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# Review

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# ECG diagnosis of acute ischaemia and infarction: past, present and future

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## Introduction

A century has passed since Einthoven published his description of the human electrocardiogram (ECG), recorded using a string galvanometer. The basic principles of this technique have remained unchanged, and it has revolutionized the diagnosis and management of cardiac pathology. At present, its sensitivity in diagnosing life-threatening myocardial infarction and ischaemia is inferior to that of biochemical markers. However, the ECG monitors cardiac function in real time, while biochemical assays can delay the diagnosis of acute myocardial infarction (AMI) and treatments that need to be delivered promptly. We review the historical development of the ECG and its limitations as a diagnostic tool for AMI, and highlight recent research into higher-resolution technologies for real-time cardiac monitoring, and how they may impact on chest pain management. Many distinguished scientists and clinicians have devoted their life's work to the use and understanding of the technique. This short review will merely highlight some of the more important contributions.

## Development of the ECG

The electrical activity of the heart was an incidental finding of Kolliker and Muller in 1856.[1] When a frog sciatic nerve/gastrocenemius preparation fell onto an isolated frog heart, both muscles contracted synchronously, suggesting that the heart generates electrical impulses. This activity was directly recorded and visualized using a Lippmann capillary electrometer by the British physiologist John Burdon Sanderson.[2] In 1887, Augustus Desire Waller used this technique to show that cardiac electrical potentials could be recorded via the limbs and directly from the chest of intact animals and humans.[3] The electrical activity preceded the heart's contraction, excluding an artefact caused by 'a mechanical alteration of contact between the electrodes of the chest wall caused by the heart's impulse'. However, the clinical importance of his recordings was overlooked.

Inspired by a demonstration by Waller, the Dutch physiologist Willem Einthoven began to develop capillary electrometer technology. This instrument produced unstable, poor-resolution recordings that were easily disturbed by horses and carriages passing, despite the addition of a stone floor to his laboratory. Abandoning this approach, he designed a more sensitive and reliable recording instrument, a modified version of the galvanometer invented independently by D'Arsonval and Ader, but consisting of a 3 μm thin oscillating silver string stretched across a strong electromagnetic field.[4] Einthoven used the device to record an ECG from a human, and published his findings between 1902 and 1903 in Dutch, English and German.[5–7] He also

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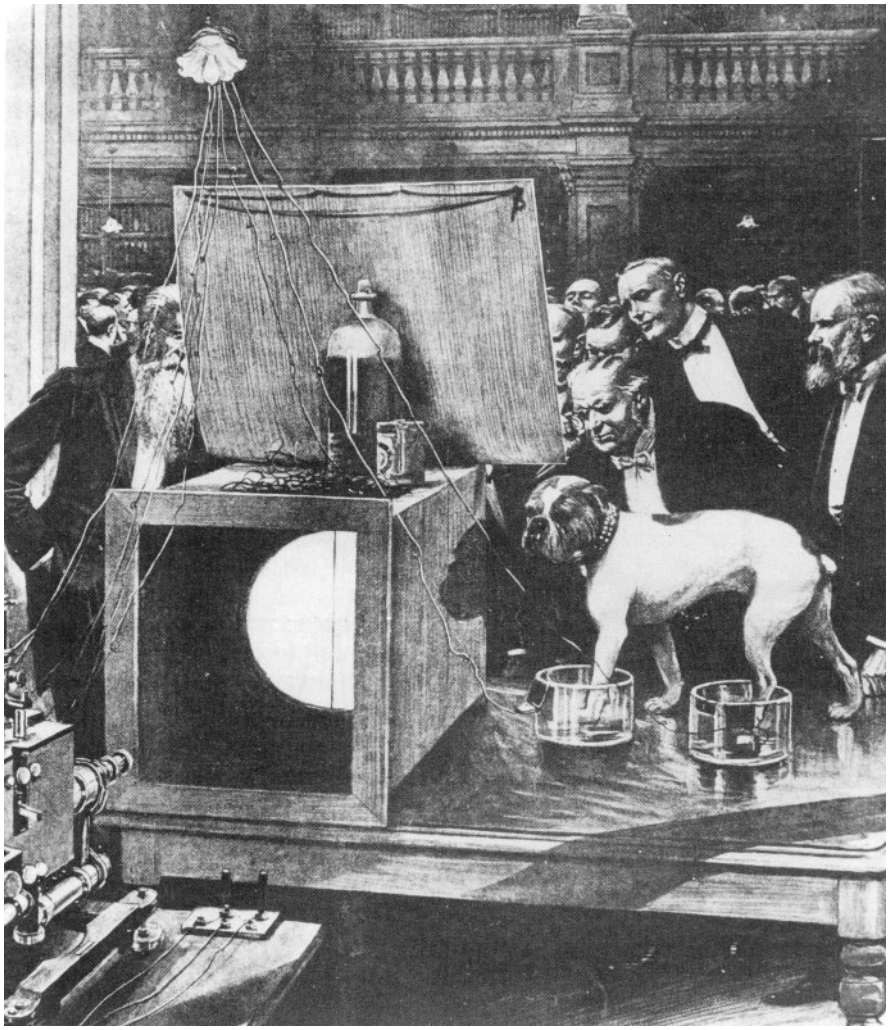

**Figure 1.** A demonstration to the Royal Society by Waller's pet bulldog 'Jimmie' (*Illustrated London News, May 22nd 1909*). *The Times* newspaper of July 9, 1909 reported that the demonstration had caused debate in parliament over whether the Cruelty to Animals Act (1876) had been contravened. On being questioned on this 'public experiment' on a dog with 'a leather strap with sharp nails secured around the neck, his feet being immersed in glass jars containing salts . . . connected by wires with galvanometers', the Secretary of State replied as follows: Mr Gladstone '*I understand the dog stood for some time in water to which sodium chloride had been added or in other words a little common salt. If my honourable friend has ever paddled in the sea he will understand the sensation. (Laughter) The dog—a finely developed bulldog—was neither tied nor muzzled. He wore a leather collar ornamented with brass studs. Had the experiment been painful the pain would no doubt have been immediately felt by those nearest the dog. (Laughter)*' Mr MacNeill (MP Donegal South) '*Will the right honourable gentleman inform the person who furnished him with his jokes that there are members in this House who regard these experiments on dogs with abhorrence?' (Hear)* Mr Gladstone '*I certainly shall not. The jokes, poor as they are, are mine own' (Laughter and cheers)* (from Levick JR, *An Introduction to Cardiovascular Physiology*, 4th edn Reprinted by permission of Edward Arnold).

recorded and labelled the P, Q, R, S and T waves of the ECG, his choice of letters reflecting a tradition in mathematics first used by Rene Descartes in the 17th century. The string galvanometer remains the basis by which ECGs are recorded today.

Einthoven recognized the clinical potential of his invention and built a one mile cable from the University hospital to his research laboratory in order to study pathological traces in man.[8] Subsequent work by Einthoven and Sir Thomas Lewis, one of the first to use a commercially available string galvanometer from the Cambridge Scientific Instrument Company, led to the electrocardiographic description of sinus arrhythmia, heart block, atrial fibrillation and hypertrophy (e.g. reference 9). Although Waller initially maintained that 'the finger tips of the physician will hardly be helped by an instrument as difficult to manage and to interpret as is the string galvanometer', his many demonstrations using the ECG (Figure 1) stimulated

wide interest from clinicians and researchers alike. This was helped greatly by the development of less cumbersome machines after WWI that could be moved to the bedside. The original device had occupied two rooms and required five people to operate.

Einthoven also studied the spread of action potentials, and introduced the three standard limb leads and the concept of Einthoven's triangle, from which he determined the electrical axis of the heart. The use of just three limb leads continued until the 1930s, when many additional precordial lead configurations were tested. In 1938, the American Heart Association and the Cardiac Society of Great Britain recommended the use of a single precordial lead in a standard position,[10] and subsequently recommended six positions for placement of electrodes named V1–V6, which were then adopted for routine use.[11] Unipolar limb leads, first described by Wilson in 1931,[12] were adapted by Goldberger in 1942[13] to produce the augmented unipolar limb leads. These leads were added to the standard limb leads and the unipolar chest leads, to give the so-called standard 12-lead ECG.

Einthoven received the Nobel Prize for Physiology or Medicine in 1924, and paid great tribute to Lewis whom he considered to 'have given to medicine at least as much' as he had. Had Waller still been alive at the time, he would have probably shared the prize. Einthoven gave half of the prize money to the living relatives of the laboratory assistant who helped him develop the string galvanometer.

## ECG changes during myocardial ischaemia and infarction

Although the ECG improved diagnosis of cardiac dysrhythmias, it had little influence on their management until the 1950s. In terms of diagnosis and management of chest pain, however, it had a rapid impact. In 1910, Obrastzow and Straschesko correlated persistent chest discomfort and dyspnoea with coronary artery thrombosis at autopsy.[14] Around this time, the Chicago-based physician James Herrick noticed that the ECG changes observed in such patients were similar to those he recorded during experimental coronary artery occlusion in dogs,[15] and suggested that the ECG could be used to help diagnose the cause of chest pain.

The temporal changes in ST segment morphology during myocardial ischaemia and infarction were first described by Pardee in 1920.[16] In the first few minutes of infarction, T waves become tall and upright before ST elevation (relative to the end of the PR segment) occurs. The elevation of the ST segment is thought to be due to opening of ATP-sensitive $K^+$ channels, as mice with the gene for this protein knocked out show no ST elevation in limb leads during ligation of the left anterior descending artery. Conversely, ST elevation in wild types can be prevented by pharmacological blockers of the channel.[17] As cells become hypoxic, K-ATP channels open, and local areas of hyperkalaemia may develop, causing injury currents to flow between them and the normal myocardium, which could potentially produce ST elevation on the ECG. However, ST elevation is not solely attributable to AMI secondary to coronary artery thrombosis. For example, the majority of healthy adult men have concave ST elevation of 0.1 mV or more in at least one precordial lead, and ST elevation can occur during pericarditis (widespread and saddle shaped), hyperkalaemia (widespread and down-sloping) and pulmonary embolism (reviewed in reference 18).

In lesser degrees of ischaemia, where ST depression occurs without reciprocal ST elevation in the standard 12-lead ECG, it is unclear whether K-ATP channels contribute. Opening of K-ATP channels and other ischaemic changes that shorten action potential duration may also eventually reverse the epi- to endo-cardial gradient of repolarization, causing T waves to invert after the first few hours.

Myocardial infarction can also produce broad and deep negative deflections in the ECG known as Q waves (also described by Pardee), although their pathological substrate is unclear. Q waves remain permanently. However the ST segment eventually returns to normal, and T waves may return to upright, as the infarcted area becomes electrically inexcitable and then necrotic before forming scar tissue. Any Q waves in V1–3, or Q waves $\geqslant 0.03$ s in duration in I/II, aVL, aVF and V4–6 (in two contiguous leads of greater or equal than 0.1 mV in depth) may retrospectively define an established MI, if permanent.[19] However, this must be in the absence of left ventricular hypertrophy, Wolf-Parkinson-White syndrome, bundle branch block, or other conditions that may produce Q wave deflections that mask those related to infarction. Q waves of $< 0.03$ s with ST/T wave depression may represent infarction, but this, along with the depth criteria stated here, requires more research. In a recent study using cardiac magnetic resonance imaging (with and without contrast enhancement or dobutamine stress), the percentage of the left ventricular mass that formed a scar was the single best predictor of Q waves on the ECG, better than either the spatial extent of the infarct or whether it was transmural in thickness. A cut-off value of 17% infarcted tissue of the left ventricle yielded a sensitivity and specificity of 90% for predicting the presence/absence of Q waves.

## Assessing the sensitivity of the ECG to detect myocardial ischaemia

Several factors limit the ability of the ECG to detect AMI or transient ischaemia. Temporal variations in ST segment changes mean that a single, isolated recording may not pick up diagnostic changes. Non-Q-wave infarcts are likely to give smaller, non-specific ECG changes that do not meet diagnostic criteria. The interpretation of smaller ECG changes is also heavily dependent on the pre-test probability of the individual having ischaemic heart disease. With large transmural infarcts, multiple events combined with conduction defects may obscure diagnostic changes. Given the position of the 12 conventional ECG leads, posterior infarcts often produce ECG changes (a tall R wave in V1 with ST depression in V1–3) that are difficult to interpret and often missed. The severity and location of ischaemia relative to the position of exploring electrodes therefore limit the sensitivity of the ECG in detecting ischaemia.

### ECG changes during provoked ischaemia

The ability of the ECG to detect transient ischaemia has traditionally been investigated by correlating the results of exercise tolerance tests (ETTs) with coronary angiography. Even in the presence of symptomatic stenosis, the lag in the development of diagnostic ECG changes behind chest pain onset or factors limiting exercise performance may lower their sensitivity. A large meta-analysis of over 132 studies amassing over 24 074 patients found the overall sensitivity of the ETT to be 68%, with a specificity of 77%, although values range widely between studies, depending on patient group and severity of disease.[21] The specificity of the ETT is based on true positives being patients with significant stenosis on an angiogram. Coronary perfusion can be more accurately monitored using technetium-99n isonitrile single-photon-emission computed tomography (SPECT)-based dobutamine stress testing. A standard 12-lead ETT can identify patients to a similar degree of accuracy (64%), with impaired coronary perfusion proven via this method.[22] However, there may be non-cardiac obstacles (e.g. mobility) to a patient completing an ETT, whereas a SPECT stress test can be performed with pharmacological stimulation alone.

A more rigorous approach would be to assess changes in the ECG during episodes of independently documented ischaemia. This has been observed whilst monitoring the partial pressure of oxygen in blood from the coronary sinus ($pO_2$) and haemodynamic variables in patients with variant angina in coronary care units. Such studies have shown ischaemia significant enough to affect left ventricular function and reduce coronary sinus blood oxygenation with little or no ECG changes, if the episodes are either brief, or prolonged and mild (e.g. reference 23). However such studies lack a high statistical power, due to the small number of patients involved, and cannot provide accurate values for overall ECG sensitivity in detecting ischaemia.

### Autopsy-proven infarction and ECG changes

The crudest way of assessing the ability of the ECG to detect AMI is by retrospective analysis in those who have proven infarction at autopsy. In such studies, ECG evidence of infarction can be found in 50 to 90% of cases.[24–27] However, the patients in these studies died of severe extensive disease, which may not reflect the ability of the ECG to detect less severe ischaemia. Multiple infarctions combined with conduction defects also often obscure Q waves and produce non-diagnostic ECG changes.

### Angiography and ECG changes

A prospective way of assessing the ability of the ECG to detect AMI is to follow-up patients with angiography. Such studies are small in terms of the number of subjects ($n = 84$ to 245), and report that admission ECGs successfully identify patients with proven stenosis on angiography in 36–87% of cases.[28–32] While angiography is a useful and accurate way of diagnosing coronary artery occlusion following AMI, occasionally symptomatic disease is restricted to the coronary microcirculation, which is not viewed by angiography. Rarely, vasospasm may also produce cardiac ischaemia without permanent stenosis (e.g. Prinzmetal's angina), and equally, thrombotic occlusion of a coronary vessel may resolve before angiography, giving the false impression that the ECG changes were misleading. Not all of the earlier studies use the same criteria for identifying a significant degree of stenosis, and without more recent biochemical evidence of AMI, it is not clear whether they always equate to infarction, if there is a good collateral circulation.

The use of angiography and catheterization does allow an assessment of the ability of the ECG to localize infarcts when single-vessel disease is present (reviewed in references 33 and 34). Once ST elevation or Q waves occur, their accuracy in delineating infarct location is high (91–98%), but due to the variation in coronary

anatomy, determining the relevant artery is less accurate.[33]

## Troponins and ECG changes

The gold standard for diagnosing an AMI is a significant rise in plasma troponin levels. The cardiac troponin complex is found on every seventh actin molecule of the sarcomere thin filament and is composed of C, T and I subunits, which bind calcium, attach to tropomyosin and inhibit calcium dependent ATPase activity, respectively. Troponins also have a cytosolic pool, and therefore display plasma kinetics characteristic of both cytosolic and structural proteins. They display a marked rise in plasma concentrations following myocardial injury, peaking at 12–24 h. Troponin T and troponin I are encoded by separate genes in skeletal and cardiac muscle. They are therefore highly specific, and an AMI is virtually ruled out if no changes in troponins are recorded within 12 h of the onset of chest pain. For these reasons, the diagnostic criteria for AMI were redefined as a significant troponin rise accompanied by either (i) a consistent clinical history; (ii) new Q waves on an ECG; (iii) ST elevation or depression; or (iv) *post mortem* findings consistent with AMI.[19] However, not all patients with a troponin rise have had a myocardial infarction; this marker is elevated in a variety of other conditions, including pulmonary embolism and myocarditis.

The ideal method of assessing ECG sensitivity is therefore to compare cases of suspected AMI that result in a significant troponin rise. The GUSTO IIa trial of 755 consecutive admissions found that 232 had no change in their ECG despite a significant rise in troponin T being found in 38%.[35] This may be an underestimate of the number of AMIs missed by the ECG, as troponin T levels were measured on admission, rather than 12 h after the onset of chest pain. McClelland *et al*.[36] studied 103 similar patients admitted consecutively, 53 of whom were diagnosed with AMI on the basis of troponin and creatine kinase MB (CK-MB) assays. A computer algorithm for analysing 12-lead ECG changes detected AMI in this group of patients with a sensitivity of 32%, versus physician reading of ECGs, which had a sensitivity of 45%. The specificities of the computer and physician diagnoses were documented as 98% and 94%, respectively. Specificity is unlikely to reach 100%, as early ischaemia from coronary occlusion may resolve or be successfully thrombolysed before significant cell death occurs. Alternatively, pericarditis, left ventricular hypertrophy or old left bundle branch block (LBBB) may complicate the reading of the ECG.

## The impact of diagnostic criteria on sensitivity and specificity

The exact degree of ST elevation required for diagnosis of an evolving AMI will also influence the sensitivity of the ECG and determine which patients receive thrombolysis. The Minnesota code for diagnosing significant ST elevation is based on ST/junctional ST elevation of $\geqslant 0.1$ mV elevation in $\geqslant 1$ inferior/lateral leads, or $\geqslant 0.2$ mV in $\geqslant 1$ anterior leads. Trials performed by the GUSTO group looking at the benefit of thrombolysis have used more strict definitions such as $\geqslant 0.1$ mV in $\geqslant 2$ contiguous limb leads or $\geqslant 0.2$ mV in $\geqslant 2$ contiguous precordial leads. This difference in the criteria for ST-elevation MI between the Minnesota code and the criteria for thrombolysis in clinical trials has led to some confusion.

In a study of different diagnostic criteria in 603 chest pain and 149 non-chest-pain admissions,[37] the Minnesota code had a sensitivity of 56% and a specificity of 94% for AMI (defined by clinical history and biochemical evidence). Other criteria, such as that used by the GUSTO investigators, had a lower sensitivity but higher specificity. Altering the diagnostic criteria varied sensitivity between 45% and 69%, but reduced specificity from 98% to 81%. The importance of the ECG in the thrombolytic trials was to identify the presence of a coronary artery occluded by thrombus that might benefit from thrombolytic agents. When faced with the potentially harmful effects of these agents, these trials were performed using criteria with a higher specificity for detecting occluded arteries. A significant proportion of patients with occluded coronary arteries do not meet the ST elevation criteria. While thrombolysis in patients with an ECG showing isolated ST depression does not result in any clinical benefit, the role of thrombolysis for lesser degrees of ST elevation is unknown, and unlikely to be tested in future clinical trials.

# Implications for management of cardiac chest pain

In the acute setting, the ECG is the primary tool for identifying patients who are likely to benefit from thrombolysis. In treating AMI, if a patient presents with chest pain consistent with AMI and has the degree of ST elevation or new LBBB described in GUSTO, thrombolysis is an effective treatment within 12 h of pain onset. If available, primary percutaneous coronary angioplasty (PCA) may be even more effective,[38] and should be the treatment

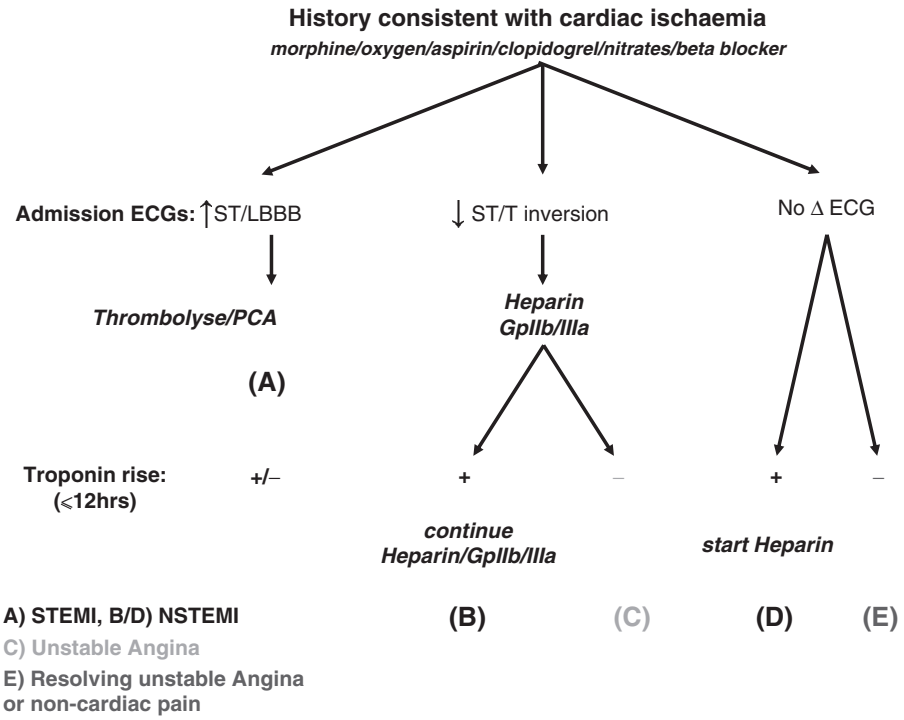


**Figure 2.** Managing suspected acute myocardial infarction. ST elevation (STEMI) or new onset left bundle branch block (LBBB) on the ECG (**A**) is diagnostic of acute myocardial infarction (AMI) and is followed by a rise in plasma troponin levels (Tn) unless infarction is aborted by revascularization. This can be attempted by thrombolysis or, if available, primary coronary angioplasty (PCA). ST depression or T wave inversion may be a result of a smaller non ST elevation MI (**B**: NSTEMI) or unstable angina (**C**), only the former being accompanied by a Tn rise within 12 h. Such patients can be anticoagulated with heparin/LMWH until Tn results are known. If they continue to have episodes of chest pain at rest further investigation including angiography is required. Those with Tn rises may benefit from additional treatments such as glycoprotein (Gp) IIb/IIIa inhibitors. Patients with no ECG changes may also be experiencing a NSTEMI (**D**), or resolving unstable angina/non-cardiac chest pain (**E**). Those who go on to have a significant rise in plasma Tn levels (**D**) may benefit from treatment with heparin until pain-free for 48 h. However, patients in this group may benefit from earlier initiation of treatment (which only occurs in practice if there is a high clinical suspicion) if they could be identified earlier. Those patients with no Tn rise in whom suspicion of coronary artery disease is high should be further evaluated with exercise tolerance testing or dobutamine stress testing as appropriate, and treated with anti-anginals as necessary.

of choice in the presence of contraindications to thrombolysis.

However, the limited sensitivity of the ECG in detecting infarction has several implications in the management of cardiac chest pain. Patients presenting with ischaemic cardiac pain and a normal ECG have an incidence of myocardial infarction of up to 7% (e.g. reference 39). Given the sensitivity of the ECG, establishing a diagnosis of AMI can often remain problematic for the clinician until the result of a 12-h troponin level is known. This limits the initiation of potentially more effective treatments that need to be delivered promptly. Figure 2 outlines how suspected AMI is often managed, highlighting delays in diagnosis and associated treatments.

Many new methods for earlier detection of AMI are now being researched, including rapid serial measurements of multiple biochemical markers and myocardial perfusion imaging.

The ECG changes of ischaemia rather than infarction present similar problems. The demonstration of a normal ECG during chest pain is an important factor in excluding a cardiac cause. Even minor degrees of ST depression however (0.05mV[40]) have a major impact on the prognosis of patients presenting with cardiac chest pain and are included in scoring systems for non-ST-elevation acute coronary syndromes (TIMI risk score[41]). The sensitivity of the ECG in detecting ischaemia and assessing prognosis is greatly improved with continuous ST segment monitoring, and dynamic as opposed to fixed changes improve the diagnostic accuracy of the findings. The value of T-wave inversion is controversial, although it is an important marker of severe coronary artery disease,

particularly when present in the anterior chest leads (Wellens' syndrome[42,43]). The specificity of ST–T change is however low, and may be encountered in a variety of other clinical conditions.

As the ECG monitors cardiac function in real time, an improvement in its sensitivity for detecting myocardial ischaemia and infarction without a compromise in specificity could vastly improve chest pain management.

# New technologies

## Combining ECG information with clinical history

The ability of an isolated ECG recording to detect ischaemia and infarction depends on the pre-test probability of a patient having coronary artery disease, as determined from their clinical history and the nature of their chest pain. This principle has been exploited by Selker and colleagues to develop a predictive instrument that combines ECG criteria and clinical details (initially as a series of seven yes/no questions) to estimate a probability of acute myocardial ischaemia, guiding physician management.[44] This algorithm has now been incorporated into modern computerized ECG machines that can themselves measure ST/T wave changes, and give a probability of an acute myocardial infarction, based on currently measured data assessed against information stored on a database. It has therefore been named the acute cardiac ischaemia time-insensitive predictive instrument (ACI-TIPI).[45,46] It relies mainly on the age and sex of the patient, the presence of Q waves and detailed ST/T wave analysis. It has been used to supplement decision-making on discharging emergency department patients or admitting them to hospital or coronary care units. In a clinical trial, it increased the proportion of patients with no ischaemia that were discharged home and reduced CCU admissions without impacting on appropriate admissions for patients with AMI or unstable angina.[46]

## Computer measurement of ST changes and Q waves in the 12-lead ECG

Many commercially available computerized ECGs now display measurements of ST/T wave changes and the presence of Q waves as supplementary information to the traces themselves to assist in their reading. While this does not necessarily improve on the sensitivity and specificity of the 12-lead ECG in detecting ischaemia/infarction *per se*, it has been used to guide the administration of early, out-of-hospital thrombolytic therapy by ambulance crews. Thrombolysis in the presence of the ECG criteria described earlier in this article is at its most useful within 3 h of the onset of chest pain, with very little benefit after 9–12 hours.[47] Several techniques have been used to guide early thrombolysis via the ambulance service, including interpretation of the ECG by a physician based in the ambulance or following telephonic transmission to the receiving centre, or following computer interpretation of the ECG on board the ambulance. Regardless of the method used, pre-hospital administration of thrombolysis results in treatment often within 100 min following the onset of symptoms, resulting in a time gain vs. hospital administration of at least 45 min, in clinical trials.[48]

Concerns regarding unjustified thrombolysis with computer-assisted diagnosis have been investigated recently. A recent study[49] compared the results of pre-hospital, computerized ECG diagnosis ($n=118$), cardiologist interpretation of the ECG by telephone transmission ($n=132$), and ECG interpretation and administration of thrombolysis in hospital ($n=269$) in three separate cities in Holland. Both aborted AMI and unjustified treatment include a non-significant rise in cardiac enzymes, but the former was defined as resulting in no changes in ST deviation within 48 h of thrombolysis. Given their definitions and despite not using troponins to detect AMI, unjustified treatment occurred equally frequently in all three groups, whilst aborted AMI was associated with pre-hospital thrombolysis.[49]

## Increasing the ability of the 12-lead ECG to detect transient ischaemia

While traditional ETTs rely on clinician assessment of ST depression and blood pressure monitoring, more information can be gained by correlating ST depression with heart rate (HR) throughout the exercise and recovery phases. This was first done by Bruce and McDonough[50] in 1969, who observed differences in ST depression/heart rate (ST-HR) hysteresis between normal patients and those with ischaemic heart disease. With the advent of computer analysis of ECG waveforms, programs have been developed that extract the prevailing direction and average magnitude of the ST/HR hysteresis during the first 3 min of post-exercise recovery, and use this as a continuous diagnostic variable for improved detection of ischaemia. A trial of this method in 347 patients referred for a routine bicycle ETT found ST-HR hysteresis to have a superior discriminative capacity compared to ST depression alone (89% vs. 76%).[51] The superior diagnostic performance of the method also appears to be relatively insensitive to the ST segment measurement point, or to the ECG lead selection.

As well as changes in repolarization measurements, computer analysis of perturbations in depolarization characteristics during ischaemia may also improve upon the diagnostic ability of the ETT. Scoring systems for exercise-induced changes in Q, R, and S wave amplitudes (such as the Athens score[52]) have been devised to improve the accuracy of ETT. These have been determined by retrospective analysis of ETT ECGs, and the scoring system then tested prospectively in new patient groups. For example, an Athens score of 5 mm (sensitivity 86%, specificity 79%) improves on ST depression as a diagnostic criterion (sensitivity 62%, specificity 70%, 160 patients) for coronary artery disease, although the score performs less well in patients with multivessel disease.[52] Transient myocardial ischaemia is also accompanied by changes in the waveform morphology of the high-frequency signal-averaged QRS, including the development of time zones of reduced amplitude, which may represent slow conduction in ischaemic regions of the heart. This has been investigated using computer analysis of the ECG during angioplasty of the LAD, which provoked angina during balloon inflation. These reduced amplitude zones were found in 90% of individuals studied, compared to ST or T wave changes, which were only present in 54%.[53]

A recent study has directly compared depolarization analysis (such as the Athens QRS score) and HR-related repolarization measurements (ST-HR hysteresis) to standard ETT criteria in patients with angiographically-proven stenosis,[54] Both techniques improved upon monitoring of ST depression (sensitivity 65%, specificity 66%), with ST-HR hysteresis (sensitivity 90%, specificity 79%) performing better than depolarization scores (sensitivity 78%, specificity 81%). Combining both depolarization and repolarization analyses into a composite scoring system may further improve the accuracy of ETT in diagnosing coronary artery disease.

## Increasing the ability of the 12-lead ECG to detect AMI

As with ETT, scoring systems such as those devised by Selvester *et al* have been used for the diagnosis and estimation of prior and acute myocardial infarct size, initially focusing on variations in the QRS wave,[55] and then being validated and refined in patients with proven single anterior, inferior, posterolateral and multivessel infarcts (e.g. references 56 and 57). A more accurate score has been devised using statistical multivariant discriminant analysis on normal ECGs and those from patients with Q wave infarctions, which have identified the value of measurements outside the QRS complex in diagnosing AMI.[57] In an analysis of 159 normal subjects and 53 with non-Q wave infarcts, requiring ST/T wave criteria (in addition to QRS scoring thresholds) improved sensitivity from 32% to 72% (specificity 95%).[58] These complex scoring systems have now been incorporated into commercial ECG programs, and are continuously being refined in studies comparing normal patients and those with biochemical and other evidence of AMI despite no ST changes on their ECG.[59] However, bi-group comparisons of patients with AMI versus non-MI patients can avoid patients with left ventricular hypertrophy and other causes of ST/T wave changes not due to myocardial infarction. Specificity in such studies can be misleading, and may very well drop in real-world clinical practice.

## Improving sensitivity and specificity by the addition of more recording leads

The sensitivity of the ECG could also be improved by increasing the number of recording leads, and adding posterior leads to detect AMIs with posterior or right ventricular wall involvement. Interpretation of results from these body surface maps (BSM) of electrical activity becomes increasingly more complicated as more electrodes are added, and computer interpretation may be required to assist diagnosis. A BSM using 80 electrodes (64 anterior and 16 posterior) with a computerized algorithm for diagnosing AMI has recently been assessed in 103 consecutive patients presenting to hospital with suspected AMI. Of these, 53 had AMI diagnosed using biochemical (troponin and CK-MB) criteria. The BSM had a sensitivity of 64% for diagnosing AMI, compared to only 45% for the 12-lead ECG, while both had a specificity of 94%, the improvement mostly being due to the increased number of posterior and right ventricular AMIs detected by the BSM.[36] A similar result was obtained using the BSM compared to a 12-lead ECG to diagnose early AMI in patients prior to hospital arrival.[60] As with the 12-lead ECG, multivariant discriminant analysis could be performed on body surface maps to produce scoring systems that improve their diagnostic ability and identify an optimal number of leads and positions.

Biophysicists have tried for years to calculate the temporal changes in body surface potentials based on the electrical activity of the ventricles within the chest. The 'holy grail' of electrocardiology is to solve the so called 'inverse problem', i.e. to directly determine ventricular activity from body surface recordings. Several mathematical algorithms for this

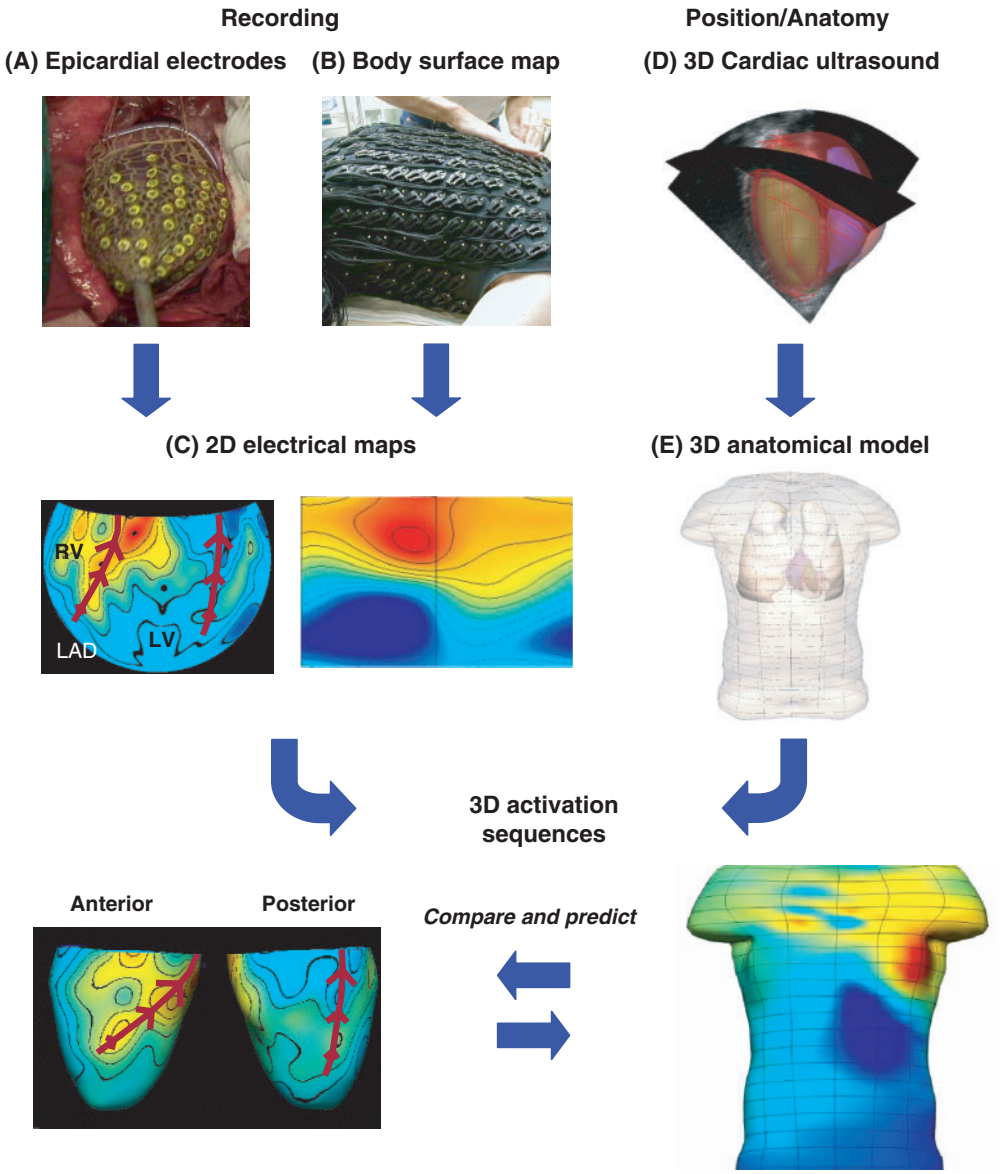


**Figure 3.** Experimental validation of inverse algorithms. Up to 339 epicardial electrodes (**A**) record activity in the closed chested human during cardiac surgery, while 256 electrodes map body surface potentials either simultaneously or post-operatively (**B**). The positions of the body electrodes are determined using a mechanical digitalised arm or laser scanner and epicardial electrodes via sonomicrometric crystals. The dimensions of the torso are digitalized and the position of the heart determined using 3D ultrasound (**D**) to produce a computerized geometrical model of the human torso (**E**). The electrical activation sequences from epicardium and torso (**C**) are then mapped onto the 3D models so that actual and predicted epicardial electrical activity can be compared.

exist (e.g. reference 61), and suggest that the activation sequence of the ventricle (rather than the magnitude of the potential changes) could be predicted, although such theories need to be validated experimentally (reviewed in reference 62). If they prove to be correct, accurate 3D activation patterns of the ventricles could be obtained from BSMs (so-called ECG imaging) that could be highly sensitive for ischaemic disturbances of conduction occurring before the onset of angina and infarction.

Recently, an experimental approach has been devised to validate these inverse solutions by recording from the both the body and ventricular surfaces *in vivo* in anaesthetized pigs[63] and dogs,[64] and also in humans both awake[65] and during open heart surgery.[66] The ability of the algorithm to predict changes in ventricular activation during pathophysiological conditions such as LAD artery occlusion, ventricular pacing and hyperkalaemia have been investigated. These experiments often involve accurately determining the position of the

heart in the torso using 3D ultrasound. In cardiac surgery patients, the chest is then opened and a sock containing up to 339 electrodes is placed around the ventricles before closing the chest wall again. The position of the ventricular electrodes in 3D space can be determined by implanting small piezo-electric transducer crystals and monitoring the distances between them and a receiver (sonomicrometry). A jacket containing 256 electrodes then records body surface potentials and these electrodes are also located in 3D space using a mechanical digitalizing arm or laser scanner. Recordings are projected onto a computerized geometrical model of the torso and heart that is customized to the individual. The body surface mapping system can identify changes in ventricular activation and recovery time during 4 min of LAD artery occlusion that cannot be detected using the standard 12-lead ECG,[67] and in the electrophysiology laboratory, can locate the physical source of pacing electrodes in patients to within 17.3 mm.[68] Whether the inverse algorithms will reliably calculate changes in ventricular activation during AMI and other conditions, remains to be determined.

## Concluding comments

Over the last 60 years, the principles of recording the ECG have changed very little. Ways of interpreting the 12-lead ECG to diagnose ischaemia and infarction and guide therapy continue to advance with pace. Once AMI is detected, the ECG diagnosis is highly specific and effective in localizing the region of ischaemia. However it is less accurate at predicting the coronary artery involved and, used in the conventional fashion, detects only around 50% of life-threatening AMIs in patients admitted with chest pain. Given that coronary artery disease is the main cause of death in the Western world, and therapeutic interventions are more effective when initiated early, there is a strong demand for more rapid and sensitive means of detection. Definitive diagnosis using biochemical markers currently may delay treatment by up to 12 h, while new technologies based upon the traditional ECG have the advantage that they can monitor cardiac activity in real time and provide rapid, computer assisted diagnosis. Although in their infancy, these technologies are already improving the sensitivity of the ECG and/or the delivery of treatment in clinical trials.

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