECG in DCM due to *DMD* pathogenic variants classically mimics a posterior, inferior and/or lateral myocardial infarction, with abnormal Q waves in leads I, aVL and V6 or in leads II, III and aVF, associated with high voltage R waves in leads V1 and V2 which is due to the progressive accumulation of a transmural scar in the posterolateral region of the LV36 **(Figure 1C)**. Short PR interval and sinus tachycardia are also frequent, along with right axis deviation and RBBB37.

Desmin (*DES*)

Desmin is a cytoskeletal protein which forms muscle-specific intermediate filaments.

Pathogenic variants in the gene encoding Desmin cause a wide spectrum of phenotypes of

different cardiomyopathies, skeletal myopathies, and mixed skeletal and cardiac

myopathies. Desmin mutations account for 1–2% of all cases of DCM1. ECG abnormalities are common in this setting (up to 60% of the cases)38. Conduction abnormalities are frequently observed (AV-blocks and RBBB), followed by supraventricular and ventricular arrhythmias38.

Cardiac sodium channel type 5 α-subunit (*SCN5A*)

SCN5A encodes the major sodium channel expressed in the heart. Variants in SCN5A gene have been associated with primary arrhythmia syndromes, including the long QT and Brugada syndromes and missense variants have been described also in familial DCM. *SCN5A* variants lead to various phenotypical expressions, including isolated conduction defects, NSVT and familial, early-onset AF which may be associated with LV systolic dysfunction42,43**(Figure 1D)**.

Desmosomal genes

Although desmosomal variants have been historically associated with ARVC, this disease has been recently shown to affect the left ventricle (LV) not only at the end stage but also as a primary target8,19. A recent study reported desmosomal genes pathogenic variants in 3.5% of patients with DCM19. The ECG in patients harbouring variants in desmosomal genes may be characterized by low voltages on both limb and precordial leads, delayed ventricular depolarization and repolarization abnormalities including TWI that may extend to the lateral leads (V5-V6)39 **(Figure 2).** Low voltages are due to the typical subepicardial distribution of fibrofatty replacement within the LV, often circumferential, preventing electrical transmission from the inner layers. Patients with DCM harbouring desmosome gene variants often develop ventricular arrhythmias and are at risk of sudden cardiac death19.

RNA-binding motif 20 (RBM20)

RBM20 is an RNA binding protein expressed highly in both atria and ventricle involved in alternative splicing process. DCM in RBM20 variants is frequently associated with early onset, severe heart failure, and arrhythmic potential1. Although RBM20 mouse models showed a prolonged PR and heart rate–corrected QT interval, these features are not exhibited in humans and a typical ECG pattern has not been described. A genetic diagnosis is important as a distinct propensity to sustained ventricular arrhythmias has been observed in patients harbouring RBM20 variants40.

Phospholamban *(PLN)*

The PLN gene encodes phospholamban, a protein responsible for inhibition of sarco-/endoplasmic reticulum Ca2+ –ATPase (SERCA) function. Variants in the PLN gene

result in increased SERCA inhibition with defective calcium reuptake, with consequent

reduction in contractility and DCM phenotypic expression. In some DCM cohorts, especially in The Netherlands and in Germany (due to founder mutations), the prevalence of PLN variants is high. Typical ECG features are low QRS complex potentials and decreased R wave amplitude, mainly in anterior-lateral precordial leads41.

In summary, the genetic background of DCM may be complex and the ECG may suggest specific genetic abnormalities. ECG “red flags” may indeed point toward particularly aggressive genetic forms which would require specific management, such as ICD implantation in primary prevention at an early stage of the disease.

**The ECG in other cardiomyopathies with dilated-hypokinetic phenotype**

Left ventricular or biventricular dilatation and systolic dysfunction is a common final result of various disease processes. Cardiomyopathies characterized by myocardial infiltration or by LV hypertrophy at an initial stage may progress toward LV dilatation and dysfunction. Typically cardiac amyloidosis (especially the AL form) may be characterized by significant reduction of the QRS voltages, a feature that may be shared also by hypertrophic cardiomyopathy in the so called “burn-out” phase. While this electrocardiographic sign reflects significant infiltration in cardiac amyloidosis, it underlies high myocardial fibrosis burden in HCM20.

**The ECG in non-genetic forms of DCM**

A number of chemical compounds can induce DCM, the most common of which are chemotherapeutic agents, cocaine and alcohol. Inflammation and auto-immune response can result in particularly malignant forms of DCM12. Although specific ECG features are often absent, it is possible to recognize some patterns in these acquired forms of DCM (**Table 3**).

Inflammatory cardiomyopathies

Acute myocarditis may result in chronic inflammation and evolution to DCM in a variable proportion of patients44. The spectrum of ECG features in DCM resulting from previous myocarditis is wide and often non-specific. However, especially in the acute inflammatory phase, low-voltages (reflecting concomitant pericardial effusion or myocardial fibrosis), conduction abnormalities (especially in myocarditis due to Lyme disease), lateral TWI, increased QRS duration and frequent VPBs or NSVT might be present45 **(Figure 3A)**. A specific form of inflammatory cardiomyopathy is Chagas disease, caused by the parasite Trypanosoma cruzi and common in South America and Central America. Chagas disease is characterized by conduction system abnormalities, most commonly RBBB with left anterior fascicular block and AV-blocks46.

A clinically manifest cardiac involvement with LV or biventricular systolic dysfunction with or without chamber enlargement occurs in approximately 5% of patients affected by systemic sarcoidosis, but a silent disease is far more common, according to autopsy studies47. The most common ECG manifestations are abnormalities in the conduction system, such as AV blocks, bundle branch blocks and fascicular blocks48,49 **(Figure 3B)**. Unexplained advanced AV-blocks in young individuals, especially if associated with LV systolic dysfunction should raise the suspicion of cardiac sarcoidosis50. Frequent VPBs and non-sustained or sustained ventricular tachycardia are also common, and might be the first presentation of the disease51.

Tachycardia-induced cardiomyopathy

Tachycardia-induced cardiomyopathy (TIC) is defined as the reversible impairment of ventricular function with or without chamber dilatation induced by persistent arrhythmia12. Both atrial and ventricular arrhythmias may cause or at least promote LV or biventricular systolic dysfunction. The exclusion of underlying structural heart disease may be challenging as current imaging techniques, for example CMR, cannot easily identify diffuse fibrosis which may be a substrate for arrhythmias. In this setting the ECG (and prolonged ECG monitoring) may provide useful insights in the diagnosis **(Figure 3C)**. For example the demonstration of high VPBs burden or of atrial arrhythmias especially if poorly controlled in terms of heart rate may suggest TIC where a timely diagnosis is important given the potential for recovery with appropriate treatment25.

DCM caused by drugs and toxins

A series of drugs and toxins can cause DCM. Anthracyclines and several other agents used for oncologic treatment may be toxic for the heart resulting in a clinical picture that is generally characterized by LV systolic dysfunction with or without LV dilatation, often without a specific ECG pattern. Prolonged QTc interval and decreased QRS voltages have been shown to correlate with LV systolic dysfunction52 **(Figure 3D)**. The burden of arrhythmia in patients with anthracycline-related cardiomyopathy is not different from patients with other forms of DCM53.

The relationship between alcohol intake and heart failure is influenced by various genetic and environmental factors. The diagnosis of alcoholic DCM is based on a history of heavy alcohol intake (>80–100 g/day for >10 years) in combination with otherwise unexplained cardiomyopathy54. On ECG, non-specific abnormalities like complete or incomplete left bundle branch block, atrio-ventricular conduction disturbances, alterations in the ST segment can be found comparable to those of idiopathic DCM55.

Cocaine and methamphetamines are sympathomimetic drugs that induce heightened inotropic and chronotropic effects. The effects on the heart are multiple, including coronary vasospasm and atherosclerosis and LV systolic dysfunction. Although in the acute setting ECG ischemic changes are often present, specific ECG patterns are often absent in the chronic phase.

**Differential diagnosis with cardiac adaptation to exercise**

Long-term athletic training is associated with a series of alterations in cardiac structure, function and electrical activity and chamber dilatation is commonly observed especially in endurance athletes56. Significant LV dilatation in athletes may pose a challenge in the differential diagnosis with DCM . Recent international recommendations for ECG interpretation in athletes underscore which abnormalities should be considered as reflective of physiological adaptation to exercise and which instead should be regarded as highly suggestive of pathology4. While isolated voltage criteria for LVH or left axis deviation are highly suggestive of a normal process, low voltages, LBBB, repolarization abnormalities and pathological Q waves are more likely expression of DCM. Although sinus bradycardia and first-degree AV block are normal findings in athletes, extreme bradycardia (< 30 bpm) and advanced AV blocks suggest a pathologic process and should be further investigated.

In summary, unexplained dilatation and or systolic dysfunction is a description of a phenotype, but not a diagnosis. Although DCM may be genetic/familial in up to 25% of the cases1, secondary causes should be excluded. In this context, a correct ECG interpretation in conjunction with a detailed personal and family history may provide useful clues in the final diagnosis. A correct identification of a possible secondary process underlying the LV systolic dysfunction, is relevant as in some cases, the LV systolic dysfunction may be reversible after specific treatment.

**The standard ECG for risk stratification**

DCM is a dynamic condition and ECG abnormalities reflect the natural history of the disease. The presence of LBBB at baseline has been reported as an independent predictor of worse outcomes (all-cause mortality and SCD) in patients with severely impaired systolic function57. Moreover, a significant proportion of patients develop a new-onset LBBB during follow-up, which likewise is a strong and independent predictor of all-cause mortality58. Selection of patients who may potentially benefit from CRT is based on the severity of their LV systolic dysfunction, of their symptoms (as assessed by NYHA class), and most importantly, ECG criteria indicative of ventricular dyssynchrony. In general terms, current European and American guidelines recommend CRT in symptomatic HF patients (NYHA class ≥II) with an EF of ≤35%, left bundle branch block (LBBB), and a QRS duration of ≥150 msec59,60. Although patients with LBBB are more likely to respond to CRT compared to patients with right bundle branch block (RBBB) or non-specific interventricular conduction delay61, both these guidelines also state that CRT should be considered in non-LBBB with QRS ≥150 msec. American guidelines widen their indication for CRT to include patients with ischemic cardiomyopathy and NYHA class I symptoms with an EF of <30% and LBBB with a QRS duration of ≥150 msec60. A wider QRS has also emerged as a predictor of ventricular arrhythmias57,62 and, more interestingly, has been independently associated with early (< 6 months) arrhythmic events65.

The impact of new-onset arrhythmias is also relevant for DCM prognosis. Atrial fibrillation (both at baseline and development during follow-up) has been associated with poor long-term survival and need for heart transplantation in patients with DCM66.

Fragmentation of the QRS complex (i.e. the presence of notching of the QRS or an additional R wave) carries a higher risk for major ventricular arrhythmias and major adverse cardiac events64,67–70. More recently, low QRS amplitude and anterolateral T wave inversion emerged as independent predictors of major ventricular arrhythmias and SCD in patients with DCM 2,45. Merlo et al.2 recently showed that specific ECG features, including T-wave inversion in antero-lateral leads, left ventricular hypertrophy (according to Sokolow-Lyon criteria) and higher heart rates are predictors of heart transplant and death.

Although many ECG features may underlie a propensity for potentially fatal cardiac arrhythmias, none of these are included in the recommendations for ICD implantation in primary prevention, which are still based on LV ejection fraction and NYHA class only71.

**Clinical implications**

A learned ECG interpretation is extremely valuable when approaching patients with unexplained LV systolic dysfunction and/or LV dilatation. A systematic approach to ECG interpretation may reveal features pointing toward specific forms of DCM with implications on clinical management. Certain ECG “red flags” may suggest to look beyond the echocardiogram and to request additional tests as CMR, Holter monitoring and ETT, avoiding an LV ejection fraction- centred approach **(Central Illustration)**.

**Gaps in evidence and future suggestions**

Most studies on ECG in DCM are single center retrospective studies. Despite the rapid increase in the understanding of the genotype-phenotype correlations in DCM and the role of the ECG in this context, the knowledge on the modifications of the ECG during the natural history of the disease is still partial. As the definition of DCM is based mainly on structural features as LV dilatation and systolic dysfunction, clinical research has focused mainly on imaging tools as echocardiography and more recently CMR. Future studies should include ECG data systematically in order to identify possible additional roles of the ECG in the diagnosis and risk stratification of the disease.

**CONCLUSIONS**

The ECG is a cornerstone in the diagnosis and management of cardiomyopathies. While traditionally the ECG was considered non-specific in DCM, a deeper understanding of the genotype-phenotype correlations and of the complex aetiological background underlying the DCM phenotype, increasingly reveals ECG patterns and “red flags” that provide the opportunity to early identify or suspect specific genetic and acquired forms. A “cardiomyopathy oriented” ECG interpretation in the setting of patients exhibiting LV or biventricular systolic dysfunction may suggest clinical scenarios requiring a specific approach in terms of clinical management. For example the finding of just a mild LV systolic dysfunction at echocardiography in a young patient may wrongly reassure the clinician. In fact if this feature is combined with certain ECG “red flags” such as AV blocks and/or atrial fibrillation, a laminopathy should be excluded; if instead the ECG exhibits low voltages and TWI in the lateral leads a desmosomal disease should be suspected with major implications not only for the patient but also for first-degree family members who may potentially at risk. A learned ECG interpretation combined with a wise use of the most advanced imaging techniques and genetic testing is extremely useful in the approach to patients where clinical management is often complex, despite continuous developments in cardiovascular medicine.

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**Table 1.** Main ECG features in DCM.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ECG feature** | **Number** | **Males (%)** | **mean LVEF (%)** | **Prevalence (%)** |
| **LVH\*** |  |  |  | **17-69** |
| Roberts et al., 19875 | 152 | 72 | - | 39 |
| Momiyama et al., 199411 | 45 | - | - | 69 |
| Merlo et al., 20192 | 414 | 71 | 32 | 17 |
| **LA enlargement** |  |  |  | **17-51** |
| Roberts et al., 19875 | 152 | 72 | - | 35 |
| Wilensky et al., 19883 | 56 | 82 | - | 51 |
| Kamiyama et al., 19976 | 41 | 71 | - | 51 |
| Merlo et al., 20192 | 414 | 71 | 32 | 17 |
| **LBBB** |  |  |  | **23-28** |
| Grimm et al., 200372 | 343 | 78 | 31 | 28 |
| Merlo et al., 20192 | 414 | 71 | 32 | 23 |
| **Abnormal Q waves** |  |  |  | **26-36** |
| Wilensky et al., 19883 | 56 | 82 | - | 36 |
| Merlo et al., 20192 | 414 | 71 | 32 | 26 |
| **AF** |  |  |  | **3-25** |
| Roberts et al., 19875 | 152 | 72 | - | 25 |
| Wilensky et al., 19883 | 56 | 82 | - | 14 |
| Aleksova et al., 201066 | 539 | 73 | 30 | 10 |
| Merlo et al., 20192 | 414 | 71 | 32 | 3 |
| **First degree AV-block** |  |  |  | **10-23** |
| Hamby et al., 18689 | 60 | - | - | 18 |
| Roberts et al., 19875 | 152 | 72 | - | 23 |
| Merlo et al., 20192 | 414 | 71 | 32 | 10 |
| **Inferior T wave inversion** |  |  |  |  |
| Merlo et al., 20192 | 414 | 71 | 32 | 14 |
| **Anterolateral T wave inversion** |  |  |  |  |
| Merlo et al., 20192 | 414 | 71 | 32 | 13 |
| **RBBB** |  |  |  | **2-6** |
| Roberts et al., 19875 | 152 | 72 | - | 6 |
| Wilensky et al., 19883 | 56 | 82 | - | 6 |
| Merlo et al., 20192 | 414 | 71 | 32 | 2 |
| **RA enlargement** |  |  |  | **3-6** |
| Roberts et al., 19875 | 152 | 72 | - | 6 |
| Wilensky et al., 19883 | 56 | 82 | - | 3 |
| Merlo et al., 20192 | 414 | 71 | 32 | 4 |
| **Abbreviations:** AF: atrial fibrillation; AV: atrio-ventricular; LA: left atrial; LBBB: left bundle branch block; LVH: left ventricular hypertrophy \*based on Sokolow-Lyon or Cornell voltage criteria; RA: right atrial | | | | |

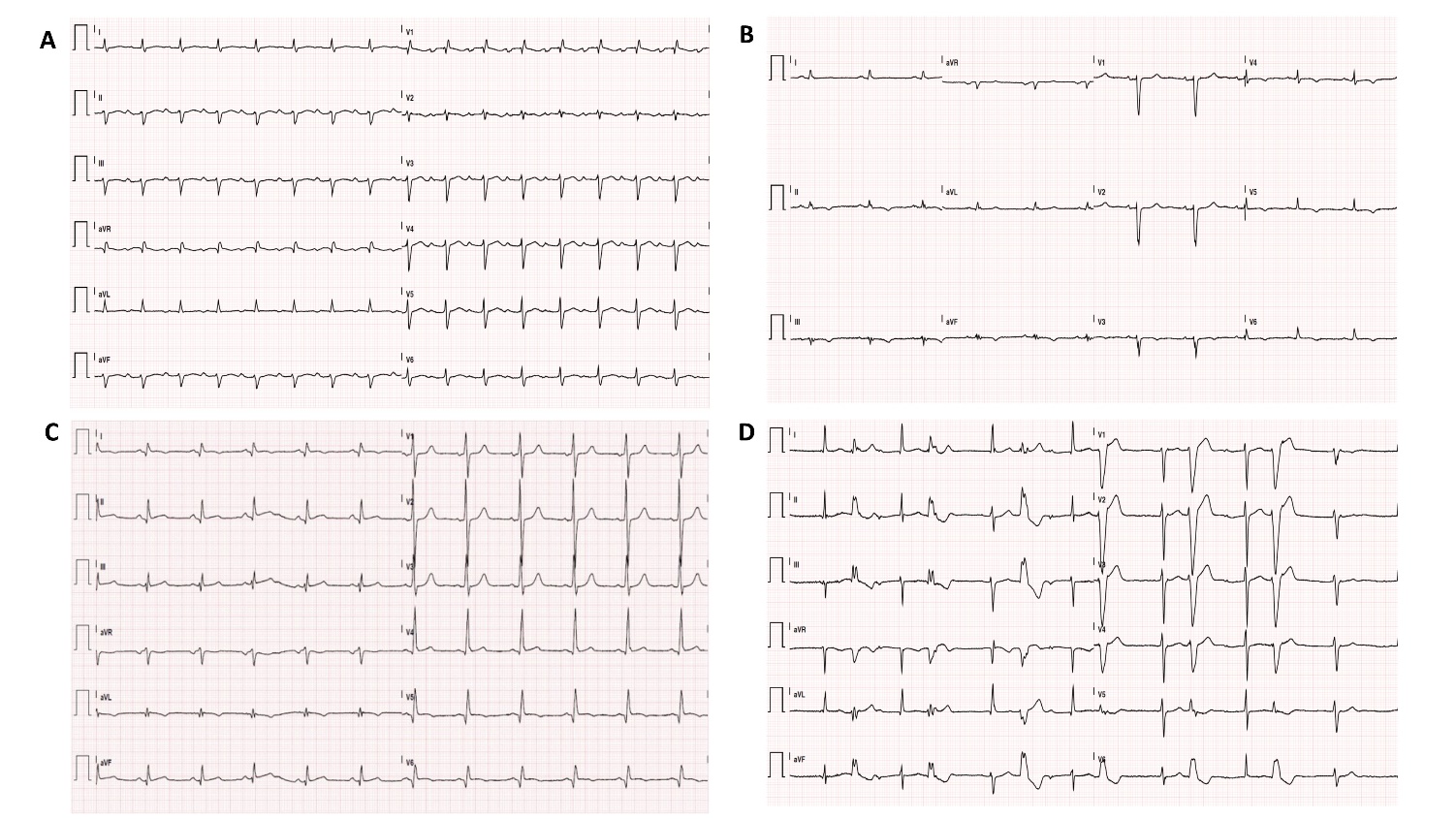
**Table 2.** Electrocardiographic “red flags” for genetic forms of DCM.

|  |  |  |  |
| --- | --- | --- | --- |
| **Red flag** |  | **Possible underlying**  **genetic variant** | **Reported prevalence** |
| **Sinus node disease**1,43 | Sinus bradycardia or sinus node arrest | *LMNA*  *SCN5A* | 13%  - |
|  | AV-block (various degree) | *LMNA*  *EMD*  *DES*  *SCN5A* | 45-77%  -  -  - |
| **Conduction system disease**7,43 | Short PR interval | *DMD* | 35% |
|  | RBBB | *DMD*  *DES* | -  - |
|  | Low voltages | *FLNC*  *DSP*  *PLN* | 36%  -  46% |
| **Depolarization abnormalities**19,21,41 | Inferolateral Q waves | *DMD* | 13% |
|  | T wave inversion | *FLNC*  *DSP* | 62%  - |
| **Repolarization abnormalities**35,73 | AF | *LMNA*  *EMD*  *DES*  *SCN5A* | 36-76%\*  -  -  - |
| **Supraventricular arrhythmias**1,74 | Atrial flutter | *LMNA*  *EMD* | -  - |
|  | Atrial tachycardia | *LMNA*  *EMD* | -  - |
|  | Sinus tachycardia | *DMD* | - |
|  | Frequent VPBs | *LMNA*  *FLNC*  *DES*  *DSP*  *SCN5A* | -  70%  -  -  - |
| **Ventricular arrhythmias**19,21,25,35,43 | NSVT | *LMNA*  *FLNC*  *DES*  *DSP*  *SCN5A* | 37%  83%  -  -  - |
| **Abbreviations:** AF: atrial fibrillation; AV: atrio-ventricular; *DES*: desmin; *DMD*: dystrophin; *EMD*: emerin; *FLNC*: filamin C; *LMNA*: lamin A/C; NSVT: non-sustained ventricular tachycardia; RBBB: right bundle branch block; *SCN5A*: cardiac sodium channel type 5 α-subunit; VPBs: ventricular premature beats.  \*The number refers to the prevalence of any supraventricular arrhythmia | | | |
|  | | | |

**Table 3.** Non-genetic forms of DCM.

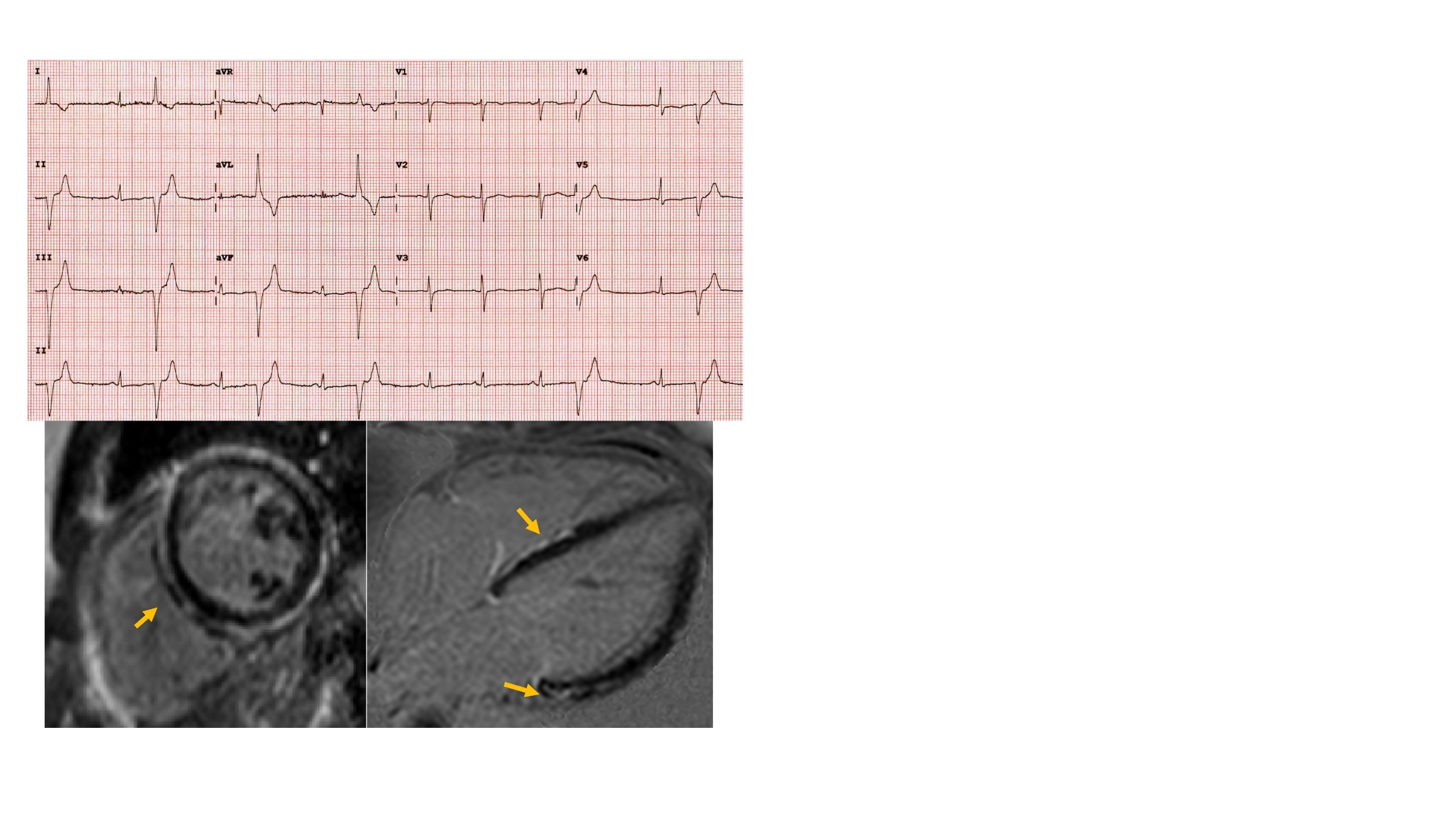
|  |  |
| --- | --- |
| **Non genetic DCM** |  |
| * **Post-inflammatory DCM** | - Low voltages (diffuse)  - T wave inversion (especially in the lateral leads)  - Prolonged QRS duration  - Frequent VPBs and NSVT  - RBBB and LAH or high-degree AV blocks (Chagas disease) |
| * **Cardiac sarcoidosis** | - High degree AV blocks  - RBBB  - Frequent VPBs and NSVT |
| * **Tachycardia-induced DCM** | - AF  - Frequent VPBs |
| * **Chemotherapy-induced DCM** | - Non-specific findings (low QRS voltages and prolonged QTc correlate with disease prognosis) |
| * **Toxic-induced DCM** | - Non-specific findings (LBBB, various degree AV blocks, non specific ST segment alterations) |
| Abbreviations: AF: atrial fibrillation; AV: atrio-ventricular; DCM: dilated cardiomyopathy; LAH: left anterior hemiblock; LBBB: left bundle branch block; NSVT: non-sustained ventricular tachycardia; RBBB: right bundle branch block; VPBs: ventricular premature beats; | |

**Figure 1.** ECG of DCM patients with underlying pathogenic variants. **A.** First degree AV-block and RBBB with left anterior hemiblock in a carrier of *LMNA* pathogenic variant. **B.** Low voltages in the limb leads and inferolateral T wave inversion in a carrier of *FLNC* pathogenic variant. **C.** Inferolateral pseudo-necrosis in a carrier of *DMD* pathogenic variant. **D.** First degree AV-block and frequent VPBs in a carrier of *SCN5A* pathogenic variant.

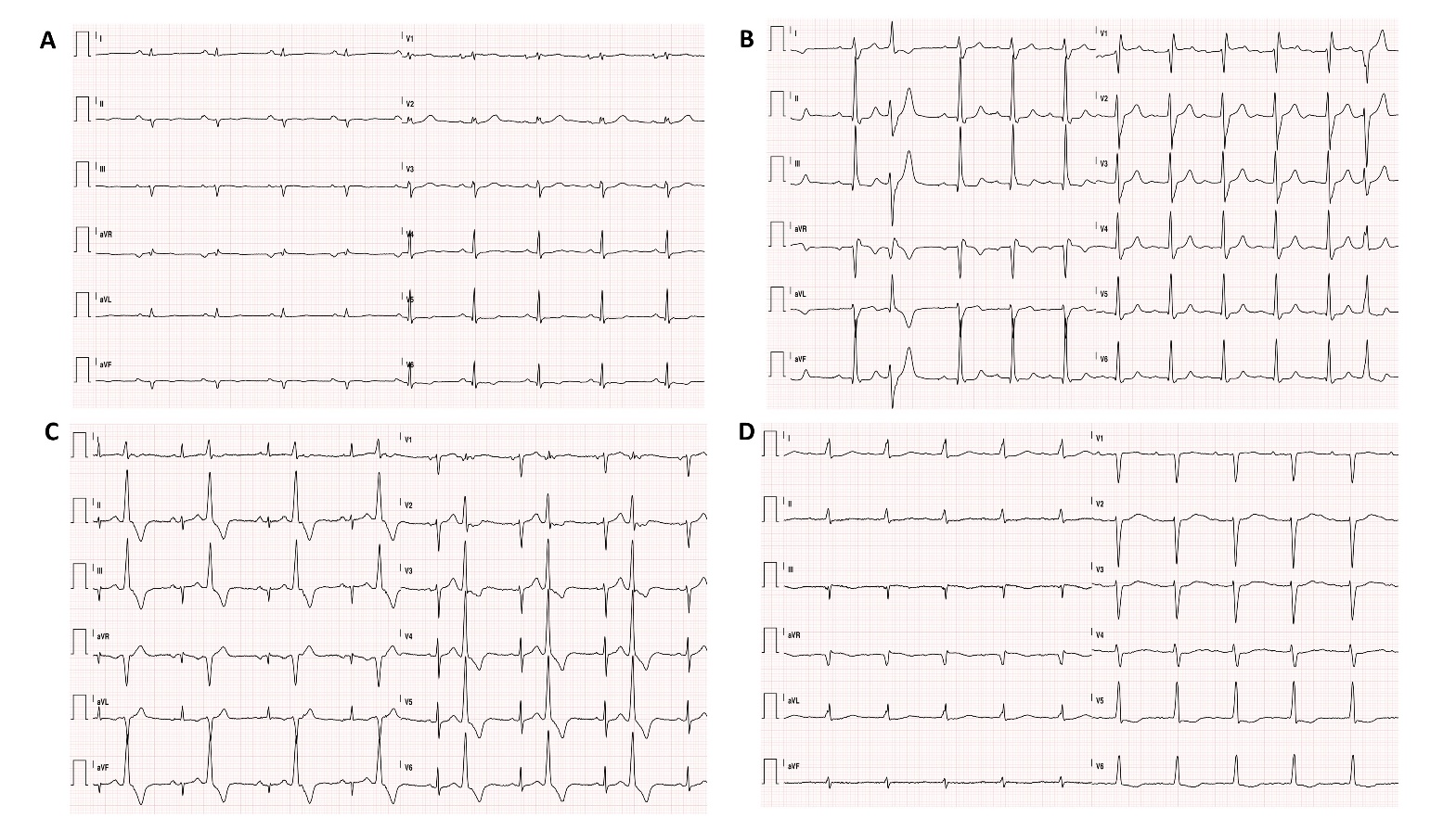


**Abbreviations:** AV: atrioventricular; *DMD*: dystrophin; *FLNC*: filamin C; *LMNA*: lamin A/C; VPBs: ventricular premature beats; *SCN5A*: cardiac sodium channel type 5 α-subunit; RBBB: right bundle-branch block.

**Figure 2.** ECG of a 32 year-old-woman exhibiting a DCM phenotype, found to have a DSP pathogenic variant. Note the diffused low voltages and frequent ventricular premature beats. The cardiovascular magnetic resonance (late gadolinium enhancement sequences) shows subepicardial late gadolinium enhancement which is more evident at the level of the right side of the interventricular septum and the basal lateral wall.



**Figure 3.** Non-genetic forms of DCM. **A.** Diffuse low amplitude of the QRS complexes, prolonged QRS duration and lateral T wave inversion in a patient with post-myocarditis DCM. **B.** First-degree AV block and complete RBBB in a patient with cardiac sarcoidosis and frequent premature ventricular contractions. **C.** Frequent fascicular VPBs in a patient with tachycardia-induced-cardiomyopathy. **D.** Non-specific ECG abnormalities, such as first-degree AV block and prolonged QRS duration in a patient affected by chemotherapy-induced DCM. Notably, a long QTc can be seen, which is associated with worse long term prognosis.



**Central illustration.** Red flags at the ECG in patients presenting with unexplained LV systolic dysfunction.

