Cardiac evaluation of the survivor of sudden cardiac arrest

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INTRODUCTION

Sudden cardiac arrest (SCA) and sudden cardiac death (SCD) refer to the sudden cessation of cardiac activity with hemodynamic collapse, typically due to sustained ventricular tachycardia/ventricular fibrillation. These events mostly occur in patients with structural heart disease (that may not have been previously diagnosed), particularly coronary heart disease. (See "Pathophysiology and etiology of sudden cardiac arrest".)

The event is referred to as SCA (or aborted SCD) if an intervention (eg, defibrillation) or spontaneous reversion restores circulation. The event is called SCD if the patient dies. However, the use of SCD to describe both fatal and nonfatal cardiac arrest persists by convention. (See "Overview of sudden cardiac arrest and sudden cardiac death", section on 'Definitions'.)

Evaluation of the survivor of SCD includes the following:

- Identification and treatment of acute reversible causes
- Evaluation for structural heart disease
- In patients without obvious arrhythmic triggers or cardiac structural abnormalities, an evaluation for primary electrical diseases
- Neurologic and psychologic assessment

- In selected patients with a suspected or confirmed heritable syndrome, evaluation of family members

The evaluation of the survivor of SCD will be reviewed here. The pathophysiology of SCD and the management of survivors of SCD are discussed separately. (See "Overview of sudden cardiac arrest and sudden cardiac death" and "Pathophysiology and etiology of sudden cardiac arrest" and "Approach to sudden cardiac arrest in the absence of apparent structural heart disease" and "Secondary prevention of sudden cardiac death in heart failure and cardiomyopathy".)

ETIOLOGY OF SCD

Accurate and precise measures of the relative frequencies of various causes of SCD are difficult to obtain. Case definitions are inconsistent and etiologies vary according to the population studied. Common causes of SCD include coronary heart disease, structural heart disease not related to CHD (eg, hypertrophic cardiomyopathy, nonischemic cardiomyopathy, etc), arrhythmias caused by primarily electrical disease (eg, Brugada syndrome, long QT syndrome, etc), and transient or reversible causes (eg, medication toxicity, electrolyte abnormalities, etc).

A detailed review of the causes of SCD is presented separately. (See "Pathophysiology and etiology of sudden cardiac arrest", section on 'Etiology of SCD'.)

INITIAL EVALUATION

The evaluation begins immediately after resuscitation. The first concern is to exclude any obvious reversible factors that may have led to the event (table 1).

History and physical examination — The patient (if awake) and family should be questioned, with particular attention to the following:

- Prior diagnoses of heart disease
- Use of any medications, especially antiarrhythmic drugs, diuretics, and drugs that might produce long QT syndrome
- Ingestion of toxins or illicit drugs
- Antecedent symptoms, especially evidence of ischemia
- Antecedent stressful events or activities

Unfortunately, the cardiac arrest is frequently unwitnessed. In addition, the patient resuscitated from VF often has retrograde amnesia and is unable to remember what occurred prior to the cardiac arrest. Thus, a coherent history may not be ascertainable. Obtaining a history from an observer, when available, is important.

Laboratory testing — Immediate evaluation should include standard laboratory testing and, in many cases, an arterial blood gas to exclude electrolyte abnormalities and acidosis. Any reversible metabolic abnormalities should be identified and corrected, particularly hypokalemia and hypomagnesemia which can predispose to ventricular tachyarrhythmias [1,2]. Toxicologic screening for drugs of abuse should be considered when relevant as drug overdose has been documented in significant numbers of patients with apparent sudden cardiac death [3].

When interpreting the test results, two important limitations should be considered:

- Electrolyte abnormalities during and shortly after resuscitation may be secondary to cardiac arrest and hypoperfusion as opposed to a cause of SCD [4].
- Electrolyte abnormalities by themselves are usually insufficient to cause SCD. Clinical settings that increase the proarrhythmic effect of hypokalemia and hypomagnesemia include acute myocardial infarction [5], overt heart failure, and long QT syndrome. (See "Acquired long QT syndrome: Definitions, pathophysiology, and causes", section on 'Metabolic abnormalities'.)

It is potentially hazardous to ascribe a cardiac arrest to an electrolyte or metabolic derangement alone, unless there is compelling evidence of an association. Mistaken attribution of a major arrhythmia to an innocent or merely potentiating laboratory abnormality can place the patient at high risk if appropriate therapy to prevent recurrent SCD is delayed or not given. Importantly, electrolyte and pH abnormalities may be secondary to the arrhythmia itself.

This risk was illustrated in a review of 169 patients treated with an ICD for sustained ventricular arrhythmia in whom the plasma potassium concentration was measured on the day of the arrhythmia [6]. The likelihood of a recurrent sustained ventricular arrhythmia was 82 percent at five years. The long-term risk was similar in patients with low, normal, and high plasma potassium concentrations at presentation.

Electrocardiogram — The ECG can reveal evidence of both acute abnormalities and chronic conditions. It should be part of the immediate evaluation and repeated as necessary once the patient's cardiac, hemodynamic, and metabolic condition stabilizes. The ECG should be evaluated for evidence of the following:

- Ongoing ischemia or prior myocardial infarction. (See 'Coronary angiography' below and "Electrocardiogram in the diagnosis of myocardial ischemia and infarction".)

- Conduction system disease, including bundle branch block, second degree heart block, and third degree heart block. (See "Left bundle branch block" and "Right bundle branch block" and "Second-degree atrioventricular block: Mobitz type II" and "Third-degree (complete) atrioventricular block".)

Less common abnormalities that also may be evident include:

- Brugada syndrome, evidenced by a pseudo-RBBB and J point elevation with a downsloping ST segment to a negative T wave in lead V1 and often lead V2. In contrast, with an ST segment myocardial infarction the J point is elevated and the ST segment remains elevated as well (waveform 1). (See "Brugada syndrome: Clinical presentation, diagnosis, and evaluation".)

- Wolff-Parkinson-White syndrome, evidenced by a short PR interval and a slurred QRS complex upstroke known as a delta wave (as a result the QRS complex has a broad base and narrow peak) (waveform 2). (See "Wolff-Parkinson-White syndrome: Anatomy, epidemiology, clinical manifestations, and diagnosis", section on 'Electrocardiographic findings'.)

- Arrhythmogenic right ventricular cardiomyopathy (ARVC), suggested by VT or ventricular ectopy with a left bundle branch block configuration and an inferior axis. In addition, abnormalities of the baseline QRS may be present, including an epsilon wave in the right precordial leads (ie, leads V1-V2) (waveform 3A-B).

- Long QT syndrome (waveform 4), possibly with torsades de pointes (waveform 5). (See "Congenital long QT syndrome: Epidemiology and clinical manifestations" and "Acquired long QT syndrome: Definitions, pathophysiology, and causes".)

- Hypertrophic cardiomyopathy. (See "Hypertrophic cardiomyopathy: Clinical manifestations, diagnosis, and evaluation".)

EVALUATION FOR STRUCTURAL HEART DISEASE

Excluding patients with an obvious noncardiac etiology (eg, trauma, hemorrhage, or pulmonary embolus), structural heart disease is present in up to 90 percent of patients with SCD (table 2) [7-13]. (See "Pathophysiology and etiology of sudden cardiac arrest".)

It is essential that all survivors of SCD undergo a complete cardiac examination to determine the nature and extent of underlying heart disease. The initial history, physical examination, and laboratory tests may provide evidence of one of these disorders, but further testing is usually necessary to confirm a diagnosis.

The standard evaluation typically includes:

- ECG (see 'Electrocardiogram' above)
- Cardiac catheterization with coronary angiography
- Echocardiography

In the appropriate clinical setting, coronary angiography and echocardiography may be part of the urgent initial evaluation.

In selected patients, cardiac magnetic resonance imaging (MRI) and, rarely, myocardial biopsy are performed. (See 'Cardiac MR' below.)

Coronary angiography — Coronary angiography is performed in most survivors of SCD for one of two indications: management of an acute coronary syndrome or diagnosis of chronic CHD.

Acute coronary syndrome — Patients with evidence of STEMI following resuscitation from SCD should undergo urgent cardiac catheterization and, when indicated by the anatomy, revascularization with primary PCI or surgical revascularization [14]. Similarly, patients with a confirmed NSTEMI and those with a high suspicion of ongoing myocardial ischemia should also undergo cardiac catheterization with revascularization as indicated. (See "Primary percutaneous coronary intervention in acute ST elevation myocardial infarction: Determinants of outcome" and "Non-ST-elevation acute coronary syndromes: Selecting an approach to revascularization".)

SCD may be the presenting manifestation of an acute coronary syndrome (ACS). Among patients with an ACS, malignant arrhythmias are significantly more common in the setting of an acute ST elevation MI (STEMI), but are also seen in approximately 2 percent of patients with a non-ST elevation MI (NSTEMI). In patients with an ACS and ischemia, the arrhythmia is usually polymorphic VT, rapid VT (ventricular flutter), or VF. (See "Ventricular arrhythmias during acute myocardial infarction: Incidence, mechanisms, and clinical features".)

Patients who experience SCD during the first 48 hours after an STEMI have a higher in-hospital mortality compared with STEMI patients who do not experience sustained VT or VF. However, among patients who survive to hospital discharge there is little or no difference in mortality at one to two years. (See "Ventricular arrhythmias during acute myocardial infarction: Incidence, mechanisms, and clinical features".)

Diagnostic angiography — In SCD survivors without an ACS, angiography is still considered to exclude stable, chronic CHD, which, as indicated above, is the leading cause for SCD [15]. Malignant arrhythmias and SCD occur in such patients, usually those who have had a prior infarction with residual myocardial scar. In contrast to patients with an ACS, the culprit arrhythmia is usually scar-related monomorphic VT, which is not the result of ischemia. However, monomorphic VT can ultimately degenerate to VF, particularly if the arrhythmia induces ischemia. Because SCD may be the first clinical evidence of chronic CHD, most SCD survivors undergo diagnostic angiography prior to discharge.

Even for patients arriving at the hospital in refractory VT/VF who are receiving ongoing cardiopulmonary resuscitation (CPR), immediate coronary angiography appears beneficial in a carefully selected group of patients (18 to 75 years of age with VT/VF as initial rhythm who received three shocks and amiodarone loading dose and who can be in the catheterization lab in <30 minutes post-arrest) [16]. Among a cohort of 55 patients who met these criteria (after excluding 7 of 62 who were declared deceased on arrival to the catheterization lab), all of whom were started on extracorporeal life support and underwent immediate coronary angiography, 46 patients (84 percent) had significant obstructive CHD, including 35 patients (64 percent) with acute thrombus, all of whom underwent percutaneous coronary intervention [16]. Among the cohort, 26 patients (42 percent) were discharged alive with favorable neurologic function, compared with 15 percent of historical controls.

Diagnostic coronary angiography may not be necessary in selected patients without signs or symptoms of CHD if another clear cause for SCD is identified (eg, long QT syndrome, WPW, Brugada, hypertrophic cardiomyopathy, left ventricular noncompaction, or arrhythmogenic right ventricular cardiomyopathy).

Angiography is suggested in younger patients without an apparent cause for SCD in whom angiography may also detect an anomalous origin of a coronary artery. Among competitive athletes under age 35, anomalous origin of a coronary artery was present in 13 percent of SCD survivors in one series [17]. (See "Athletes: Overview of sudden cardiac death risk and sport participation", section on 'Etiology of sudden death'.)

Patients with stable CHD who experience an episode of primary SCD without evidence of simultaneous ischemia are at high risk for recurrent malignant arrhythmias, even after percutaneous or surgical revascularization [18-21]. As a result, such patients are treated with an ICD. (See "Risk stratification after acute ST-elevation myocardial infarction".)

Echocardiography — Echocardiography can detect abnormalities that suggest or confirm the diagnosis of many of the important causes of SCD. Since global left ventricular dysfunction due

to myocardial stunning can be induced by cardiac arrest and cardiopulmonary resuscitation, evaluation of left ventricular function should be performed at least 48 hours after resuscitation [22].

Detailed review of the diagnostic criteria for each disorder is presented separately. Potential causes of SCD that can be detected with echocardiography include the following:

- CHD – Left ventricular dysfunction with wall motion abnormalities suggest prior myocardial infarction. Dyskinetic wall motion is consistent with an aneurysm.
- Hypertrophic cardiomyopathy (see "Hypertrophic cardiomyopathy: Clinical manifestations, diagnosis, and evaluation")
- Arrhythmogenic right ventricular cardiomyopathy
- Aortic stenosis (see "Echocardiographic evaluation of the aortic valve")
- Dilated cardiomyopathy (see "Echocardiographic recognition of cardiomyopathies" and "Ventricular arrhythmias: Overview in patients with heart failure and cardiomyopathy")

Cardiac MR — Cardiac magnetic resonance imaging (CMR) is indicated for selected patients in whom a diagnosis is uncertain after the above evaluation. (See "Clinical utility of cardiovascular magnetic resonance imaging".)

CMR is useful in the evaluation of the following disorders:

- Hypertrophic cardiomyopathy (see "Hypertrophic cardiomyopathy: Clinical manifestations, diagnosis, and evaluation")
- Myocarditis
- Arrhythmogenic right ventricular cardiomyopathy
- Dilated cardiomyopathy
- Congenital heart disease, including anomalous origin of coronary arteries (see "Congenital and pediatric coronary artery abnormalities" and "Cardiac imaging with computed tomography and magnetic resonance in the adult")
- Cardiac sarcoidosis
- Cardiac amyloidosis (see "Cardiac amyloidosis: Epidemiology, clinical manifestations, and diagnosis", section on 'Cardiovascular magnetic resonance')

The utility of CMR angiography as an alternative to invasive coronary angiography is not well defined. Alternatively, cardiac computed tomography angiography may be used to assess both congenital and acquired coronary abnormalities. (See "Cardiac imaging with computed tomography and magnetic resonance in the adult".)

Summary — In 1997, the Joint steering committees of the Unexplained Cardiac Arrest Registry of Europe and of the Idiopathic Ventricular Fibrillation Registry of the United States published recommendations for the evaluation of SCD survivors [12]. These recommendations included the following tests, all of which are described above:

- History and physical examination
- Blood biochemistries
- ECG
- Echocardiography
- Coronary angiography

Since the publication of these recommendations, cardiac MR has come into wider use and is now a common component of this evaluation when standard tests are inconclusive.

When this evaluation has not provided a diagnosis, the patient is evaluated for primary electrical disease.

EVALUATION FOR PRIMARY ELECTRICAL DISEASES

General issues — Approximately 5 to 10 percent of SCD survivors have no evidence of a noncardiac etiology or of structural heart disease after the above evaluation. Such patients are considered to have a primary electrical disorder.

A detailed discussion of SCD in patients with a structurally normal heart is presented separately. (See "Approach to sudden cardiac arrest in the absence of apparent structural heart disease".)

The majority of these patients do not actually have "normal" hearts, but historically our diagnostic tools have been unable to identify the structural or functional derangement. In the past, the etiology of many of these deaths was unknown and deemed "idiopathic." Subsequent discoveries have identified the cause of death in many of these patients [11,23,24]. As our understanding of the mechanisms of primary electrical disorders has improved, so have our diagnostic capabilities, with important benefits for both the victims of SCD and their families.

These disorders are often detected by characteristic changes on the ECG. (See 'Electrocardiogram' above.)

Several of the disorders that cause SCD in the absence of structural heart disease are due to abnormalities of cardiac ion channels, including the following:

- Brugada syndrome (see "Brugada syndrome: Clinical presentation, diagnosis, and evaluation")
- Long QT syndrome (see "Congenital long QT syndrome: Epidemiology and clinical manifestations" and "Acquired long QT syndrome: Definitions, pathophysiology, and causes")
- Short QT syndrome (see "Short QT syndrome")
- Catecholaminergic polymorphic VT (see "Catecholaminergic polymorphic ventricular tachycardia")

Disorders associated with SCD that are not due to ion channel abnormalities include:

- Wolff-Parkinson-White syndrome (see "Wolff-Parkinson-White syndrome: Anatomy, epidemiology, clinical manifestations, and diagnosis")
- Commotio cordis (see "Commotio cordis")

Patients without evidence of any of the above structural or electrical abnormalities are said to have idiopathic VF or primary electrical disease.

Identification of a primary electrical disorder in a SCD survivor has two important benefits:

- Directing medical treatment to prevent arrhythmia recurrence (eg, beta blockers for catecholaminergic polymorphic VT). Although medical therapy alone is now uncommon in SCD survivors (the vast majority of patients receive an ICD), adjunctive medical therapy can be useful to reduce the frequency of ICD shocks. (See "Secondary prevention of sudden cardiac death in heart failure and cardiomyopathy", section on 'Other treatment options'.)

- Guiding the evaluation and management of family members.

EP study — Electrophysiologic (EP) testing is not usually performed in patients with an established etiology of SCD. However, EP study can be valuable in those whose initial evaluation reveals no etiology, and in selected patients with a previously identified disorder.

In SCD survivors with an apparently normal heart, EP testing may reveal the following:

- Abnormalities of atrioventricular conduction – The presence of severe conducting system disease suggests that a serious bradyarrhythmia may have contributed to the SCD event. However, such patients typically present with syncope rather than SCD. Furthermore, even

when conduction disease is identified, VT/VF may be the real culprit and ventricular stimulation to induce ventricular arrhythmias may be warranted.

- An accessory pathway in patients with Wolff-Parkinson-White syndrome – An accessory pathway can result in rapid conduction to the ventricle of a supraventricular arrhythmia, primarily atrial fibrillation, producing a very rapid ventricular rate that can degenerate to VF. Such patients usually have evidence of preexcitation on their ECG. If preexcitation is evident on an ECG in a survivor of SCD, EP study and ablation of the accessory pathway are usually indicated. (See "Wolff-Parkinson-White syndrome: Anatomy, epidemiology, clinical manifestations, and diagnosis", section on 'Ventricular fibrillation and sudden death'.)

- Inducible ventricular arrhythmias – VT and VF may be induced in patients with a number of underlying cardiac abnormalities. The prognostic value of inducible arrhythmias is best established in patients with prior myocardial infarction and reduced LV systolic function. (See "Incidence of and risk stratification for sudden cardiac death after myocardial infarction", section on 'Inducible VT/VF'.)

There is evidence that inducible VF, particularly when induced repeatedly with nonaggressive protocols, suggests the diagnosis of idiopathic VF and may predict recurrent arrhythmic events [25,26]. In a review of the literature, 69 percent of patients with idiopathic VF had a sustained ventricular tachyarrhythmia induced with a nonaggressive protocol; induced arrhythmia was generally polymorphic in configuration and poorly tolerated [25].

In some other conditions it is not clear that inducible VT or VF has prognostic significance (eg, Brugada syndrome, infiltrative diseases, HCM). Furthermore, aggressive stimulation protocols can induce polymorphic VT or VF in some individuals without cardiac disease. Thus, inducible arrhythmias can be a nonspecific finding. For this reason, the significance of inducible ventricular arrhythmias in patients with apparently normal hearts is unclear. On the other hand, the absence of inducible VT/VF may not preclude ICD implantation since lack of inducibility does not predict low risk.

- Myocardial scar – Substrate mapping may identify areas of scar indicating abnormal substrate and a predisposition to ventricular arrhythmia. These abnormalities are more commonly seen in patients with CHD, HCM, ARVC, or infiltrative diseases, but also occur in some cases of idiopathic VF [27]. In addition, some patients with idiopathic VF have other electrophysiologic abnormalities, including areas of slow conduction, regionally delayed repolarization, or dispersion in repolarization [28].

- Supraventricular arrhythmias – Patients in whom VT or VF was not well documented at the time of SCD may have another culprit arrhythmia, usually a supraventricular tachycardia

(SVT). In such patients, SVT may be inducible during EP study [29].

Exercise testing — Exercise testing is not usually part of the CHD evaluation in SCD survivors, since most undergo coronary angiography. However, it may be of importance for the SCD survivor in whom the sudden death episode occurred during exercise or physical activity. In addition, the provocation of ischemia with exercise, independently of coronary anatomy, is of importance in the evaluation of the SCD survivor. Although angiography alone does not prove a causal relationship to SCD or the presence of ischemia, the observation that revascularization appears to improve outcomes [9,20,21] means that a negative exercise test in a patient with significant coronary disease on angiography is not likely to affect the decision on revascularization. Also of great importance is the provocation of VT or VF in these patients, which would predict a higher recurrence rate. It is also a target for adjunctive antiarrhythmic therapy, particularly a beta blocker, in addition to an ICD. While VT (which is often scar mediated and provoked by catecholamines) may be provoked during exercise, VF most commonly occurs after exercise in the recovery period (when ischemia is more common).

In patients with apparently normal hearts, exercise testing can assist in the diagnosis of long QT syndrome (QT interval fails to shorten or may even lengthen with an increase in heart rate) and catecholaminergic polymorphic VT. It is also useful in patients with Wolff-Parkinson-White pattern as the resolution of the delta wave with exercise generally correlates with low likelihood of a rapid ventricular rate with atrial fibrillation which is the etiology for VF and SCD in these patients. (See "Congenital long QT syndrome: Diagnosis", section on 'Exercise testing' and "Catecholaminergic polymorphic ventricular tachycardia" and "Wolff-Parkinson-White syndrome: Anatomy, epidemiology, clinical manifestations, and diagnosis", section on 'Evaluation'.)

Ambulatory monitoring — In patients without a clear etiology for SCD, ambulatory monitoring may reveal recurrent sustained or nonsustained arrhythmias. However, most patients without an established diagnosis will have an ICD placed prior to discharge, and the memory features in these devices may preclude the need for ambulatory monitoring.

Pharmacologic challenge — As noted above, some of the primary electrical disorders may still be present despite no evidence of abnormalities on any of the preceding tests. ECG abnormalities may be intermittent or latent, and genetic testing is not yet comprehensive enough to exclude all possible disorders.

Investigators have evaluated the role of pharmacologic challenge to elicit diagnostic ECG changes or arrhythmias in selected SCD survivors. One report included 18 SCD survivors with no evidence of structural heart disease [30]. All patients had a normal ECG, echocardiogram,

coronary angiography, and cardiac MR. Patients were infused with epinephrine (0.05 to 0.5 microg/kg per minute) and then procainamide (1 g over 30 minutes). Epinephrine was intended to induce catecholaminergic polymorphic VT and procainamide to induce the characteristic ECG abnormalities of Brugada syndrome. (See "Catecholaminergic polymorphic ventricular tachycardia" and "Brugada syndrome: Clinical presentation, diagnosis, and evaluation".)

The following findings were noted:

- Ten patients were diagnosed with catecholaminergic polymorphic VT based upon an abnormal response to epinephrine infusion (frequent or polymorphic ventricular ectopy, nonsustained VT, or sustained VT). Four of these patients had ventricular ectopy during exercise testing, but none had sustained or nonsustained VT.
- Two patients were diagnosed with Brugada syndrome.
- Six patients were left with a diagnosis of idiopathic VF.
- Among 55 family members who were tested, eight affected members from one family were diagnosed with catecholaminergic polymorphic VT, and one relative was diagnosed with Brugada syndrome.

In summary, two-thirds of patients whose standard evaluation provided no etiology for SCD had a diagnosis established with pharmacologic provocative testing. This allowed for the addition of appropriate adjunctive therapy (beta blockers for catecholaminergic polymorphic VT) and the identification of nine additional affected family members.

MINOR CARDIAC ABNORMALITIES NOT ASSOCIATED WITH SCD

During the course of the cardiac evaluation, minor cardiac abnormalities are often detected that do not have a clear causal relationship to SCD. These findings do not preclude the diagnosis of idiopathic VF; however, their severity must be considered and monitoring is warranted since these disorders may be the initial manifestations of an underlying structural heart disease that will become clinically apparent at a later date [12].

- Disorders such as first degree atrioventricular (AV) block, transient second degree Mobitz type II AV block without bradycardia, and isolated bundle branch block do not exclude idiopathic VF.
- Thickening of the left ventricle less than 10 percent above normal and hypertension without LV hypertrophy are not clearly associated with SCD.

- A direct link between mitral valve prolapse and SCD has not been established unless there is valve redundancy or thickening, a family history of SCD, or perhaps significant mitral regurgitation, QT interval prolongation, or ST-T waves changes. (See "Mitral valve prolapse: Overview of complications and their management".)

- AF in the absence of ventricular preexcitation or hyperthyroidism is associated with an increase in total mortality, but not SCD [12,31]. (See "Epidemiology, risk factors, and prevention of atrial fibrillation".)

- Isolated ventricular premature beats, and more importantly repetitive forms (ie, couplets or nonsustained ventricular tachycardia), are associated with an increased risk of subsequent SCD only in patients with structural heart disease or with risk factors for CHD. (See "Premature ventricular complexes: Treatment and prognosis", section on 'Prognosis'.)

EVALUATION OF FAMILY MEMBERS

Some causes of SCD are familial, including a genetic predisposition to premature coronary heart disease, a cardiomyopathy or an electrophysiologic abnormality (eg, long QT syndrome or Brugada), and the risk of cardiovascular disease appears significantly higher in first- and second-degree relatives of the SCD victims, particularly young victims. In a nationwide Danish study from 2000 to 2006, 470 victims of SCD were identified who were 35 years of age or younger [32]. Among a cohort of 3073 first- and second-degree relatives of the SCD victims who were followed for up to 11 years, cardiovascular disease (CVD) was significantly more likely to be present than in the general population (standardized incidence ratio [SIR] for CVD 3.5, 95% CI 2.7-4.7). In contrast, among relatives of elderly (greater than 60 years of age) victims of SCD, there was no difference in the rates of CVD compared with the general population (SIR 0.9, 95% CI 0.8-1.1).

A general cardiologic evaluation of first- and second-degree relatives of victims of unexplained SCD can yield the diagnosis of a heritable disease in up to 40 percent of families as illustrated by the following observations [33-35].

- In a study of 32 families of victims of unexplained SCD, a general cardiologic evaluation (ECG, echocardiogram, Holter monitor and, less commonly, stress testing) was completed in 107 first-degree relatives [33]. Seven families (22 percent) were diagnosed with a heritable disease: four with long QT syndrome, one with nonstructural cardiac disease, one with myotonic dystrophy, and one with HCM.

- These findings were extended in a second report that evaluated 43 families with 183 surviving first- and second-degree relatives of victims of unexplained SCD at age ≤40 [34]. Careful history identified 26 additional cases of unexplained SCD at age ≤40. Cardiology evaluation included ECG, echocardiogram, exercise tolerance testing (ETT), and measurement of serum lipids. Additional testing, as indicated, included flecainide challenge for suspected Brugada syndrome or cardiac MR for suspected ARVC. (See "Brugada syndrome or pattern: Management and approach to screening of relatives".)

  When a clinical diagnosis was established, genetic testing for the suspected disease was performed. Where a genetic abnormality was confirmed, additional screening was done in another 150 family members. The following findings were noted:

  - A heritable disease was identified in 17 families (40 percent): five with catecholaminergic polymorphic VT, four with long QT syndrome, two with Brugada syndrome, one with Brugada/long QT syndrome, three with ARVC, one with HCM, and one with familial hypercholesterolemia. Genetic analysis confirmed the diagnosis in 10 families.

  - An average of 8.9 asymptomatic carriers per family was identified, many through the secondary genetic analysis.

  - Identification of a specific disease was more likely if ≥2 unexplained SCD events occurred in the family, and if more family members underwent evaluation.

The increased yield in the second study may reflect the more extensive evaluation, including ETT, and the inclusion of more family members.

Consistent with these findings, it has been recommended that first-degree family members of patients with SCD in the absence of structural heart disease be informed of the potentially increased risk and that an assessment should be offered at a center with experience in the diagnosis and management of inherited cardiac diseases [24]. Routine genetic screening for inherited disorders is not feasible although, in the presence of an identifiable condition, the genetic evaluation of family members may be undertaken at some centers.

NEUROLOGIC AND PSYCHOLOGIC ASSESSMENT

Patients who have been resuscitated from sudden death should be given a complete neurologic examination to establish the nature and extent of impairment resulting from the arrest. The physical examination, rather than imaging studies or other testing, is the most useful way of

elucidating the patient's degree of neurologic function, mental impairment, and of determining prognosis. A 2004 meta-analysis of 11 studies found that the following clinical signs predicted a poor clinical outcome following cardiac arrest with 97 percent specificity [36]:

- Absence of pupillary light response after 24 hours
- Absence of corneal reflex after 24 hours
- Absent motor responses to pain after 24 hours
- Absent motor responses after 72 hours

(See "Hypoxic-ischemic brain injury in adults: Evaluation and prognosis".)

Equally important is an assessment of the patient's psychologic state. Posttraumatic stress disorder (PTSD) may occur in SCD survivors. This was suggested in a study of 143 patients who had been resuscitated and discharged with no or only moderate neurologic disability [37]. All patients completed a self-rating questionnaire at a mean of 45 months after cardiac arrest: 39 (27 percent) fulfilled criteria for PTSD. (See "Posttraumatic stress disorder in adults: Epidemiology, pathophysiology, clinical features, assessment, and diagnosis" and "Posttraumatic stress disorder in adults: Treatment overview".)

MANAGEMENT

At present, most survivors of SCD are treated with an ICD. The use of ICDs in SCD survivors, the role of adjunctive antiarrhythmic medications and catheter ablation, and exceptions to the use of ICDs are discussed in detail separately. (See "Secondary prevention of sudden cardiac death in heart failure and cardiomyopathy".)

SUMMARY AND RECOMMENDATIONS

Evaluation of the survivor of SCD includes the following:

- Identification and treatment of acute reversible causes, including (see 'Etiology of SCD' above and "Pathophysiology and etiology of sudden cardiac arrest", section on 'Etiology of SCD'):
  - Acute cardiac ischemia and myocardial infarction
  - Antiarrhythmic drugs or other medication (eg, QT prolonging drugs), toxin, or illicit drug ingestion

- Electrolyte abnormalities, most notably hypokalemia, hyperkalemia, and hypomagnesemia
- Heart failure
- Autonomic nervous system factors, especially sympathetic activation (eg, physical or psychologic stress)

- Evaluation for structural heart disease
  - Initial evaluation including history, physical examination, laboratory testing (eg, electrolytes, blood gas, toxin screen, etc), and electrocardiogram (see 'Initial evaluation' above)
  - Evaluation for structural heart disease, which may include one or more of echocardiography, coronary angiography, cardiac magnetic resonance imaging, depending of the clinical scenario (see 'Evaluation for structural heart disease' above)
- In patients without obvious arrhythmic triggers or cardiac structural abnormalities, an evaluation for primary electrical diseases
  - Primary electrical diseases include Brugada syndrome, long QT syndrome, short QT syndrome, Wolff-Parkinson-White, catecholaminergic polymorphic VT, commotio cordis, and idiopathic ventricular fibrillation (see 'General issues' above)
  - The evaluation for primary electrical disease may include one or more of electrophysiology studies, exercise testing, ambulatory ECG monitoring, and pharmacologic challenge (see 'Evaluation for primary electrical diseases' above)
- Neurologic and psychologic assessment (see 'Neurologic and psychologic assessment' above)
- In selected patients with a suspected or confirmed heritable syndrome, evaluation of family members (see 'Evaluation of family members' above)

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Topic 970 Version 37.0

GRAPHICS

Treatable conditions associated with cardiac arrest

Condition	Common associated clinical settings
Acidosis	Diabetes, diarrhea, drug overdose, renal dysfunction, sepsis, shock
Anemia	Gastrointestinal bleeding, nutritional deficiencies, recent trauma
Cardiac tamponade	Post-cardiac surgery, malignancy, post-myocardial infarction, pericarditis, trauma
Hyperkalemia	Drug overdose, renal dysfunction, hemolysis, excessive potassium intake, rhabdomyolysis, major soft tissue injury, tumor lysis syndrome
Hypokalemia*	Alcohol abuse, diabetes mellitus, diuretics, drug overdose, profound gastrointestinal losses
Hypothermia	Alcohol intoxication, significant burns, drowning, drug overdose, elder patient, endocrine disease, environmental exposure, spinal cord disease, trauma
Hypovolemia	Significant burns, diabetes, gastrointestinal losses, hemorrhage, malignancy, sepsis, trauma
Hypoxia	Upper airway obstruction, hypoventilation (CNS dysfunction, neuromuscular disease) pulmonary disease
Myocardial infarction	Cardiac arrest
Poisoning	History of alcohol or drug abuse, altered mental status, classic toxidrome (eg, sympathomimetic), occupational exposure, psychiatric disease
Pulmonary embolism	Immobilized patient, recent surgical procedure (eg, orthopedic), peripartum, risk factors for thromboembolic disease, recent trauma, presentation consistent with acute pulmonary embolism
Tension pneumothorax	Central venous catheter, mechanical ventilation, pulmonary disease (eg, asthma, chronic obstructive pulmonary disease), thoracentesis, thoracic trauma

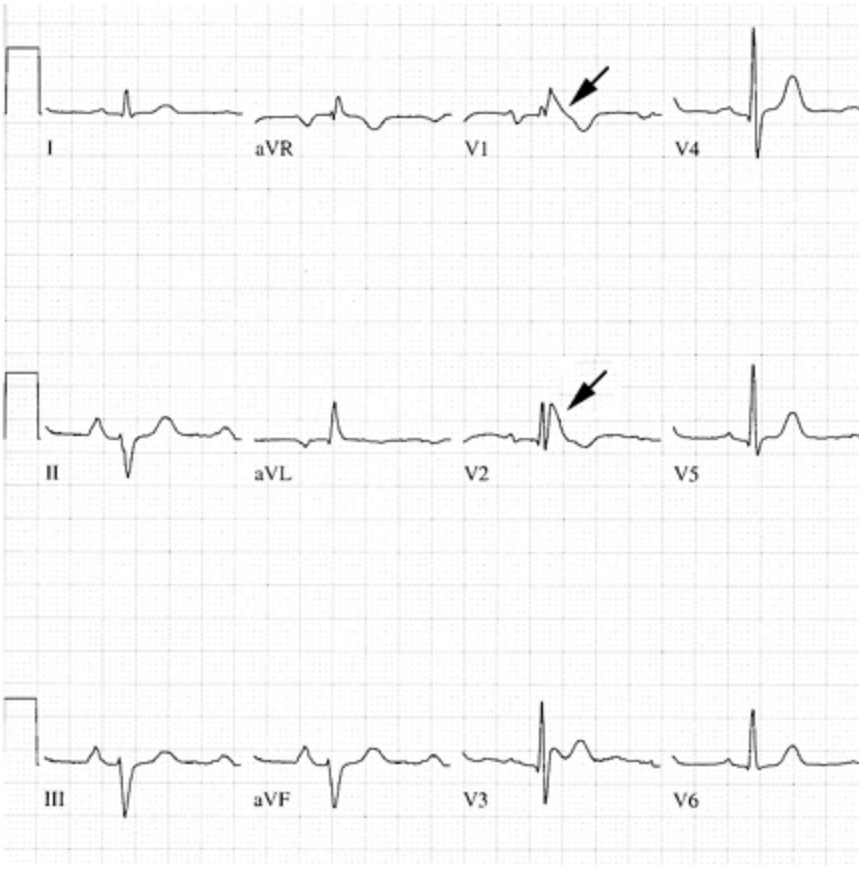
CNS: central nervous system.

* Hypomagnesemia should be assumed in the setting of hypokalemia, and both should be treated.

Adapted from: Eisenberg MS, Mengert TJ. Cardiac resuscitation. N Engl J Med 2001; 344:1304.

Graphic 52416 Version 8.0

12-lead electrocardiogram (ECG) from a patient with the Brugada syndrome shows downsloping ST elevation

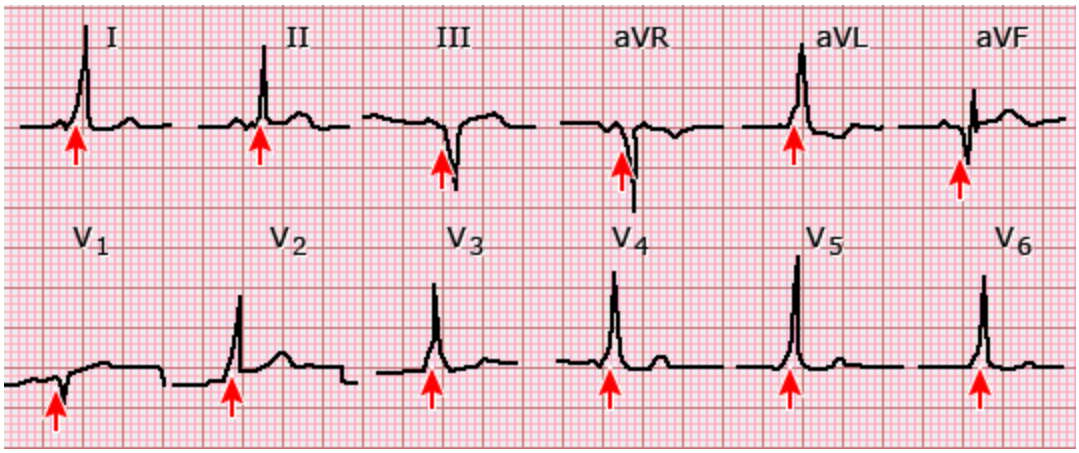


ST segment elevation and T wave inversion in the right precordial leads V1 and V2 (arrows); the QRS is normal. The widened S wave in the left lateral leads (V5 and V6) that is characteristic of right bundle branch block is absent.

Courtesy of Rory Childers, MD, University of Chicago.

Graphic 64510 Version 10.0

12-lead ECG showing the Wolff-Parkinson-White pattern

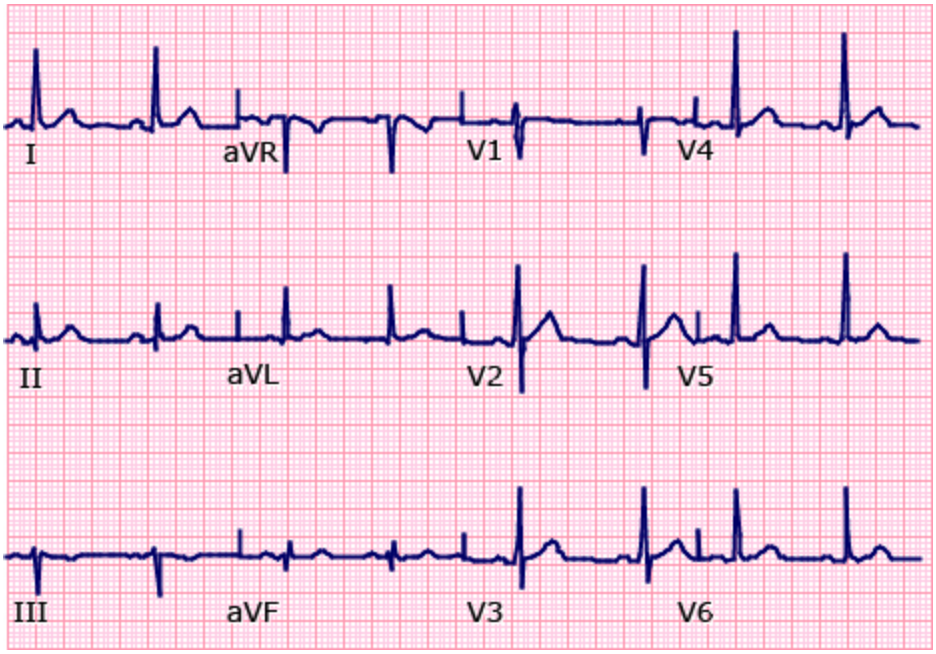


The two main ECG features of WPW pattern include a short PR interval (<0.12 seconds) and a delta wave (arrows). The QRS complex is wide (>0.12 seconds) and represents a fusion beat; the initial portion (delta wave) results from rapid ventricular activation via the accessory pathway (preexcitation), while the termination of ventricular activation is via the normal conduction system, leading to a fairly normal terminal portion of the QRS.

ECG: electrocardiogram; WPW: Wolff-Parkinson-White.

Graphic 75578 Version 11.0

Normal ECG in sinus rhythm



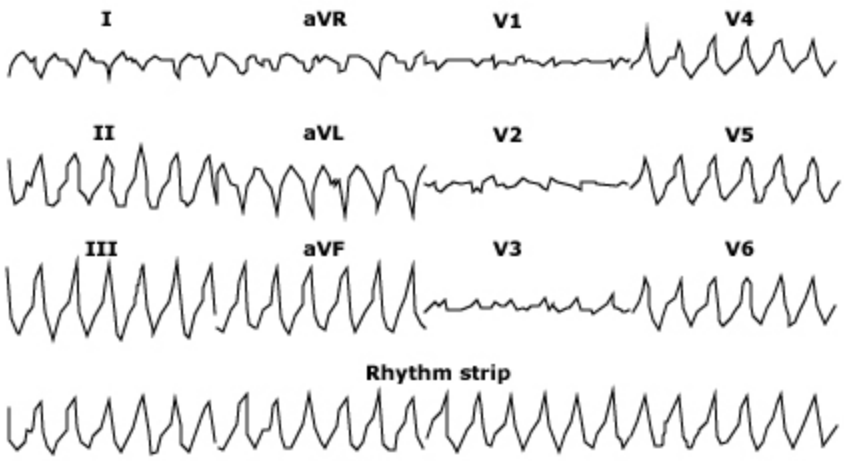
Normal sinus rhythm at a rate of 71 beats/minute, a P wave axis of 45°, and a PR interval of 0.15 seconds.

ECG: electrocardiogram.

Courtesy of Morton Arnsdorf, MD.

Graphic 58149 Version 6.0

12-lead electrocardiogram showing ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy

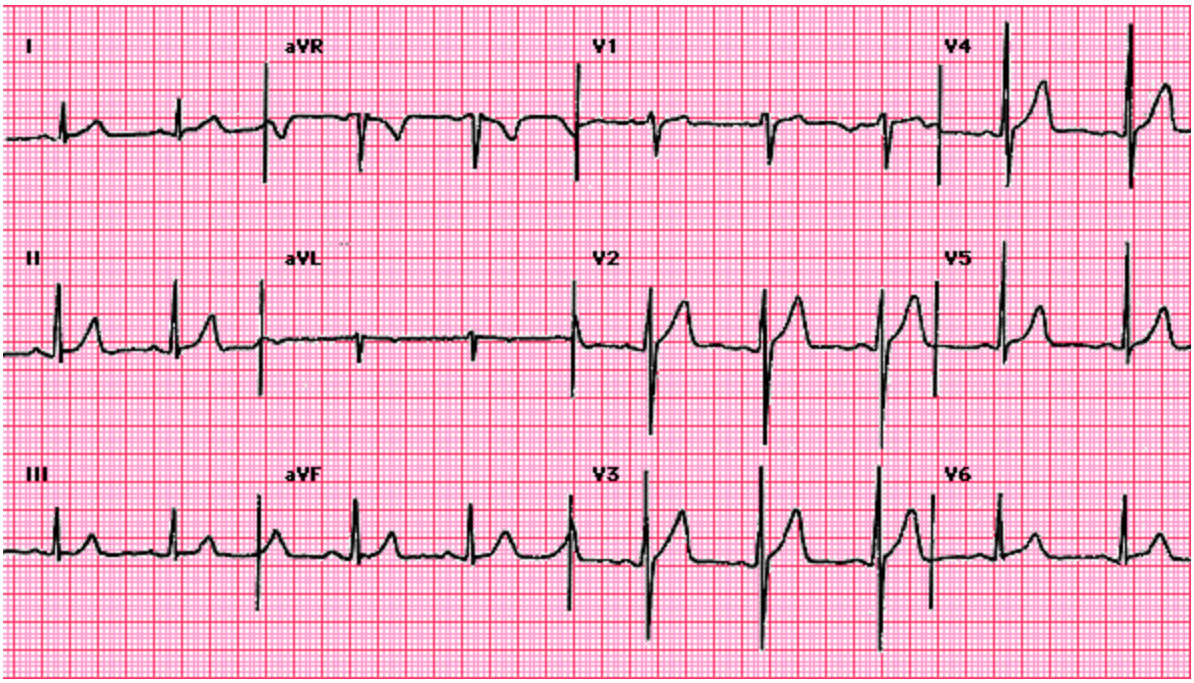


Ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy usually arises from the free wall of the right ventricle, resulting in a left bundle branch morphology.

With permission from Podrid PJ, Kowey PR (Eds), Cardiac Arrhythmia - Mechanisms, Diagnosis, and Management, Williams & Wilkins, Baltimore, 1995.

Graphic 56591 Version 9.0

Normal ECG



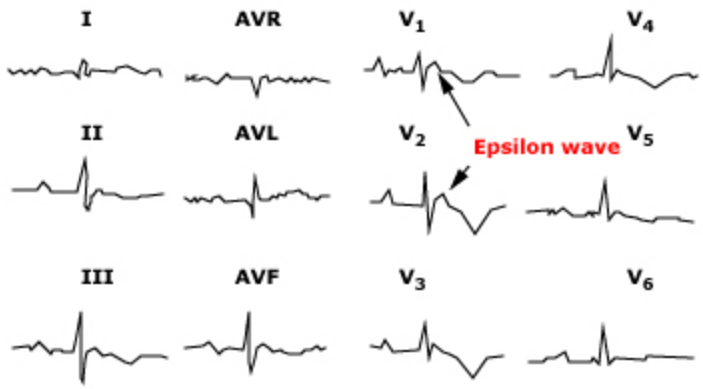
Normal electrocardiogram showing normal sinus rhythm at a rate of 75 beats/minute, a PR interval of

0.14 seconds, a QRS interval of 0.10 seconds, and a QRS axis of approximately 75°.

Courtesy of Ary Goldberger, MD.

Graphic 76183 Version 4.0

12-lead electrocardiogram showing epsilon wave and T wave inversions in arrhythmogenic right ventricular cardiomyopathy

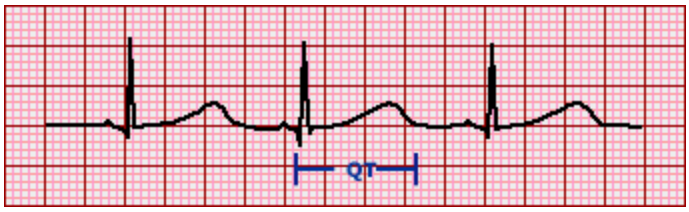


12-lead electrocardiogram in a patient with arrhythmogenic right ventricular cardiomyopathy showing deep T wave inversions in V2 to V4, compatible with right ventricular disease, and epsilon waves representing delayed right ventricular depolarization just after the QRS complex (arrows).

Data from: Jaoude S, Leclercq JF, Coumel P. Eur Heart J 1996; 17:1717.

Graphic 60781 Version 9.0

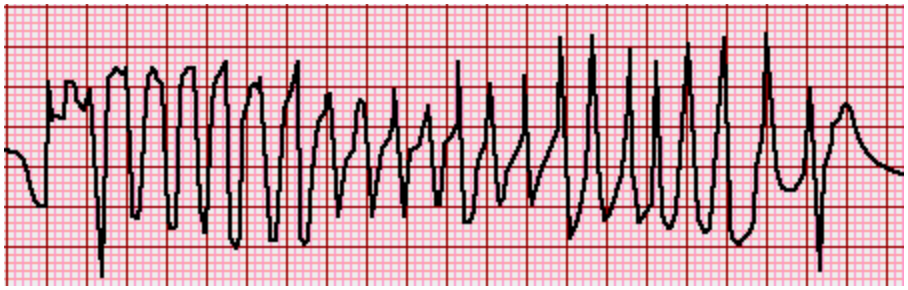
Single-lead electrocardiogram showing a prolonged QT interval



The corrected QT interval (QTc) is calculated by dividing the QT interval (0.60 seconds) by the square root of the preceding RR interval (0.92 seconds). In this case, the QTc is 0.625 seconds (625 milliseconds).

Graphic 77018 Version 7.0

Single lead electrocardiogram (ECG) showing polymorphic ventricular tachycardia (VT)



This is an atypical, rapid, and bizarre form of ventricular tachycardia that is characterized by a continuously changing axis of polymorphic QRS morphologies.

Graphic 53891 Version 5.0

Major causes of sudden death

Ischemic heart disease
Coronary artery disease with myocardial infarction or angina
Coronary artery embolism
Nonatherogenic coronary artery disease (arteritis, dissection, congenital coronary artery anomalies)
Coronary artery spasm
Nonischemic heart disease
Hypertrophic cardiomyopathy
Dilated cardiomyopathy
Valvular heart disease
Congenital heart disease
Arrhythmogenic right ventricular dysplasia
Myocarditis
Acute pericardial tamponade
Acute myocardial rupture
Aortic dissection
No structural heart disease
Primary electrical disease (idiopathic ventricular fibrillation)
Brugada syndrome (right bundle branch block and ST segment elevation in leads V1 to V3)
Long QT syndrome
Preexcitation syndrome
Complete heart block
Familial sudden cardiac death
Chest wall trauma (commotio cordis)
Noncardiac disease
Pulmonary embolism
Intracranial hemorrhage
Drowning
Pickwickian syndrome
Drug-induced

Central airway obstruction
Sudden infant death syndrome
Sudden unexplained death in epilepsy (SUDEP)

Graphic 62184 Version 3.0