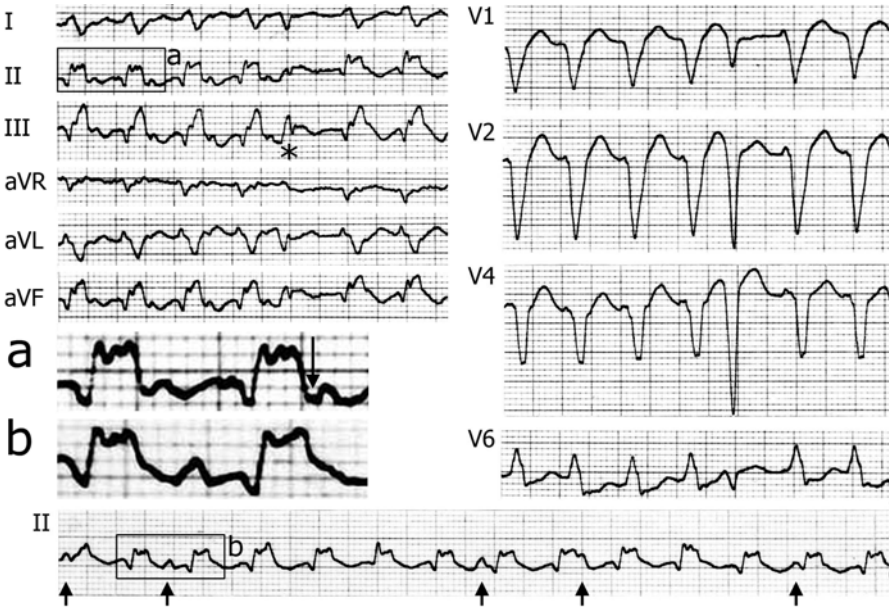

Fig. 6.4 Ventricular tachycardia with retrograde P waves apparently positive in the inferior leads. In all leads, that are simultaneous, apart from the tracing in the bottom strip, the 5th beat (*asterisk*) is a ventricular extrasystole. Beats 1–4 are followed by P waves that seem, at first glance, positive in the inferior leads and negative in aVR and aVL. The premature beat alters the relationship between QRS complexes and P waves, being the last two ventricular beats not followed by P waves. The bottom strip (lead II) has been recorded later with respect to the others and clearly shows A-V dissociation: P waves of sinus origin are positive (*arrows*) and independent of QRS complexes; some sinus P waves, occurring simultaneously with ventricular complexes, are invisible, being "buried" within the ventricular complexes. Panels (**a**, **b**) show enlarged beats: during retrograde V-A conduction, P waves are negative (*arrow* in section **a**), not positive as they seem at first glance. In section (**b**), a positive P wave is evident in between two QRS complexes, demonstrating A-V dissociation

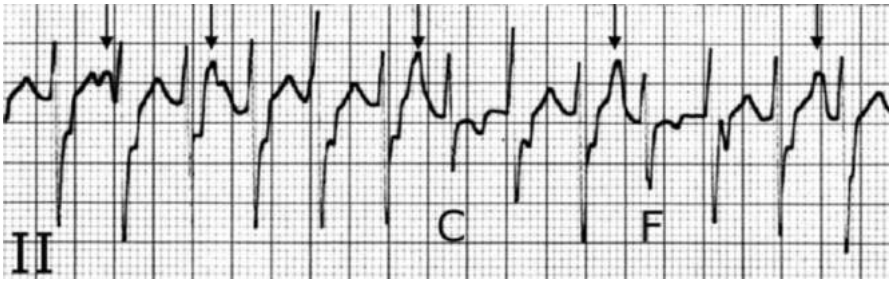

Fig. 6.5 Capture and fusion beats during ventricular tachycardia. In this ECG strip, A-V dissociation is evident (*arrows* point out sinus P waves that modify T wave morphology). In two occasions, the sinus impulse is conducted to the ventricles, giving rise to a narrow QRS complex (capture beat, labeled *C*) or to a fusion beat (labeled *F*). These are intermediate in configuration between ectopic wide complexes and capture beat

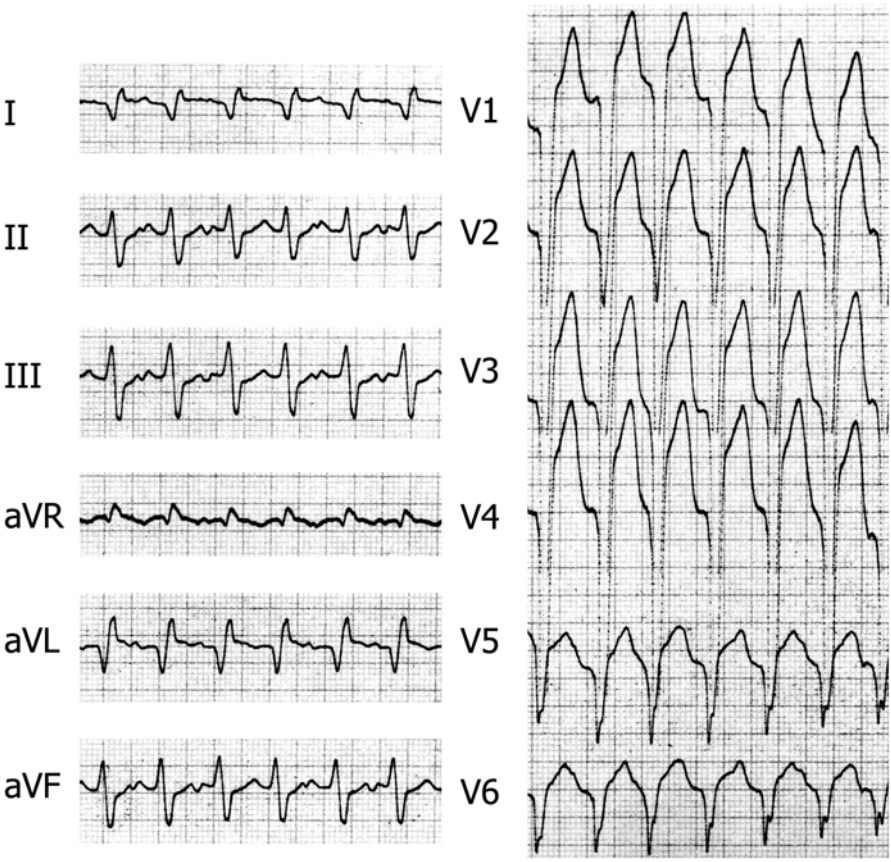

Fig. 6.6 Precordial concordance. In this tachycardia, wide QRS complexes with QS morphology are present in all precordial leads. This pattern demonstrates without any exception the ventricular origin of tachycardia. Analysis of the inferior leads also reveals a 2nd-degree V-A block with 3:2 ratio; the retrograde negative P waves modify the T wave configuration in two consecutive beats, whereas in the 3rd QRS complex, the T wave is not affected

disturbance can result in such a configuration [15]. Concordance, however, cannot be diagnosed if rS, Rs, or rs complexes occur even in one single precordial lead. In a study based on 232 electrocardiograms with bundle branch block analyzed during sinus rhythm, none showed precordial concordance, suggesting a 100 % specificity of this sign indicating the ventricular origin of the arrhythmia [16]. Negative concordance (QS morphology in all precordial leads, Fig. 6.6), however, is specific of VT, whereas positive concordance could be observed, although rarely, in a preexcited tachycardia due to a left-sided Kent bundle [7, 8]. Negative concordance in the bipolar limb leads (I, II, III) has also been proposed as a specific pattern suggesting VT; [17] such a configuration demonstrates an extreme right axis deviation, a phenomenon that never occurs in adults, apart from some cases of congenital heart disease or dextrocardia.

6.2.5 Absence of RS Complexes in the Precordial Leads

In several cases of VT, none of the precordial leads shows ventricular complexes with a configuration characterized by an R wave followed by an S wave (rs, RS, rS, or Rs). This sign, expressing in a slightly different manner the concept of "precordial concordance," suggests a ventricular origin of the arrhythmia. The sign specificity was 100 % both in the original study [5] and in another research based on 133 patients with wide QRS tachycardia; [10] in a different series, however, specificity was 81 and 98 % in the presence of positive and negative precordial QRS complexes, respectively [16].

6.2.6 Interval >100 ms from QRS Complex Beginning to S Wave Nadir in a Precordial Lead

It has been observed that whenever, in a wide QRS complex tachycardia, the interval from QRS complex beginning to S wave nadir exceeds 100 ms in a precordial lead, tachycardia is ventricular in origin [5]. The above criterion was fulfilled in 41 % of patients with previous myocardial infarction and VT [18]. In subjects with slowed down intraventricular conduction, however, leads V4–V6 show at times the above-mentioned sign even during sinus rhythm, particularly in the presence of left axis deviation. In a study based on electrocardiograms with left bundle branch block and sinus rhythm, 34 % of cases had an interval from QRS complex beginning to S wave nadir >100 ms [16], demonstrating a low specificity of this sign in revealing VT.

6.2.7 Vagal Stimulation Maneuvers

In the presence of QRS wide complex tachycardia, vagal stimulation can result in the following responses:

1. No change in tachycardia morphology or rate: the question remains open.
2. Sinus rhythm restoration: supraventricular reentrant tachycardia with a circuit incorporating the A-V node.
3. Variation in A-V conduction ratio, with appearance of P or F waves: atrial tachycardia or atrial flutter.
4. Variation in V-A conduction ratio, demonstrated by QRS complexes not followed by a retrograde P wave: ventricular origin of tachycardia.

6.3 The Electrocardiogram in the Absence of Tachycardia

An ECG recorded in the absence of tachycardia can be at times helpful, since a conduction disturbance or preexcitation observed during sinus rhythm can be the key to recognize the mechanism underlying the wide QRS complexes. In the great

majority of cases, however, no ECG recorded during sinus rhythm is available at the moment of the arrhythmic emergence. Whenever the ECG during tachycardia is identical to that obtained in sinus rhythm, the arrhythmia is supraventricular in origin, apart from a single exception: the bundle branch reentry tachycardia [19]. In the latter condition, a tracing in sinus rhythm can be misleading, since it suggests a supraventricular, rather than ventricular, origin of the arrhythmia [19].

6.4 QRS Complex Morphology in Leads V1 and V6

Analysis of QRS complex configuration represents an important tool in wide QRS complex tachycardia. Whenever other diagnostic signs (A-V dissociation, capture and fusion beats, precordial concordance, etc.) are either absent or controversial, the distinction between supraventricular and ventricular tachycardia lies on morphologic analysis of ventricular complexes, taking particularly into account leads V1 and V6. The 1st step is tachycardia classification based on QRS morphology in lead V1: whenever ventricular complex is mainly positive in this lead, tachycardia will be defined as "RBBB type," whereas if in that lead ventricular complexes are negative, tachycardia will be classified as "LBBB type." In any situation, the leads to be analyzed are V1 and V6.

6.4.1 Wide QRS Complex Tachycardia with Right Bundle Branch Block-Type Configuration (Positive QRS Complex in Lead V1)

V1. Ventricular complexes with morphology *R* or *Rr′* (the 1st R wave higher than the 2nd one), as well as *qR* or *RS* complexes, suggest VT, whereas both a triphasic (*rsR*Đ or *rSR*Đ) or biphasic configurations *rR*Đ with the 2nd R wave higher than the 1st one suggest SVT with aberrant conduction (Fig. 6.7).
V6. In this lead, *rS*, *QS,* or *qR* complexes are specific of VT (Fig. 6.8), whereas *qRs* complexes suggest aberrant conduction (specificity 95 %). Whenever the R/S ratio, however, is <1 (larger S wave than R wave voltage in lead V6), the ventricular, rather than supraventricular, origin of tachycardia is more likely [10, 16, 20].

6.4.2 Wide QRS Complex Tachycardia with Left Bundle Branch Block-Type Morphology (Negative QRS Complex in Lead V1)

V1. In the presence *of SVT with aberrant conduction and LBBB morphology, this lead shows either a QS configuration or a small and relatively narrow (≤30 ms) r wave* followed by a deep S wave with an early (<60 ms) nadir. R wave duration >30 ms or S wave nadir later than 60 ms from the QRS complex beginning suggest ventricular origin of the arrhythmia. Moreover, a notch in the proximal (descending) limb of S wave indicates VT (Fig. 6.8).

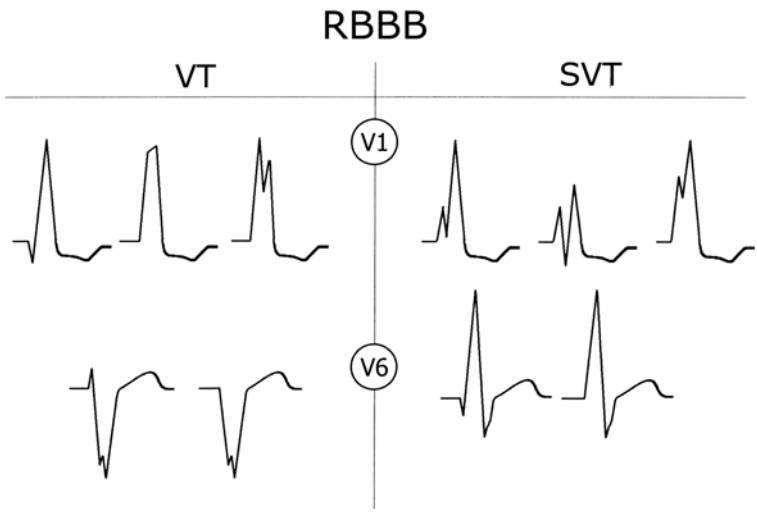

Fig. 6.7 Ventricular complex morphology suggesting either VT or SVT with aberrant conduction in wide QRS complex tachycardia with RBBB-like configuration (QRS complex mainly positive in lead V1)

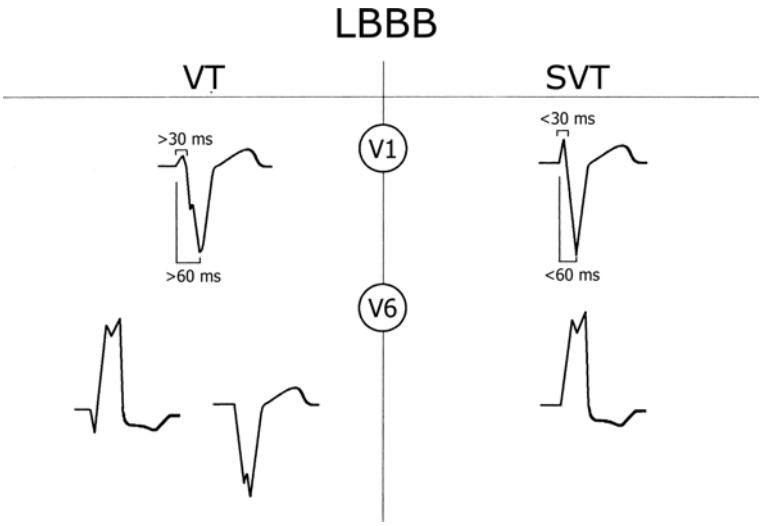

Fig. 6.8 Ventricular complex morphology suggesting either VT or SVT with aberrant conduction in wide QRS complex tachycardia with LBBB-like configuration (QRS complex mainly negative in lead V1)

V6. In a wide QRS complex tachycardia, negative or predominantly *negative QRS complexes in lead V6 suggest at first glance a ventricular origin* of the arrhythmia independent of the associated intraventricular disturbance pattern [20]. Impulses

of ventricular origin show often (69 % of cases) a negative net QRS amplitude (algebraic sum of positive and negative deflections) in V6, whereas this pattern is relatively rare (27 % of cases) in supraventricular tachycardia.

These signs based on QRS morphology in leads V1 and V6, introduced by Kindwall [21], express the slow initial progression of the ventricular wave front when the depolarization is not due to an impulse conducted over the His-Purkinje system. In true LBBB, thus, the 1st ventricular vector, expressing the right-to-left septal depolarization, is directed to the left and anteriorly: lead V1, thus, cannot show a *wide* r wave since the initial ventricular depolarization is fast, being the supraventricular impulse conducted over the Purkinje system. Accordingly, *in a broad QRS tachycardia with LBBB configuration, a relatively wide (≥30 ms) r wave in lead V1 strongly suggests a ventricular origin of the arrhythmia*. The same holds true for a relatively late (>60 ms) S wave nadir in lead V1 and for the presence of a notch in the descending S wave limb. The specificity of the above "ectopic" QRS morphologies in lead V1, however, is not 100 %: a study based on electrocardiograms with LBBB during sinus rhythm has reported a specificity of 78, 66 and 66 % for r wave duration in lead V1 >30 ms, S wave nadir >60 ms, and notch in the descending S wave limb, respectively [16].

6.4.3 Limitations of Criteria Based on QRS Morphology in Wide QRS Complex Tachycardia

Despite being useful, morphologic criteria are not absolute; the equations *typical bundle branch block = aberrant conduction, atypical bundle branch block = ventricular tachycardia* suffer some *limitations and may lead to wrong conclusions in patients treated with antiarrhythmic drugs, particularly those belonging to class 1C*. This is because these drugs slow down the intraventricular conduction, resulting in very abnormal ventricular complexes. Patients treated with 1C drugs may show extremely wide QRS complexes during SVT, to the extent that morphological analysis leads to a wrong diagnosis. This occurs not rarely in patients with atrial flutter treated with 1C antiarrhythmic drugs, that result in tachycardia rate reduction, favoring 1:1 A-V conduction of atrial impulses, and QRS complex widening.

6.5 Other Signs

6.5.1 QRS Duration >140 ms

It has been observed that a wide complex tachycardia with QRS duration >0.14 s is very likely ventricular in origin [11], but this criterion has a low specificity, ranging from 43 % [16] to 69 % [10]. Moreover, QRS complexes can be, although rarely, relatively narrow (<0.12 s) in ventricular tachycardia.

6.5.2 QRS Axis Deviation

In several cases of VT, left or right axis deviation occurs [9–11], and rarely the QRS axis is normal (between 0° and +90°) in VT. Superior QRS axis deviation, however, has been considered not suggestive of VT in the presence of ventricular complexes with LBBB configuration, whereas an RBBB morphology is often associated with VT (87 % specificity) [16].

6.5.3 Regularity

Apart from atrial fibrillation and atrial flutter or tachycardia with variable A-V conduction ratio, supraventricular tachycardias are usually regular. This is also true for sustained ventricular tachycardias, although irregularity in itself does not exclude VT, the variability of R-R intervals being not uncommon in focal tachycardias, particularly at the beginning or at the end of tachycardia. Sustained VT cycle variability has also been attributed to exit block [22] or longitudinal dissociation in the reentry pathway of tachycardia [23, 24].

6.6 Lead aVR Analysis

A new algorithm based on lead aVR analysis has recently been proposed to distinguish ectopy from aberrant conduction in wide QRS complex tachycardia [25, 26]. The procedure is based on four steps (Fig. 6.9): the first three ones are simple and quick, whereas the 4th step requires complicated voltage measurements. Whenever the sign looked for in steps 1, 2, or 3 is present, the diagnosis is VT, whereas only in step 4 becomes possible the recognition of SVT with aberrant conduction (Fig. 6.9).

6.6.1 Step 1: Dominant Initial R Wave

146 out of 482 cases of wide QRS tachycardia showed in lead aVR *a dominant initial R wave*, which was the largest ventricular complex deflection (Figs. 6.9 and 6.10). This pattern *demonstrated a ventricular origin* of the arrhythmia, confirmed by intracardiac recordings, in 144/146 cases (sensitivity 38.9 %, specificity 98.2 %).

6.6.2 Step 2: q or r initial Wave with Duration >40 ms in qR or rS complexes

A ventricular complex starting, in aVR, *not with a dominant R wave but with a low voltage q or r wave whose duration was ≥40 ms* was present in 74 out of 336 cases without a dominant initial R wave. In 65 of these, the diagnosis was VT (sensitivity 28.8 %, specificity 91.8 %).

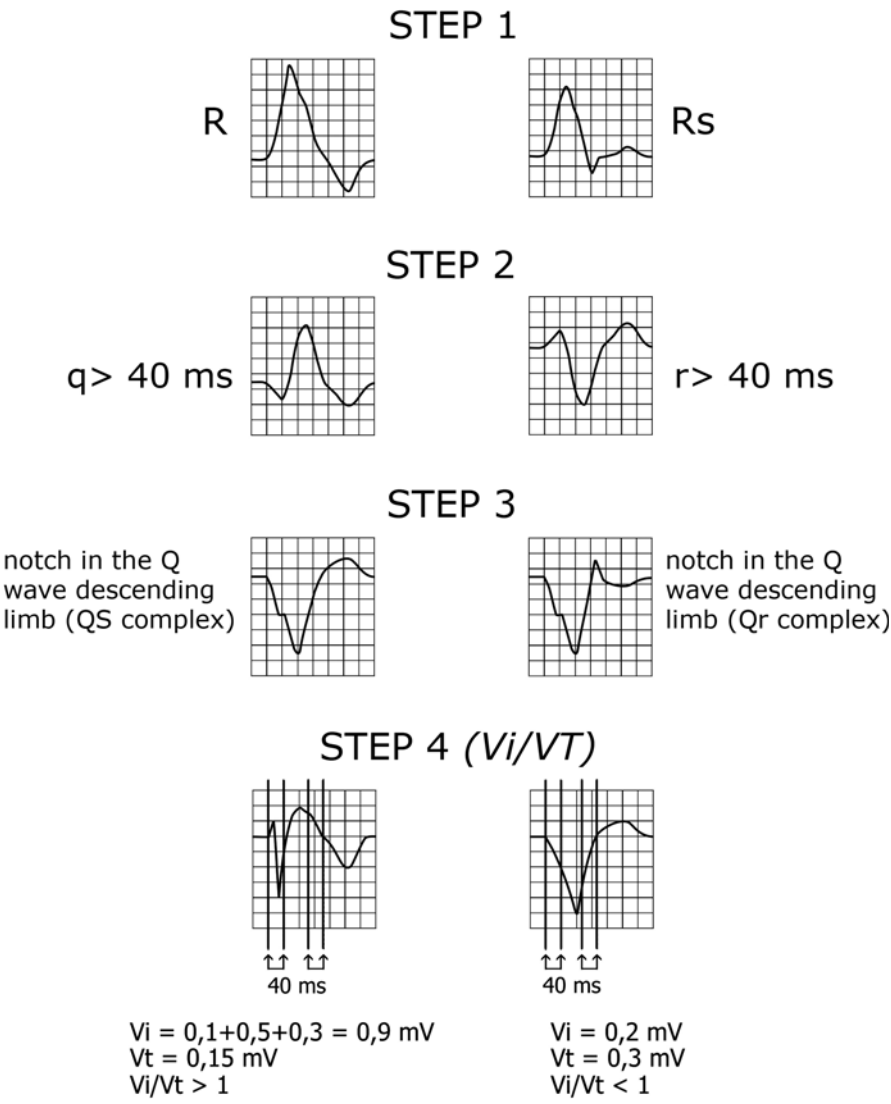

Fig. 6.9 Algorithm based on aVR analysis. *Vi* voltage of the first 40 ms, *Vt* voltage of the final 40 ms (see text)

6.6.3 Step 3: Notch in the Descending Q Wave Limb of a Negative (QS or Qr) Ventricular Complex

This pattern was present in 32 over 37 VT cases where the first 2 criteria were absent (sensitivity 19.9 %, specificity 95 %).

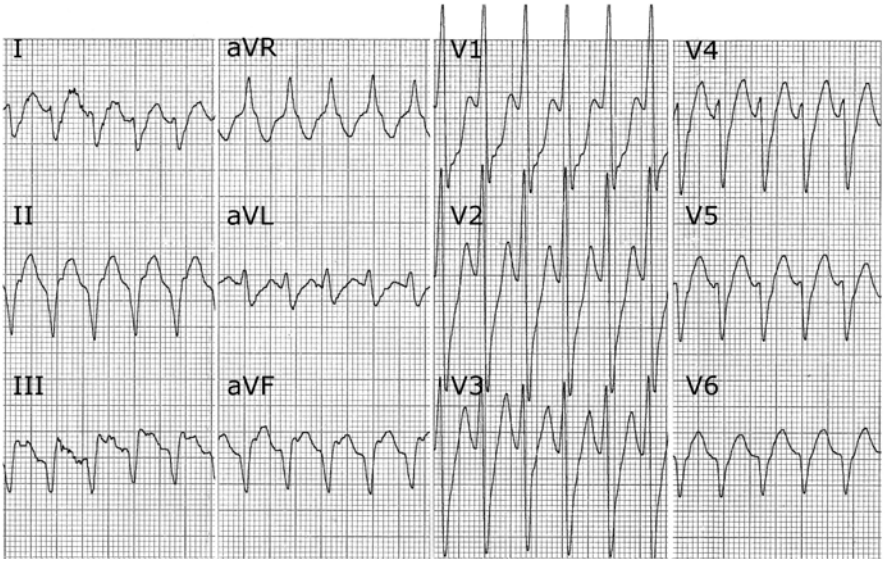

Fig. 6.10 Ventricular tachycardia. In this wide QRS complex tachycardia, negative P waves follow ventricular complexes in the inferior leads. The arrhythmia cannot be classified as "RBBB morphology" or "LBBB morphology" since lead V1 shows complexes with RS configuration. Both QS complexes in lead V6 and aVR analysis (entirely positive complexes) suggest VT

6.6.4 Step 4: *Vi*/*Vt* Ratio

The presence of any sign in steps 1–3 demonstrates the ventricular origin of the arrhythmia, but *the absence of these criteria does not permit to exclude VT and does not demonstrate SVT.* In this situation it is necessary to evaluate the *Vi/Vt ratio, namely, the ratio between the voltages recorded during the first 40 ms of the QRS complex (Vi) and those measured during the last 40 ms of the complex (Vt*). To calculate *Vi* (initial voltage) and *Vt* (terminal voltage), it is necessary to sum the amplitude of *all the deflections present in the first and the last 40 ms*, respectively (Fig. 6.10). This is not a very easy task, since the authors suggest to measure not the simple voltage of the deflection, but to take into account separately any limb of the waves. For example, if an R wave of 3 mm is present at the beginning of the ventricular complex, the corresponding calculated voltage is 6 mm (3 of the ascending limb + 3 of the descending limb). Unfortunately, it is not easy to distinguish exactly the moment of QRS complex beginning and/or termination, to the extent that the authors suggest to use a simultaneous recording of several leads (at least aVR, aVL, aVF) in order to make easier the identification of QRS complex beginning and/or termination.

A Vi/Vt ratio ≥1 suggests a diagnosis of SVT with aberrant conduction, while *a ratio ≤1 speaks in favor of VT.* This criterion has a logical basis: in VT, intraventricular conduction is totally independent of the conduction system, and the ectopic impulse is slowly conducted; accordingly, a small amount of ventricular muscle is

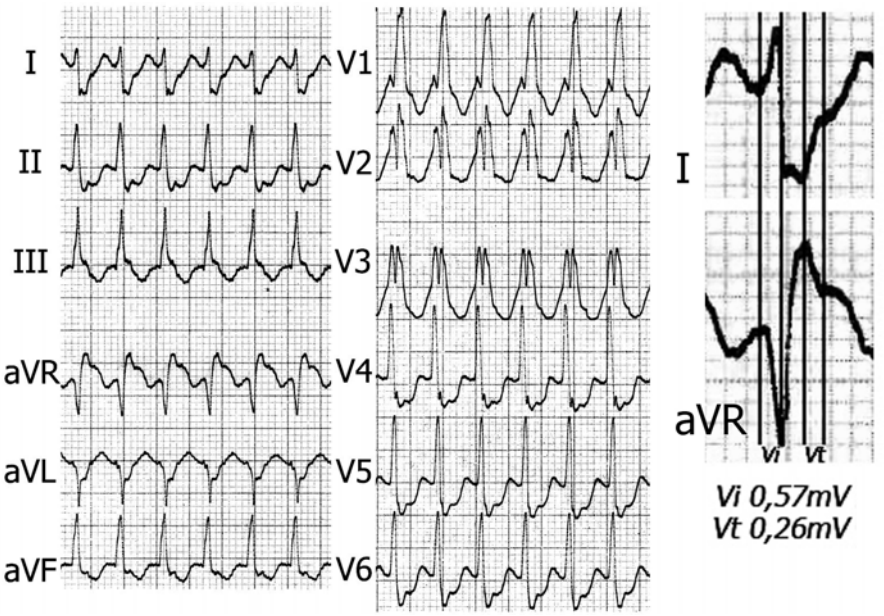

Fig. 6.11 Supraventricular tachycardia with aberrant conduction. Neither P waves nor signs of A-V dissociation are recognizable in this ECG. The morphology of ventricular complexes (rsR′ in V1, Rs with wide s wave in V6) suggests aberrant conduction. The same diagnosis results from lead aVR analysis, since neither dominant initial R wave nor wide q or r wave with duration >40 ms occurs, and is also absent a notch in the proximal q wave limb. Moreover, the ratio between the initial (first 40 ms, *Vi*) and the terminal (final 40 ms, *Vt*) voltage is >1, pinpointing the diagnosis of aberrant conduction

depolarized during the first 40 ms, resulting in a relatively low voltage of the corresponding ECG deflections. When, in contrast, the initial ventricular depolarization occurs using the Purkinje system, as it happens in bundle branch block, a relatively large myocardial mass is depolarized during the first 40 ms, resulting in relatively high voltage-related deflections. Examples of correct diagnosis arrived by means of aVR analysis are reported in Figs. 6.11, 6.12, and 6.13.

In conclusion, aVR analysis can be very helpful whenever one of the signs described in steps 1–3 is present, but becomes less useful in their absence.

6.7 R Wave Peak Time at Lead II

It has recently been reported that the *R wave peak time (RWPT) duration in lead II (the interval from the QRS complex beginning to the 1st change in polarity*) permits a quick and reliable distinction between VT and SVT [27]. The authors have observed that an *RWPT ≤50 ms demonstrates a supraventricular origin* of the arrhythmia, whereas an *RWPT ≥50 ms in lead II suggests VT*. The underlying reason why a long RWPT speaks in favor of ventricular origin of tachycardia is

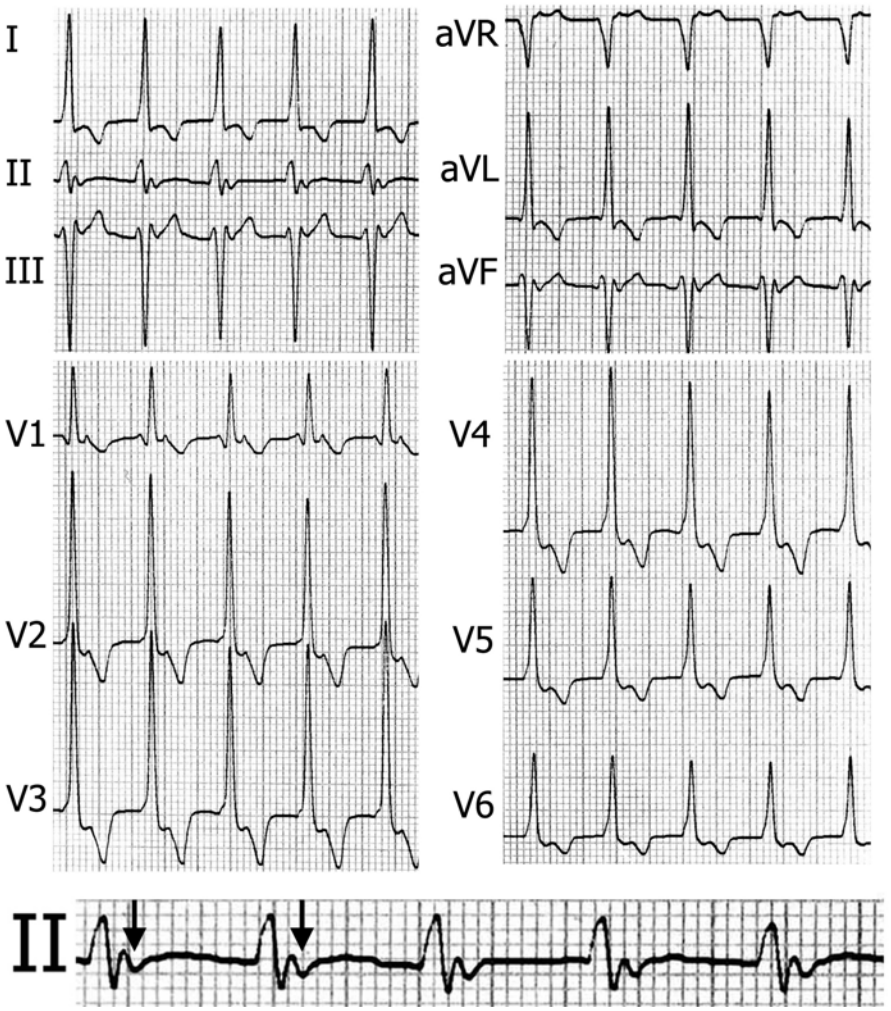

Fig. 6.12 Wide QRS tachycardia with 1:1 V-A conduction. Negative P waves follow ventricular complexes with constant R-P interval in the inferior leads (*arrows* in the *bottom strip*, representing lead II enlarged). This pattern suggests a diagnosis of ventricular (fascicular) tachycardia, despite the relatively narrow QRS complexes

likely the slow initial diffusion of the depolarization wave front in VT. In SVT, in contrast, at the beginning of ventricular depolarization, the supraventricular impulse is normally conducted over a bundle branch (or a fascicle) and the Purkinje system, in such a way that a relatively large myocardial mass is quickly depolarized, resulting in a short RWPT. In the case of VT, in contrast, the cardiac impulse slowly travels over the common myocardial tissue, resulting in a long RWPT. The efficacy of this sign in discriminating VT from SVT is very high in the study that has described such a criterion; the experience of our group,

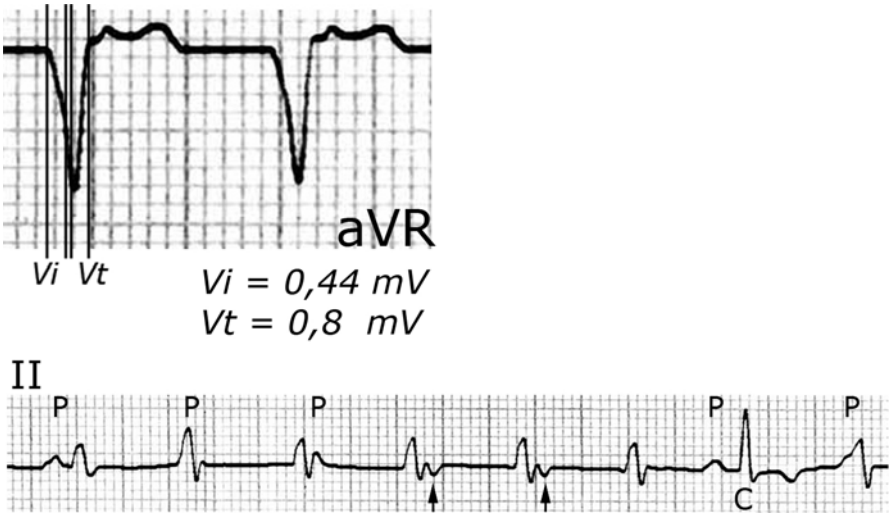

Fig. 6.13 Same case of the preceding figure. Analysis of lead aVR (*top*) and effect of verapamil administration (*bottom*). Despite the absence of (a) dominant initial R wave, (b) q wave with duration >40 ms, (c) notch in the q wave descending limb, the ratio between the voltages of the first and the final 40 ms (*Vi/Vt*) is less than 1, supporting the diagnosis of VT. The ECG recorded during intravenous verapamil administration (strip of lead II) shows A-V dissociation (the 1st three and the last QRS complex) and a capture beat (*C*); *arrows* indicate retrograde conduction restarting

however, is less satisfactory. Further research is necessary to evaluate the real efficacy of RWPT in lead II. Figure 6.3 shows a case of VT in which the RWPT does not exceed 30 ms.

In conclusion, the classic diagnostic criteria to distinguish VT from SVT with aberrant conduction include the following:

1. A-V dissociation, characterized by absence of any relationship between QRS complexes and P waves; this phenomenon is at times immediately recognizable but more often can be discovered only by means of a detailed analysis of the tracing.
2. Second-degree ventriculoatrial block, namely, a relationship between P waves and QRS complexes, but with more ventricular complexes than P waves.
3. Fusion and/or capture beats.
4. Concordant precordial pattern, a sign that can be also expressed as absence of RS (or even rs, Rs, rS) complexes in the precordial leads.
5. Analysis of QRS complexes aimed at discriminating a typical pattern of intraventricular conduction disturbance from a QRS configuration that is impossible or unlikely whenever the ventricular depolarization is dependent on a supraventricular impulse.

Several further criteria have been introduced to identify the origin of wide QRS complex tachycardia, but none of these is able to provide a simple and quick solution of the problem.

Vagal maneuvers and analysis of previous electrocardiograms recorded during sinus rhythm, if available, can provide further keys to the diagnosis. Some criteria proposed in the past, such as QRS axis or ventricular complex duration, are nowadays no longer considered; in addition, it has been demonstrated that items such as age, hemodynamic status, heart rate, and regularity of R-R intervals can be misleading and should not be taken into account.

Analysis of QRS configuration in leads V1 and V6 is a keystone in distinguishing the origin of wide QRS tachycardias: diagnostic criteria rely upon the assumption that aberration is due to a functional bundle branch block, whereas ectopy derives from a totally abnormal activation of the ventricles. Aberration, thus, results in a "typical" bundle branch block morphology, whereas ectopy is expressed by an "atypical" bundle branch block. Specific criteria, based on analysis of leads V1 and V6, have been developed to distinguish from each other the two conditions. Criteria based on QRS configuration, however, suffer from limitations since unexpected complicating factors, such as a previous myocardial infarction, can result in an "atypical" form of bundle branch block even in the presence of supraventricular tachycardia.

Recently proposed items (lead aVR analysis, peak R wave time in lead II) can be at times useful, but they need further investigation to confirm the results obtained by the authors that introduced such criteria.

6.8 Ventricular Versus Preexcited Tachycardia

In preexcited tachycardia, supraventricular impulses are conducted to the ventricles over an accessory pathway, resulting in wide QRS complexes; this is because ventricular depolarization is entirely (or, less commonly, partially) due to the impulse conducted over the abnormal conduction pathway. Such a situation may occur in the presence of (1) atrial tachycardia, (2) atrial flutter, (3) A-V nodal reentrant tachycardia, and (4) antidromic A-V reentrant tachycardia.

In all of these conditions, ventricular depolarization is due to the accessory pathway, and the QRS complexes are very wide ("pure" delta waves), mimicking a VT. It is, thus, necessary to distinguish VT from preexcited tachycardia, since at first glance QRS complex morphology suggests in the latter ventricular, rather than supraventricular, origin of the arrhythmia. In antidromic A-V reentrant tachycardia due to Mahaim fibers, however, the morphology of QRS complexes suggests supraventricular, rather than ventricular, origin of the arrhythmia, since the accessory pathway is usually connected with the right bundle branch, resulting in a typical left bundle branch block pattern [28].

Distinction between VT and preexcited tachycardia is based on the following concept: VT can originate from any part of the ventricular myocardium, whereas in preexcited tachycardia, ventricular depolarization starts (apart the rare exception represented by Mahaim fibers) from the atrioventricular rings, in correspondence of ventricular insertion of the Kent bundle. Accordingly, there is a relatively limited possible patterns, and each of them is characteristic of a defined Kent bundle

location. Since the ECG in sinus rhythm permits in most cases a reliable localization of the accessory pathways [29, 30], the question to be raised in the presence of a wide QRS complex tachycardia should be the following: "Is the morphology of this arrhythmia consistent with the typical pattern of ventricular depolarization due to an accessory pathway?" If the answer is "yes," a preexcited tachycardia is possible, whereas in the case of negative answer, such a diagnosis can be excluded.

It has been reported that in a wide QRS complex tachycardia, the following morphologies suggest VT rather than preexcitation: [4]

1. Negative QRS complexes in V4–V6
2. Negative precordial QRS concordance (negative QRS complexes in all precordial leads)
3. Deep Q waves or Qr complexes in a precordial lead except V1

Although Q waves in precordial leads other than V1 are virtually impossible in preexcitation, negative complexes in V4–V6 are not rarely observed in preexcitation due to a posteroseptal accessory pathway, since the superiorly directed vector can result in large S waves.

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Acute Management of Arrhythmias in Patients with Known Congenital Heart Disease

7

Francesca Bianchi and Stefano Grossi

7.1 Focusing on the Issue

Surgical advances for congenital heart disease (CHD) allow long-term survival for a unique group of patients who would otherwise have died during early childhood. Improved longevity had eventually exposed to late complications, atrial and ventricular arrhythmias contributing to sudden cardiac death (SCD) [1]. Arrhythmias are the consequences of both native abnormalities and surgical procedures. It seems that the arrhythmic burden is the price paid to survival and mostly occurs in adults with CHD. It is now estimated that there are over 1.8 million of adult patients with CHD in Europe [2] and one million in North America [1].

Some defects are best known since studies have focused on specific lesions with predilection for common malformations with effective surgical solution and large number of patients surviving into middle age: this is the case of tetralogy of Fallot that has been studied more extensively than other conditions and so arrhythmic mechanisms and risks are best known [1]; other conditions, less common or with a more recent improvement of survival, are less known.

The entire spectrum of arrhythmias may be encountered in adults with CHD, with several subtypes often coexisting. For some conditions, arrhythmias are intrinsic to the structural malformation itself, as is the case with Wolff-Parkinson-White syndrome in the setting of Ebstein's anomaly, twin atrioventricular (AV) node tachycardia in heterotaxy, or AV block in the setting of "congenitally corrected" transposition of the great arteries (L-TGA). For most other CHD patients, arrhythmias represent an acquired condition related to the unique myocardial substrate

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created by surgical scars in conjunction with cyanosis and abnormal pressure/volume loads of long duration [3, 4].

Arrhythmia substrate and consequent management is peculiar for any CHD, but some general principles can be identified, and recently international scientific boards have provided evidence-based recommendations on best practice procedures for the evaluation, diagnosis, and management of arrhythmias [5, 6].

Arrhythmia management is strictly connected to anatomical native and surgical substrate and to hemodynamic status. Classification of CHD complexity (simple, moderate, and great/severe) proposed by the ACC/AHA task force [7] reported in Table 7.1 is used to orientate management.

7.2 What Physicians Working in ED Should Know

Facing acute arrhythmias in CHD patients needs an early interplay between emergency physician and cardiologists.

Hemodynamically poorly tolerated tachycardia or ventricular fibrillation resulting in pulseless arrest requires management according to AHA/ACC/ESC guidelines for Adult Cardiac Life Support (ACLS) [8]. When direct current cardioversion is required, paddles or patches have to be positioned taking into account cardiac location in the chest [6].

In tolerated arrhythmias, 12-lead electrocardiogram (ECG) of the event should be registered. Knowledge of anatomical defect and collection of surgical reports are also fundamental for best acute and long-term management and should be obtained as soon as possible.

Hemodynamically tolerated tachycardia should be managed according to well-established adult guidelines, while taking into consideration CHD-specific issues [6] on drug therapy: antiarrhythmic drugs (AAD) are frequently poorly tolerated due to negative inotropic and other side effects, and few data exist on their safety and efficacy [6].

For atrial arrhythmias the *thromboembolic risk* must be assessed before cardioversion, reminding that in moderate and severe complexity CHD, it is high even when onset is <48 h [6].

Unexplained syncope in adults with CHD is an alarming event that may have several potential etiologies, including conduction abnormalities and bradyarrhythmias, atrial and/or ventricular arrhythmias, and nonarrhythmic causes [6].

In patients with CHD, the majority of *sudden cardiac deaths* (SCD) have an arrhythmic etiology, but up to 20 % may be nonarrhythmic, as in cerebral or pulmonary embolism, myocardial infarction, heart failure, and aortic or aneurysmal rupture [5]. SCD is responsible for approximately one-fifth of the mortality in adult's CHD, with a greater risk observed in certain malformations (tetralogy of Fallot, Ebstein's disease, left-sided obstructive disease). However, the annual mortality rates are low compared with adult population (0.1–0.3 % per patient-year) [1].

Table 7.1 Complexity of diagnosis in adult patients with congenital heart disease

Simple	Moderate complexity	Great/severe complexity

Native disease:
Isolated congenital aortic valve disease
Isolated congenital mitral valve disease (except parachute valve, cleft leaflet)
Small atrial septal defect
Isolated small ventricular septal defect (no associated lesions)
Mild pulmonary stenosis
Small patent ductus arteriosus
Repaired conditions:
Previously ligated or occluded ductus arteriosus
Repaired secundum or sinus venosus atrial septal defect without residua
Repaired ventricular septal defect without residua
	Aorto-left ventricular fistulas
	Anomalous pulmonary venous drainage, partial or total
	Atrioventricular septal defects, partial or complete
	Coarctation of the aorta
	Ebstein's anomaly
	Infundibular right ventricular outflow obstruction of significance
	Ostium primum atrial septal defect
	Patent ductus arteriosus (not closed)
	Pulmonary valve regurgitation, moderate to severe
	Pulmonary valve stenosis, moderate to severe
	Sinus of Valsalva fistula/ aneurysm
	Sinus venosus atrial septal defect Subvalvular or supravalvular aortic stenosis
	Tetralogy of Fallot
	Ventricular septal defect with:
	  Absent valve or valves
	  Aortic regurgitation
	Coarctation of the aorta
	  Mitral disease
	  Right ventricular outflow tract obstruction
	  Straddling tricuspid or mitral valve
	  Subaortic stenosis
		Conduits, valved or nonvalved
		Cyanotic congenital heart disease (all forms)
		Double-outlet ventricle
		Eisenmenger syndrome
		Fontan procedure
		Mitral atresia
		Single ventricle (also called double inlet or outlet, common, or primitive)
		Pulmonary atresia (all forms)
		Pulmonary vascular obstructive disease
		Transposition of the great arteries
		Tricuspid atresia
		Truncus arteriosus/hemitruncus
		Other abnormalities of atrioventricular or ventriculoarterial connection not included above (e.g., crisscross heart, isomerism, heterotaxy syndromes, ventricular inversion)

Adapted from Warnes et al. [7]; with permission

7.3 What Cardiologist Should Know

Atrial tachyarrhythmias (ATs), the most frequent in CHD, have been identified as a risk factor for SCD. The mechanism has been attributed to rapid AV conduction, most notably at times of exertion, with hemodynamic instability caused by the atrial

tachyarrhythmia itself or by its degeneration into a secondary ventricular tachyarrhythmia [7].

Prevalence of ATs is 3 times higher than what is observed in general population, and it is reported that 20-year-old patients with CHD have an equivalent risk of a 55-year-old women without CHD: patients with CHD are young with aged hearts [9]; atrial fibrillation (AF) is less common than atrial flutter accounting for 20–30 % of all ATs [10, 11].

The most common mechanism of tachycardia seen in the adult CHD patient population is macro-reentry within the atrial muscle. It is defined as *intra-atrial reentrant tachycardia (IART*) [7].

This arrhythmia usually is a late postoperative disorder, and it may arise after nearly all procedures involving a right atriotomy (even simple closure of an atrial septal defect); the incidence is clearly highest after the Mustard–Senning and Fontan operations, in which 30–50 % can be expected to develop a symptomatic episode during follow-up. Generally, IART tends to be slower than typical flutter, with atrial rates in the range of 170–250 beats per minute. In the setting of a healthy AV node, these rates will frequently allow a pattern of 1:1 AV conduction that may result in hemodynamic instability, syncope, or possibly death [3, 7]. Rate control should be achieved as soon as possible. Beta-blocking drugs and nondihydropyridine calcium channel antagonists can be used to achieve ventricular rate control with insufficient evidence to recommend one agent over another; since beta-blockers are associated with a decreased incidence of ventricular tachyarrhythmias in many conditions, it may be reasonable to liberalize their use in this patient population if well tolerated [6].

Sustained IART or AF lasting ≥48 h is an established *risk for thromboembolism* [12, 13], but moderate and complex forms of CHD have a predisposition to thromboembolic complications estimated to be10- to100-fold higher than in age-matched controls: in these patients it may be prudent to rule out intracardiac thrombus prior to cardioversion regardless of the duration of IART or AF [6].

Once atrial arrhythmia is recognized and thromboembolic risk ruled out, acute interruption can be performed with electrical cardioversion, overdrive pacing (in patients with implanted atrial or dual chamber pacemaker/defibrillators), or antiarrhythmic drugs.

Reciprocating tachycardia and some non-automatic focal atrial tachycardias may be terminated by vagal maneuvers, intravenous adenosine, or non-dihydropyridine calcium channel antagonists, with the exception of patients with an anterograde conducting accessory pathway (WPW).

There is a paucity of literature regarding pharmacologic conversion of IART or AF in adults with CHD; ibutilide has been tested in a small pediatric series [14], but there are no efficacy and safety data regarding acute conversion of IART or atrial fibrillation with class IA and IC and other class III drugs in patients with CHD [6]: *electrical cardioversion should therefore be preferred*. Anterior–posterior pad positioning may be needed in the setting of marked atrial dilation [5].

Experience with chronic pharmacologic therapy for IART in adults with CHD has been discouraging [6, 10, 11, 15], resulting in a growing preference for nonpharmacologic options in most centers.

Nevertheless, in those with moderate or complex forms of CHD, a rhythm control treatment strategy (i.e., maintenance of sinus rhythm) is generally preferred to rate control as the initial management approach [6].

Ventricular arrhythmias. There are several scenarios in which high-grade ventricular arrhythmias may develop in CHD. The most familiar involves macroreentrant VT as a late complication in postoperative patients who have undergone ventriculotomy and/or patching such as tetralogy of Fallot repair which is the best studied. Reentry circuit is caused by conduction corridors around regions of scar in the RV outflow tract (RVOT). The incidence of late VT or SCD for repaired tetralogy has been estimated between 0.5 and 6.0 % in various series [3, 7]. Some patients with slow organized VT may be hemodynamically stable at presentation, but VT tends to be rapid for the majority, producing syncope or cardiac arrest as the presenting symptom. Serious ventricular arrhythmias may also develop in a number of other malformations, even in the absence of direct surgical scarring to ventricular muscle when the right ventricle supports the systemic circulation or in the presence of a failing systemic ventricle. The appearance of ventricular arrhythmias in these cases commonly coincides with deterioration in hemodynamic status [7].

Cardioversion should be expeditiously performed for any sustained ventricular arrhythmia; electrical cardioversion in tolerated arrhythmias has the disadvantage of requiring sedation, while drugs carry the disadvantage of delayed effect.

The most efficacious pharmacologic agent is intravenous amiodarone; this agent may be associated with hypotension if administered rapidly: patients should be continuously observed and intravenous sedation and cardioversion readily available. Beta-blockers can be combined to amiodarone to improve rhythm stability, while lidocaine is a third-choice drug for short-term treatment [8].

When triggered activity is the suspected underlying mechanism, intravenous beta-blockers or calcium channel antagonists may be used, but the latter can be more harmful in the presence of scar-related macroreentry or ischemic ventricular tachycardia [6, 8].

7.4 Indications for Hospitalization, Follow-Up, and Referral

Guidelines recommend that health care for adults with CHD and arrhythmias should be coordinated by regional adult CHD centers of excellence with multidisciplinary staff that serve the surrounding medical community for consultation and referral [5–7, 16].

Syncope, ventricular arrhythmias, and in general arrhythmias in the setting of moderate to severe complexity CHD should be hospitalized.

The onset of arrhythmias may be a signal of hemodynamic decompensation, and the risk associates may be amplified in the presence of the abnormal underlying circulation [16]; a new evaluation with echocardiography and eventually further imaging (transesophageal echocardiogram, MRI/CT scan) or catheterization should be planned after a new-onset arrhythmic event.

Unexplained syncope and "high-risk" CHD substrates should be evaluated with an *electrophysiologic study,* which is also useful in life-threatening arrhythmias or resuscitated sudden cardiac death when the proximate cause for the event is unknown or there is potential for ablation [5, 6].

Before planning any invasive procedure, patients should undergo an individualized and multidisciplinary evaluation and the best knowledge of cardiac and vascular anatomy achieved [5, 6].

Patients with *AF/flutter/IART* and simple forms of CHD could be reasonably managed according to AF guidelines for AF or flutter and no or minimally heart disease [6, 12, 13] for rate/rhythm control strategies as well for anticoagulation: in *nonvalvular simple CHD,* CHADSVASC and HASBLD score should be used and either vitamin K antagonists (VKA) or a novel anticoagulant (NOAC) can be used [5].

In all patients initial therapy for atrial arrhythmias should include adequate rate control, best performed with beta-blockers, if tolerated.

Late postoperative atrial tachyarrhythmias in adults with CHD are most often due to *cavotricuspid isthmus-dependent,* and catheter ablation has proven to be safe and considerably effective, generally preferred over long-term pharmacologic management [6].

In CHD of moderate to severe complexity, an initial strategy of rhythm control is reasonable [5], and patients should be treated with VKA; NOAC is not recommended in this context due to lack of safety data [5, 6]. Non-pharmacologic strategy for rhythm control should be preferred to long-term pharmacologic therapy even if acute success rates of catheter ablation (CA) in CHD seem to be lower compared with the general adult population [5, 11]. If catheter ablation is not feasible or unsuccessful, long-term pharmacologic therapy can be necessary [6, 7]. Class I drugs and dronedarone are not recommended in this setting. *Sotalol* can be considered in patients with preserved ventricular function and without renal insufficiency, hypokalemia, severe sinus node dysfunction, or QT prolongation; *amiodarone* can be considered as first-line antiarrhythmic agent for the long-term maintenance of sinus rhythm in the presence of pathologic hypertrophy of the systemic ventricle, systemic or subpulmonary ventricular dysfunction, or coronary artery disease; in all other conditions, it is a second-line therapy due to high time and dose-dependent side effects; induced thyrotoxicosis is especially common in women with CHD and cyanotic heart disease or univentricular hearts with Fontan palliation and in those with a body mass index $\leq$21 kg/m2 [5, 14]. *Dofetilide* appears to be a reasonable alternative to amiodarone in normal QT patients if available [5].

Rate control may be the definitive therapeutic strategy after failed attempts at rhythm control and in whom rate control is well tolerated [6].

Catheter ablation is also recommended in recurrent symptomatic and/or drug-refractory supraventricular tachycardia related to accessory AV connections or twin AV nodes and in high-risk or multiple accessory pathways and can be beneficial for recurrent symptomatic and/or drug-refractory AV nodal reentrant tachycardia [5, 6].

Ventricular arrhythmias: *ICD* is the first-line therapy for the secondary prevention of sudden death in adults with CHD [17] and should be considered in high-risk patients [5, 6, 8, 15, 19].

Abnormal systemic venous pathways, impaired or lack of venous access to the ventricle, or right-sided AV valve disease may need *epicardial and/or subcutaneous coils* [5].

The subcutaneous ICD may be a reasonable option in adults with CHD in whom transvenous access is not possible or desirable and in whom anti-bradycardia and ATP functions are not essential [5].

Beta-blockers are associated with a decreased incidence of ventricular tachyarrhythmias in patients with transposition of the great arteries and atrial switch surgery, and they should be used in long-term VA prevention if tolerated [5, 6].

Catheter ablation is indicated as adjunctive therapy to an ICD in adults with CHD and recurrent monomorphic ventricular tachycardia, a ventricular tachycardia storm, or multiple appropriate shocks that are not manageable by device reprogramming or drug therapy [6]. The most common CHD associated with sustained ventricular tachycardia is tetralogy of Fallot: a macroreentry mechanism is at the base of monomorphic ventricular tachycardias, which can be cured with catheter ablation as an alternative to drug therapy; in limited Fallot series after VT ablation, ICD was considered necessary only if CA was unsuccessful [16, 18].

Frequent ventricular ectopy associated with deteriorating ventricular function can reasonably be treated by catheter ablation.

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Acute Management of Arrhythmias in Patients with Channelopathies

8

Francesca Bianchi and Stefano Grossi

The term "channelopathies" defines a group of inherited arrhythmic syndromes caused by mutations of genes encoding for proteins that regulate ion currents [1] in patients without structural heart disease. Mutations disrupt the balance in the cardiac action potential favoring peculiar ECG abnormalities and the risk of life-threatening arrhythmias.

A gain or a loss of function of ionic channels or trafficking proteins underlies the development of arrhythmogenic triggers and substrate and the amplification of transmural heterogeneities [2]. It is estimated that inherited arrhythmia disorders (long and short QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, early repolarization syndrome, idiopathic ventricular fibrillation) cause 10 % of the1.1 million sudden deaths in Europe and the USA [3].

Due to the peculiarity of these rare disorders, some of the commonly used emergency protocols should be applied with caution, since some of antiarrhythmic and resuscitation drugs could be contraindicated and potentially worsen arrhythmias in this specific group of patients.

The congenital *long QT syndromes (LQTS)* are the most common channelopathies, with an estimated prevalence of 1:2000–2500 [4], and are characterized by prolonged repolarization, resulting in a prolonged QT interval on the ECG, and by a susceptibility to polymorphic ventricular arrhythmias known as torsades de pointes [2]. Causes for this primary electrical myocardial disease are mutations in genes coding for cardiac potassium and sodium channels and proteins associating with potassium channels, or mutations in the ankyrin-B gene, that reduce net repolarization currents in the ventricular myocardium prolonging repolarization phase and predispose to early afterdepolarization (EAD)-induced triggered activity. Once

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triggered by EADs, torsades de pointes can be maintained by a reentrant mechanism [1, 4–6].

Short QT syndrome (SQTS), characterized by a short QT interval on ECG with a high sharp T wave and a reduced repolarization phase, has a high familial incidence of palpitations, atrial fibrillation, syncope, and SCD [7, 8], typically during childhood. It is considered the most lethal channelopathy; incidence and prevalence are difficult to determine due to limited data [4, 6–8].

The *Brugada syndrome (BrS)* is an autosomal dominant inherited arrhythmic disorder characterized by an ECG pattern consisting in coved-type ST segment elevation in atypical right bundle branch block in right precordial leads (V1–V3) and risk of SCD resulting from episodes or polymorphic ventricular arrhythmias [9–11]; men are affected with a ratio 8:1 in respect to women; reported prevalence in Europe is 1:2000, while in Asian population, it is 2,4:2000; life-threatening events typically involve young male adults (30–40 years old) during sleep [6, 11].

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a rare but highly malignant genetic disease leading to an increase in intracellular Ca^{++} concentration, resulting in polymorphic arrhythmias due to a cascade of delayed afterdepolarization and triggered activity occurring during emotional or physical stress that cause syncope and high mortality (30 % by the age of 30 years); the estimated prevalence is 1:10,000 [4, 12].

Recently, several studies have reported that J-point and ST segment elevation in the inferior or lateral leads, which is also called early repolarization (ER) pattern, can be associated with ventricular fibrillation (VF) and SCD in patients without apparent structural heart diseases. However, J-wave elevation is fairly commonly seen in young healthy individuals (estimated prevalence, 1–9 %) and frequently considered to be benign [6]: the vast majority of patients with the ECG pattern are asymptomatic and have a low arrhythmic risk, while strategies for risk stratification remain suboptimal. It is reported that unexplained syncope in patients with an ER pattern, particularly with a "malignant variant" of the pattern, may be an important predictor of future arrhythmic events [4, 13]; the presence of an ER pattern with otherwise unexplained ventricular arrhythmia is commonly referred to as *ER syndrome* [4, 6, 13, 14].

8.1 Focusing on the Issue

The ED physician could deal with a patient with an already established diagnosis of inherited arrhythmia, eventually already treated with drugs and or implanted cardiac defibrillator (ICD).

On the other hand, the referral event could be the first clinical manifestation of an unrecognized inherited arrhythmogenic disorder that, especially in young and otherwise healthy subject, must be suspected, investigated, and finally confirmed or ruled out.

All patients with a known or suspected channelopathy who refer for arrhythmic suggestive symptoms should be ECG monitored and a cardiologic evaluation sought.

Patients resuscitated from cardiac arrest must be rapidly evaluated for the presence of structural heart disease, an inherited arrhythmia syndrome, a triggering ventricular arrhythmia focus, or a noncardiac cause [15].

Most of inherited arrhythmic disorders could be diagnosed on the basis of a standard 12-lead ECG that should therefore be obtained as soon as possible as the chance to make a correct diagnosis is highest in proximity of the arrhythmic event [15]. This is a simple and useful instrument to confirm the presence or suspect a channelopathy, aside from excluding other acquired acute cardiac conditions (such as acute coronary syndrome); however, a single normal resting ECG may not exclude all forms of channelopathies. ECG recording of arrhythmic event, when possible, could be useful for the subsequent management [15].

In all cases it is indicated to avoid pro-arrhythmic triggering conditions and discontinue potentially harmful drugs that are specific for any different channelopathy: currently used antiarrhythmic and resuscitation drugs may hasten the electrical instability in these particular patients and should be therefore avoided when a specific channelopathy is known or suspected (see below).

8.2 Different Ways of Presentation

Cardiac arrest and hemodynamic nontolerated arrhythmias should be managed with early defibrillation [15] with special considerations required for drug administration.

Polymorphic ventricular tachycardia is defined as ventricular rhythm faster than 100 bpm with clearly defined QRS complexes that change continuously from beat to beat; it is the typical life-threatening arrhythmia observed in patients with channelopathies; its occurrence, in the absence of structural heart disease, suggests the presence of an inherited arrhythmia syndrome [15]; it could be self-terminating or degenerate into VF.

Bidirectional ventricular tachycardia, characterized by two alternating QRS complex morphologies with different polarity, is recognized as a hallmark of CPVT; it can degenerate into polymorphic ventricular tachycardia and VF. It may be encountered also in the rarest Andersen-Tawil syndrome and in several other conditions which predispose to delayed afterdepolarizations (DADs) and triggered activity (i.e., digitalis intoxication) [4, 16] See Fig. 8.2.

The term *torsades de pointes* (TdP) was coined by Dessertenne [17] in 1966 as a polymorphic ventricular tachycardia characterized by a pattern where the QRS complexes appear to be twisting around the isoelectric baseline [15]. The trigger for TdP is thought to be a PVC that results from an EAD generated during the abnormally prolonged repolarization phase; this arrhythmia has a typical long-short ventricular cycle length as initiating sequence and is typical for congenital or acquired long QT syndrome. TdP usually self-terminates and it is often responsible for syncopal episodes but when it deteriorates into VF may cause sudden death [4] see fig. 8.2. Since TdP is strongly associated with drugs or electrolyte imbalances that further delay repolarization, precipitating factors should promptly be searched and corrected [15, 18, 19].

Ventricular tachycardia/ventricular fibrillation storm represents a true medical emergency that requires a multidisciplinary approach to care [15] (see Chap. 11).

In patients with known diagnosis of channelopathy (including known gene carriers), the occurrence of *syncope* is an independent predictor of life-threatening arrhythmic events [4].

In most patients, syncope is the first clinical manifestation of inherited arrhythmic disorders that should therefore be evaluated.

Atrial fibrillation (AF) affects 1–2 % of the population and increases in prevalence with aging [20]. Ion channel disorders can predispose to atrial fibrillation, and prevalence in this population is increased, since the same imbalance of the action potential that causes ventricular arrhythmias could affect the atria. On the contrary, AF could be the first manifestation of an inherited cardiac arrhythmia (sometimes unmasked by drug administration [21]) which should be always considered in young otherwise healthy subjects.

Since commonly used drugs for rhythm or heart rate control may be contraindicated due to the potentially life-threatening pro-arrhythmic effect, a non-pharmacological strategy should be considered, with immediate electrical cardioversion always indicated in poorly tolerated AF, but also drugs for anesthesia/sedation should carefully be considered as potentially harmful: for example, propofol should be avoided in Brugada patients, who have a reported prevalence of atrial fibrillation between 9 to 25 and 39 % [21]. Short QT syndrome is characterized by atrial fibrillation [7, 8] with young age onset, being the first clinical manifestation in several reported SQTS cases, since a short repolarization time is a known mechanism in AF [22]: it was observed in 15 % of SQTS population, also younger than 35 years [23]. Adrenergically mediated atrial arrhythmias are also common manifestation of CPVT [4]. In LQTS frequent short-lasting atrial arrhythmias have been reported [23, 24].

Patients presenting with *ICD discharge* should be ECG monitored and device interrogation, even by remote monitoring when available, performed as soon as possible: appropriate shocks due to ventricular arrhythmia should be promptly managed, according to the peculiar diagnosis of the patient. Inappropriate shocks (which may have a high incidence in this population due to young age, high incidence of AF, and sometimes peculiar ECG [25] leading to incorrect recognition of the rhythm) and discharges on non-sustained VT should be avoided as part of the emergency treatment: painful shocks can increase the sympathetic tone and trigger further arrhythmias leading to a malignant cycle of ICD shocks and even death [15]; inhibition through magnet application could be the first intervention before device specialist intervention in case of incessant and clearly inappropriate shocks.

Therapy: The first step of management of acute events in these patients is to avoid and correct potentially triggering conditions:

Fever: In *Brugada* syndrome avoidance of fever is generally accepted to be an important part of prophylactic treatment since it is a well-known trigger of cardiac events [26, 45, 27]. Fever can also be a risk factor for the development of life-threatening ventricular arrhythmias in the *LQT2* form of congenital long QT syndrome [28, 29].

Autonomic influences play an important role in unmasking the electrocardiographic phenotype and precipitating lethal arrhythmias. Sympathetic stimulation precipitates tachyarrhythmias and sudden cardiac death in CPVT and LQTS, while in BrS and ER, it can prevent them [30]. Most episodes of VF in patients with Brugada syndrome and some in LQT3 are observed during periods of high vagal tone, such as at rest, during sleep, or after alcohol intake [30]. In LQTS 1 and 2 and CPVT patients, sympathetic stimulation and sympathomimetic drugs should be avoided, and the use of sedation to reduce emotional stress may be considered as a support to drug therapy.

Drugs to avoid: Several AAD as well as noncardiac drugs may have a pro-arrhythmic effect in this group of disease. Arrhythmias are due to the effects of drugs on ion channels (with worse harm for potassium channel blockers in LQTS and sodium channel blockers in Brugada), that is, a target effect in AAD and a collateral effect of several other compounds. These drugs should be avoided or discontinued as a principal part of acute arrhythmia management in channelopathies; two panels of experts have created a web-based platform reporting and periodically updating all drugs that should be avoided in LQTS and Brugada syndrome: www.crediblemeds.org and www.brugadadrugs.org, respectively [18, 19, 26, 45].

These websites should be promptly consulted while managing these patients, mostly in emergency setting. In SQTS, at present, only one drug is known to have pro-arrhythmic effect and should be avoided (rufinamide, an antiepileptic drug), but other molecules may shorten QT in experimental isolated hearts and the list could grow in the future. *Electrolyte* abnormalities should be corrected (see Chap. 8) and sometimes overcorrected: *Potassium* repletion to 4.5–5 mmol/L may be considered for patients who present with torsades de pointes [31]; in CPVT patients calcium should not be administered.

Management with intravenous *magnesium sulfate* is reasonable for patients who present with *LQTS* and episodes of *torsades de pointes. Beta-blockers* can be combined with pacing for patients who present with TdP and sinus bradycardia [31]. In LQT3 intravenous *lidocaine or oral mexiletine* may be considered.

Acute drug therapy of *polymorphic ventricular arrhythmia in Brugada* syndrome is based on isoproterenol infusion which increases the L-type calcium currents (1–2 μg bolus i.v. followed by continuous infusion of 0.15–2.0 μg/min) and/or quinidine (300–1500 mg/day) [18, 21, 26]; quinidine is also useful for atrial fibrillation in Brugada patients and should be considered in chronic prevention of recurrences of both atrial and ventricular arrhythmias [4, 18, 21, 45]. Electrical storm in patients with early repolarization syndrome has to be managed by *isoproterenol infusion* (initiated at 1 μg/min targeting a 20 % increase in heart rate or an absolute heart rate >90 bpm, titrated to hemodynamic response, and suppression of recurrent ventricular arrhythmia); *quinidine* can be helpful for acute and long-term treatment [4, 32].

In CPVT patients therapy of acute ventricular arrhythmias is mainly based in adrenergic suppression; *verapamil* i.v. could be of use for short-term therapy [4, 16, 33].

8.3 What Cardiologists Should Know

Cardiologist should be promptly involved in the management of "channelopathy patients" in the setting of acute arrhythmias in order to:

1. Rule out structural heart disease and secondary causes that mimic channelopathies.
2. Define diagnosis.
3. Provide risk stratification in order to plan long-term management.

Diagnosis in channelopathies is essentially 12-lead ECG based, and more than 1 recording is usually indicated; triggering conditions could give a clue. *LQTS* diagnosis is based on QT measurement [34] corrected with Bazett formula: a QTc value ≥480 ms in repeated 12-lead ECG is diagnostic [45]; LQTS is diagnosed also in the presence of a risk score ≥3 [4, 35, 36, 45] or in the presence of an unequivocally pathogenic mutation in one of the LQTS genes. LQTS can be diagnosed in patients with QTc > or = 460 ms and unexplained syncope in the absence of secondary causes [4, 45].

Most arrhythmic events occur during physical or emotional stress in LQT1, at rest or in association with sudden noise in LQT2, and at rest or during sleep in LQT3 [37].

The use of provocative tests have been proposed to unmask LQTS in patients with normal QTc at resting ECG, like measurement during change from supine to standing position, in the recovery phase of exercise testing; clinical use of epinephrine for unmasking LQTS, however, is not unequivocally accepted [4].

SQTS is diagnosed in the presence of QTc ≤340 ms and diagnosis should be considered if QTc ≤360 ms in the presence of a pathogenic mutation or family history of SQTS/SCD at age <40 years or a VT or VF episode in the absence of heart disease [4, 45]. In one of the largest published SQTS series, it is reported that more than 60 % of the subjects had symptoms at presentation: cardiac arrest, the first clinical manifestation in one third of the patients, can occur in children during first year of life and in males between the second and fourth decade; syncope is the second most frequent clinical manifestation (15 % of cases). Events may occur both at rest and during effort, so it is not possible to identify a uniform trigger.

Brugada syndrome is diagnosed when a type 1 ST segment elevation is observed in at least one right precordial lead placed in a standard or superior position (up to the 2nd intercostal space) spontaneously or after intravenous administration of a sodium channel-blocking agent, as aymaline or flecainide [4, 9–11, 45]. Arrhythmic events typically occur during sleep or vagal stimulation. Risk stratification is based on the presence of spontaneous type 1 pattern and symptoms; there is no consensus on the value of electrophysiologic study in predicting long-term arrhythmic events [4].

CPVT is diagnosed in the presence of unexplained exercise or catecholamine-induced bidirectional or polymorphic ventricular tachycardia in individual without structural heart disease and with normal resting ECG [45]. In individuals >40 years of age, it can be diagnosed, but in this population, coronary artery disease should be excluded. CPVT is also diagnosed in patients with a pathogenic mutation [4, 45]. Arrhythmic events are typically induced by exercise and emotional stress and since basal ECG is usually normal and exercise stress test and loop recorders are pivotal investigations for diagnosis [4].

8.4 A Possible Algorithm/Pathway for Diagnosis and Treatment (Fig. 8.1; Table 8.1)

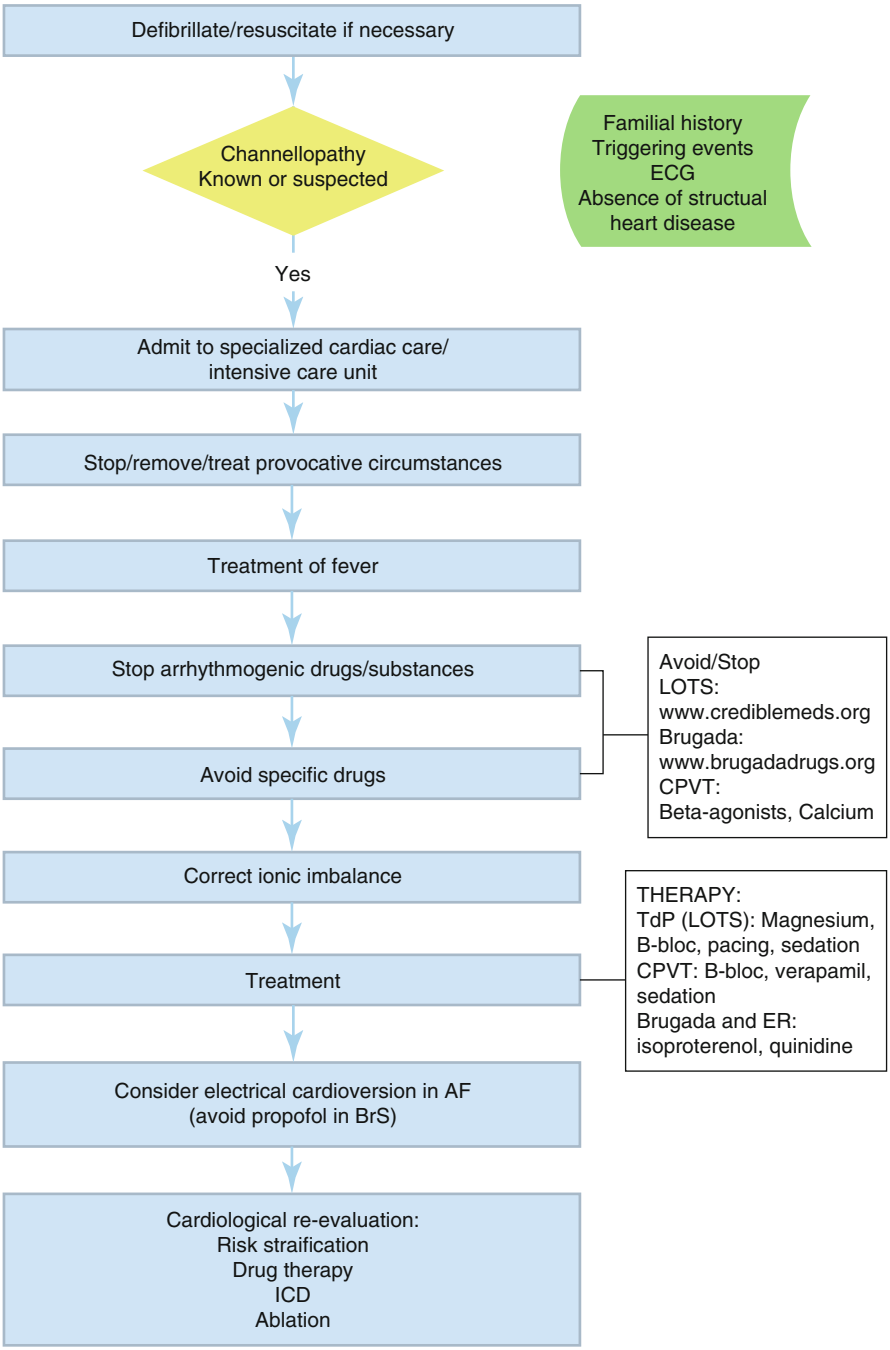

Fig. 8.1 A possible algorithm/pathway for diagnosis and treatment of arrhythmias in patients with channelopathies

Table 8.1 Conditions that can cause PVT/VF and potential therapies

Clues	Test to consider	Diagnoses	Therapies
Long QT/T wave alternans TdP History of seizures Specific triggers (loud noise)	ECG/monitor Epinephrine challenge Exercise stress test Genetic testing	Congenital LQTS	Beta-blockers Avoid QT-prolonging drugs In LQT3: mexiletine/flecainide PM/ICD Stellatectomy
Incomplete RBBB with STE in leads V1–V2 Fever	ECG Drug challenge Genetic testing	BrS	Isoproterenol/quinidine Antipyretic Ablation ICD
J-point elevation	ECG	Early repolarization	ICD
Short QT interval	ECG	SQTS	ICD Quinidine or sotalol
Bidirectional VT exercise induced	Exercise stress test Genetic testing	CPVT Andersen-Tawil syndrome	Beta-blockers/flecainide/verapamil ICD

Adapted from [15]: with permission

8.5 Indications for Hospitalization, Follow-Up, and Referral

Following the arrhythmic index event, channelopathy patient should be reevaluated for risk stratification and prevention of recurrences. Expert centers with a focus on inherited arrhythmias should be involved in complex cases [4].

Atrial arrhythmias in low-risk patients could be managed in out-of-hospital setting with referral to arrhythmia experts to set up indication for pharmacological or non-pharmacological strategy. Thromboembolism should be managed according to AF guidelines using CHA_2DS_2VASC score [20]. First line therapy consists in avoiding potentially pro-arrhythmic drugs and conditions: a complete list should be supplied to the patient and to the general practitioner.

CPVT and LQT patients should be advised to limit/avoid competitive sport, strenuous exercise, and exposure to stressful environments (which in LQT2 should include exposure to loud/abrupt noises, i.e., alarm bell); Brugada patients should avoid excessive alcohol intake and large meals and should be advised to a prompt treatment of fever [45].

Syncope and life-threatening arrhythmias require hospitalization.

Aborted sudden death and sustained ventricular arrhythmias require an ICD for secondary prevention [4, 15, 31, 45] with or without adjunctive therapy.

CPVT and LQTS patients should be treated with *beta-blockers: nadolol and propranolol* are the drugs of choice [1, 4, 33]; in patients with recurrent symptoms/arrhythmias already on beta-blockers, it should be considered *flecainide for CPVT*

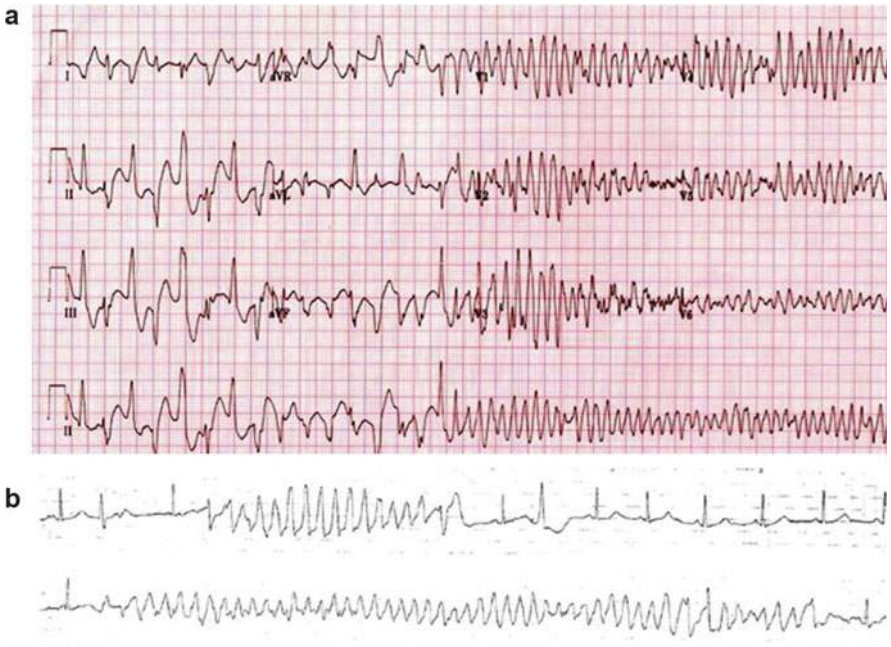

Fig. 8.2 Panel (**a**):12-lead ECG from a 9-year-old boy with ryanodine-positive CPVT shows a transition from triggered bidirectional ventricular tachycardia followed by brief polymorphic ventricular tachycardia to reentrant ventricular fibrillation. With permission from Elsevier Roses-Noguer F. et al. [43]: Copyright © 2014 Heart Rhythm Society. Panel (**b**): torsades de point. With permission from Van der Heide et al. [44]

patients [33] and *flecainide or ranolazine or mexiletine in LQT3* patients [4]; ICD and left cardiac denervation should be considered in patients refractory to pharmacological therapy [4, 33]. Repeated exercise stress test is used in CPVT patients to evaluate drug efficacy.

Brugada and SQTS patients symptomatic for syncope should be treated with *ICD*; quinidine therapy could be used as adjunctive therapy or in cases in which ICD is refused or contraindicated or in recurrent appropriate ICD intervention [22, 26].

Hydroquinidine has proven to play a role in AF recurrence prevention in Brugada patients [4, 21].

Refractory electrical storm could be evaluated for catheter ablation of triggers [15, 39–41, 45].

All clinically diagnosed patients with LQTS and CPVT should undergo *genetic evaluation* if not previously performed, and it can be useful in Brugada (type1) patients and SQTS [42]. Routine genetic testing is not indicated for the survivor of an unexplained out-of-hospital cardiac arrest in the absence of a clinical index of suspicion for a specific cardiomyopathy or channelopathy [42] (Figs. 8.2 and 8.3)

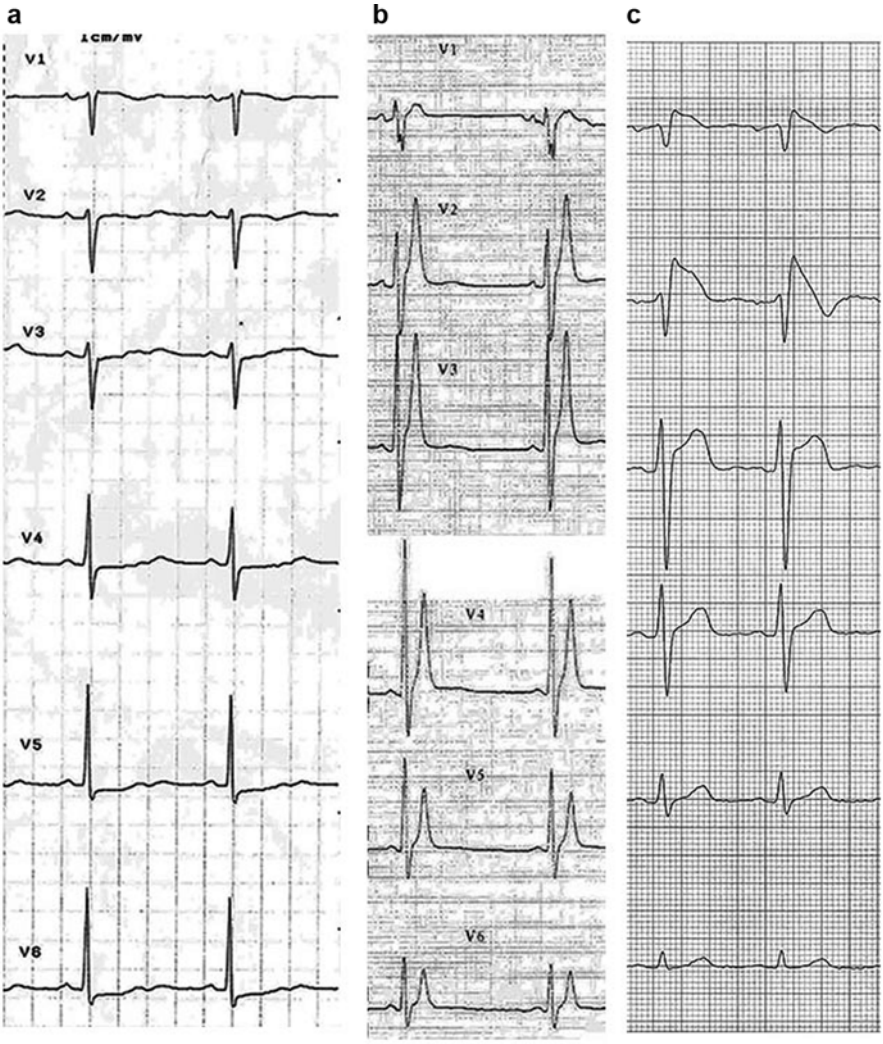

Fig. 8.3 Precordial leads ECG in patients with panel (**a**), long QT syndrome, heart rate 58 beats per minute, QTc 600 ms; panel (**b**), short QT syndrome, heart rate 52 beats per minute (bpm), QT 280 ms*; panel (**c**), Brugada syndrome, coved ST elevation in V1–V2. *With permission from Gaita F. et al. [7]

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9 Acute Management of Patients with Arrhythmias and Non-cardiac Diseases: Metabolite Disorders and Ion Disturbances

Stefano Bardari, Biancamaria D'Agata, and Gianfranco Sinagra

9.1 Focusing on the Issue

Acute metabolic disorders are relatively common amongst medical and surgical patients, especially if critically ill. Whilst increasing the complexity of management plans, these circumstances also increase the risk of cardiac complications, such as arrhythmias, and furthermore are associated with increased mortality. Arrhythmic risk is promoted by electrolyte, acid-base and fluid balance disturbance, increased sympathetic drive and cardiac ischaemia. Particularly, electrolyte abnormalities may generate or facilitate clinical arrhythmias, even in the setting of normal cardiac tissue, by modulating ion conduction across (specific) cardiac cell membrane channels [1], and management of the underlying pathology may be all that is required to allow rapid normalisation of the metabolic profile. Moreover, complex pharmacological regimes may exacerbate the situation [2].

9.1.1 Metabolite Disorders

Endocrine disorders can induce ventricular tachycardia (VT) and sudden cardiac death (SCD) by excess or insufficient hormonal activity on myocardial receptors (e.g. pheochromocytoma, hypothyroidism). The endocrinopathy can also cause myocardial changes (e.g. acromegaly) or electrolyte disturbances produced by

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hormone excess (e.g. hyperkalaemia in Addison disease and hypokalaemia in Conn syndrome), and certain endocrine disorders can accelerate the progression of conditions such as underlying structural heart disease secondary to dyslipidaemia or hypertension, increasing the risk of serious arrhythmias [3].

In addition to electrolyte shifts and ischemia, other systemic influences found in the critically ill patient, such as acid-base abnormalities, hypoxia and enhanced catecholamine levels, can also predispose to ventricular arrhythmias [4]. The mechanism of these arrhythmias is due to automaticity or triggered activity through stimulation of the β-adrenergic receptor, sympathetic activation or exogenous catecholamines. Re-entry may also be facilitated, particularly in the presence of ischemia [5]. The management of ventricular arrhythmias secondary to endocrine disorders should address the electrolyte (potassium, magnesium and calcium) imbalance and the treatment of the underlying endocrinopathy.

9.1.1.1 Thyroid Disorders

Thyrotoxicosis commonly causes atrial arrhythmias; cases of VT/SCD are extremely uncommon but may occur with concomitant electrolyte disturbances. VT/SCD is more common in hypothyroidism, the basic underlying mechanism being possibly related to prolongation of the QT interval [6, 7]. Thyroxin replacement therapy usually corrects this abnormality and prevents any further arrhythmias, but antiarrhythmic drugs, such as procainamide, have been used successfully in an emergency.

9.1.1.2 Phaeochromocytoma

Phaeochromocytoma may present with VT/SCD, but there are no data to quantify its incidence, best mode of management or response to treatment. Conventional antagonism of catecholamine excess with α-receptor blockers followed by β-blockade helps control hypertension and reverses or prevents any further structural deterioration [8], but there is only anecdotal evidence that it prevents recurrence of ventricular arrhythmia [9]. Early definite surgical treatment of the phaeochromocytoma should be a priority, especially in cases with documented life-threatening arrhythmias. In some patients with VT associated with phaeochromocytoma, a long QT interval has been identified [10, 11].

9.1.1.3 Acromegaly

SCD is an established manifestation of acromegaly, and life-threatening arrhythmias are likely to be an important cause [12]. Up to one half of all acromegalic patients have complex ventricular arrhythmias on 24-h Holter recordings, and of these, approximately two thirds are repetitive [13]. Appropriate surgical management of the pituitary tumour is paramount for improved long-term outcome, as cardiac changes are reversible, especially in the young [14, 15]. Somatostatin analogues such as octreotide and lanreotide have both been shown to improve the ventricular arrhythmia profile [16–18].

9.1.1.4 Primary Aldosteronism, Addison Disease, Hyperparathyroidism and Hypoparathyroidism

Severe electrolyte disturbances form the basis of arrhythmogenesis and VT/SCD associated with the previously mentioned endocrinopathies. Electrocardiographic (ECG) changes including prolongation of QRS and QTc intervals can accompany

the electrolyte disturbance. Electrolyte imbalance requires immediate attention before definitive treatment of the underlying cause [19–21].

9.1.1.5 Diabetic Ketoacidosis (DKA)

As its name suggests, DKA is defined by the presence of metabolic acidosis, along with hyperglycaemia, as a result of insulin deficiency. These factors are generally accompanied by severe dehydration, catecholamine release and disordered potassium homeostasis; deviation of magnesium, sodium and other electrolytes can also occur. The syndrome is most often precipitated by sepsis or poor medication compliance with direct cardiac consequences, such as arrhythmias [22]. With appropriate insulin and fluid therapy, the acidosis is reversed and concomitantly potassium is forced into cells, often resulting in rebound hypokalaemia. Without frequent biochemical monitoring, such dynamic metabolic changes may deviate from normality without being acted upon, so increasing the likelihood of cardiac compromise.

During the acute phase of treatment, the rapid transition of potassium gradients changes the type of arrhythmia susceptibility. Initially, hyperkalaemia slows conduction and normal automaticity favouring bradycardias, re-entrant VT and ventricular fibrillation (VF). Later, hypokalaemia favours re-entrant arrhythmias, polymorphic VT and atrial fibrillation (AF) due to triggered activity. However, the broader spectrum of dynamic metabolic changes present in DKA will also impact upon the risk of arrhythmia, potentially through complex interactions between all of the mechanisms outlined earlier. This has led to recommendations of continuous electrocardiographic monitoring during the acute phase of treatment, although the evidence of benefit for this as a routine approach is lacking [23].

9.1.2 Ion Disturbances

Electrolyte abnormalities are commonly associated with cardiovascular emergencies. These abnormalities are amongst the most common causes of cardiac arrhythmias, and they can (cause or) complicate resuscitation attempts and post-resuscitation care. If extreme, even isolated electrolyte deficiency or excess can cause life-threatening cardiac involvement in patients with structurally normal hearts. Clinical syndromes that create hypo- and hyper-concentrations of potassium, calcium and magnesium are associated with the most common and clinically important disturbances of cardiac rhythm related to electrolyte abnormality. Despite the frequency of sodium abnormalities, particularly hyponatraemia, its electrophysiological effects are rarely clinically significant. It is important to identify clinical situations in which electrolyte problems may be expected. In some cases therapy for life-threatening electrolyte disorders should be initiated even before laboratory results become available. Of all the electrolyte abnormalities, hyperkalaemia is the most rapidly fatal. A high degree of clinical suspicion and aggressive treatment of underlying electrolyte abnormalities can prevent these abnormalities from progressing to cardiac arrest [24]. Electrocardiographic findings associated with these disturbances can provide clues to the diagnosis as well as guide therapeutic interventions. Although discussed individually, it is important to remember that there is a dynamic physiologic interrelationship to electrolyte homeostasis and that aberration in one ‘compartment’ may have impact on another [25].

9.1.2.1 Potassium

Potassium (K^+) is the most abundant intracellular cation with only 2 % of the total body potassium in the extracellular space, and hypokalaemia is the most common electrolyte abnormality in clinical practice. Potassium plays an important role in maintaining the electrical potential across the cellular membrane as well as in depolarisation and repolarisation of the myocytes. The electrophysiological effects of potassium depend not only on its extracellular concentration but also on the direction (hypokalaemia *vs* hyperkalaemia) and rate of change. Although the mechanism of potassium regulation between compartments is complex, there are two main transport processes. An active transport process involves the Na^+/K^+ ATPase pump, insulin, beta-adrenergic agents and mineral corticosteroids and a passive transport that results from alterations in the pH and extracellular cellular fluid osmolality. Homeostatic serum potassium concentration is maintained by terminal nephron segments of the kidney. Factors that lead to alterations in serum potassium regulation include renal failure and medications such as non-steroidal anti-inflammatory agents, angiotensin-converting enzyme inhibitors, diuretics and digitalis [26, 27]. Alterations in serum potassium levels can have dramatic effects on cardiac cell conduction and may lead to EKG changes, and the electrocardiogram is a useful screening tool for gauging the severity of the serum potassium abnormality and the urgency of therapeutic intervention [28, 29].

Hyperkalaemia

Hyperkalaemia is a common disorder, although less common than hypokalaemia, occurring both in the outpatient setting and in up to 8 % of patients who have been admitted to hospital, mainly in the setting of compromised renal function [30–33]. Hyperkalaemia is defined as an excess concentration of potassium ions in the extracellular fluid compartment above the normal range of 3.5–5.0 mEq/L. Moderate (6–7 mEq/L) and severe (>7 mEq/L) hyperkalaemia is life-threatening and requires immediate therapy. Although mild hyperkalaemia is often asymptomatic and easily treated, acute and severe hyperkalaemia, if left untreated, can result in fatal cardiac arrhythmias [34–36].

The most common clinical presentation of severe hyperkalaemia involves patients with end-stage renal failure. Identification of potential causes of hyperkalaemia will contribute to rapid identification and treatment of patients who may be experiencing hyperkalaemic cardiac arrhythmias [37–39]. Potassium-sparing diuretics such as spironolactone, triamterene and amiloride are well-recognised causes of hyperkalaemia. Use of angiotensin-converting enzyme (ACE) inhibitors can also lead to elevation of serum potassium, particularly when combined with oral potassium supplements. Moreover, non-steroidal anti-inflammatory medicines can cause hyperkalaemia through direct effects on the kidney.

Physical symptoms of hyperkalaemia include weakness, ascending paralysis and respiratory failure.

Electrocardiographic manifestations of hyperkalaemia. The EKG manifestation of hyperkalaemia depends on serum K^+ level. Studies validate a good correlation with hyperkalaemia and EKG changes, but 50 % of patients with potassium levels greater than 6.5 mEq/L will not manifest any ECG changes.

The increased extracellular concentration of K^+ causes an influx of K^+ into the cells. There is an alteration of the transmembrane potential gradient, a decrease in

magnitude of the resting potential and a decrease in velocity of phase 0 of the action potential. The K^+ influx causes a shortening of the action potential and results in delayed conduction between the myocytes and ECG change, such as the *T wave tenting*, classically described as symmetrically narrow or peaked, though the deflection is often wide and of large amplitude [40]. In addition, inverted T waves associated with left ventricular hypertrophy can *pseudonormalise* (i.e., flip upright) [41]. These T wave changes occur as a result of the acceleration of the terminal phase of repolarisation, are most prominently seen in the precordial leads and are often seen when potassium levels exceed *5.5 mEq/L*. With higher levels of serum potassium, cardiac conduction between myocytes is suppressed. Reduction in atrial and ventricular transmembrane potential causes an inactivation of the sodium channel, decreasing the cellular action potential. Atrial tissue is more sensitive to these changes earlier, and, as a result, P wave flattening and PR interval prolongation may be seen before QRS interval prolongation. These changes generally occur when potassium levels exceed *6.5 mEq/L* [42]. As the serum level continues to rise to levels above *twice the normal value*, there is suppression of sinoatrial and atrioventricular conduction, resulting in sinoatrial and atrioventricular blocks, often with escape beats. Other blocks including intraventricular conduction delay, bundle branch block and fascicular blocks have been reported. The bundle branch blocks associated with hyperkalaemia are atypical in the sense that they involve the initial and terminal forces of the QRS complex. Shifts in the QRS axis indicate disproportionate conduction delays in the left bundle fascicles [43]. As hyperkalaemia progresses, depolarisation merges with repolarisation, expressed in the ECG with *QT shortening* and *apparent ST segment elevation* simulating acute injury [44]. Atypical bundle branch blocks (LBBB and RBBB), intraventricular conduction delays, VT, ventricular fibrillation and idioventricular rhythm are more commonly seen in cases of severe hyperkalaemia.

Hypokalaemia

Hypokalaemia, defined as a serum potassium level *<3.5 mEq/L*, is the most common electrolyte abnormality encountered in clinical practice. It is observed in over 20 % of hospitalised patients [45], because of the high prevalence of patients on medications that can result in hypokalaemia, as 10–40 % of patients on thiazide diuretics have low potassium levels [46]; moreover, almost 50 % of patients resuscitated from out-of-hospital VF [47].

The most common causes of low serum potassium are gastrointestinal loss (diarrhoea, laxatives), renal loss (hyperaldosteronism), severe hyperglycaemia, potassium depleting, diuretics, carbenicillin, sodium penicillin, amphotericin B, intracellular shift (alkalosis or a rise in pH) and malnutrition.

The major consequences of severe hypokalaemia result from its effects on nerves and muscles (including the heart). The myocardium is extremely sensitive to the effects of hypokalaemia, particularly if the patient is taking a digitalis derivative. Symptoms of mild hypokalaemia are weakness, fatigue, paralysis, respiratory difficulty, constipation, paralytic ileus and leg cramps; more severe hypokalaemia will alter cardiac tissue excitability and conduction.

Electrocardiographic manifestations of hypokalaemia. In cases of severe hypokalaemia, EKG changes can be a very useful, quick, inexpensive and widely

available diagnostic tool. The ECG manifestations of hypokalaemia [48] are due to its effects on repolarisation and conduction. As serum potassium levels decline, transmembrane potassium gradient decreases. The effect on cell membrane is elevation in resting membrane potential and prolongation of the action potential, particularly phase 3 repolarisation and refractory periods.

The *earliest ECG change* associated with hypokalaemia is a *decrease in the T wave amplitude*.

As potassium *levels further decline*, *ST segment depression and T wave inversions* can be seen and the *U wave becomes more prominent*. The *PR interval can be prolonged,* and there can be an *increase in the amplitude of the P wave*.

With *even lower serum potassium levels*, the classic ECG change associated with hypokalaemia is the development of *U waves*. The U wave is described as a positive deflection after the T wave that is often best seen in the mid-precordial leads, such as V2 and V3. These changes have been reported in almost 80 % of patients with potassium levels <2.7 mEq/L [49].

With *extreme hypokalaemia*, *giant U waves* may often mask the smaller preceding T waves or following P waves [50]. The characteristic reversal in the relative amplitude of the T and U waves is the most distinctive change in waveform morphology in hypokalaemia. The U wave in hypokalaemia is caused by prolongation of the recovery phase of the cardiac potential, the relative refractory period predisposing to re-entrant tachyarrhythmias.

Magnesium

Although magnesium is the fourth most common mineral and the second most abundant intracellular cation (after potassium) in the human body, the significance of magnesium disorders is controversial partly because of the frequent association of other electrolyte abnormalities. Magnesium is an important cofactor in several enzymatic reactions contributing to normal cardiovascular physiology.

The average adult contains about 24 g of magnesium, with only 1 % found in the extracellular space [51]. One third of extracellular magnesium is bound to serum albumin. Therefore, serum magnesium levels are not reliable predictors of total body magnesium stores. It plays an important role in stabilising excitable membranes and may influence the incidence of cardiac arrhythmias through a direct effect, by modulating the effects of potassium, or through its action as a calcium channel blocker. Magnesium deficiency is thought to interfere with the normal functioning of membrane ATPase and thus the pumping of sodium out of the cell and potassium into the cell [52].

Hypermagnesaemia. Hypermagnesaemia is defined as a serum magnesium concentration *>2.2 mEq/L* (normal: 1.3–2.2 mEq/L). Magnesium balance is influenced by many of the same regulatory systems that control calcium balance and by diseases and factors that control serum potassium. As a result, magnesium balance is closely tied to both calcium and potassium balance. The most common cause of hypermagnesaemia is renal failure. Hypermagnesaemia may also be iatrogenic (caused by overuse of magnesium) or caused by continued use of laxatives or antacids containing magnesium (an important cause in the elderly). Severe symptoms include neurological symptoms, areflexia, muscular weakness, paralysis, ataxia,

drowsiness, confusion, respiratory failure and, rarely, cardiac arrest. Gastrointestinal symptoms include nausea and vomiting. Moderate hypermagnesaemia can produce vasodilation, and severe hypermagnesaemia can produce hypotension. Extremely high serum magnesium levels may produce a depressed level of consciousness, bradycardia, hypoventilation and cardiorespiratory arrest [53].

Electrocardiographic manifestations of hypermagnesaemia. ECG changes of hypermagnesaemia include the following:

- Increased QRS duration
- Increased PR and QT intervals
- Variable decrease in P wave voltage
- Variable degree of T wave peaking
- Complete AV block and asystole

Hypomagnesaemia. Hypomagnesaemia, defined as a serum magnesium concentration <1.3 mEq/L, is far more common than hypermagnesaemia. It is caused by decreased intake, increased losses or altered intracellular-extracellular distribution. Hypomagnesaemia usually results from decreased absorption or increased loss, either from the kidneys or intestines (diarrhoea). Alterations in parathyroid hormone and certain medications (e.g. pentamidine, diuretics, alcohol) can also induce hypomagnesaemia. Lactating women are at higher risk of developing hypomagnesaemia.

Measurement of serum levels do not correlate well with clinical manifestations. Hypomagnesaemia is associated with far-reaching adversity across the physiologic spectrum, including central nervous system effects (seizures, mental status changes), cardiovascular effects (dysrhythmias, vasospasm), endocrine effects (hypokalaemia, hypocalcaemia) and muscle effect (bronchospasm, muscle weakness) [54].

Electrocardiographic manifestations of hypomagnesaemia. A number of ECG abnormalities occur with low magnesium levels, including the following:

- ST segment depression
- Prolonged QT and PR intervals
- T wave inversion
- Flattening or inversion of precordial P waves
- Widening of QRS
- Torsades de pointes, treatment-resistant VF (and other arrhythmias) and worsening of digitalis toxicity [55]

Calcium

Calcium (Ca^{++}) is the most abundant mineral in the body. It is essential for bone strength and neuromuscular function and plays a major role in myocardial contraction. The human body has a nearly inexhaustible reservoir of Ca^{++} stored as hydroxyapatite in skeletal bone. Of the total 1–2 kg of adult total body Ca^{++}, only 1 g of calcium is present in plasma. Ca^{++} is important in a myriad of regulatory mechanisms, skeletal muscle contraction and control of enzymatic reactions and is a key ion in myocyte electrical activity and myocardial contraction [56]. Although total

serum calcium $Ca^{++,}$ is directly related to serum albumin, the ionised Ca^{++} is inversely related to serum albumin. The lower the serum albumin, the higher the ionised calcium. Isolated abnormalities of extracellular Ca^{++} produce clinically significant electrophysiological effects only when they are extreme in either direction.

Hypercalcaemia. Hypercalcaemia is defined as a serum Ca^{++} concentration above the normal range of 8.5–10.5 mEq/L (or an elevation in ionised calcium above 4.2–4.8 mg/dL).

Hypercalcaemia is the cardinal feature of *hyperparathyroidism*. Primary hyperparathyroidism and malignancy account for >90 % of reported cases [57]. It is typically chronic, mild and well tolerated. Severe hypercalcaemia with serum levels *above 14 mg/dL* can be precipitated in these patients by dehydration from gastrointestinal losses, diuretic therapy or ingestion of large amounts of calcium salts.

Symptoms of hypercalcaemia usually develop when the total serum Ca^{++} concentration reaches or exceeds 12–15 mg/dL and can be relatively vague, including fatigue, lethargy, motor weakness, anorexia, nausea, constipation and abdominal pain. Effects on the kidney include diminished ability to concentrate urine; diuresis, leading to loss of sodium, potassium, magnesium and phosphate; and a vicious circle of calcium reabsorption that further worsens hypercalcaemia. At higher levels patients may exhibit hallucinations, disorientation, hypotonicity and coma. Cardiovascular symptoms of elevated Ca^{++} levels are variable. Myocardial contractility may initially increase until the Ca^{++} level reaches *15–20 mg/dL. Above* this level myocardial depression occurs. Automaticity is decreased, but arrhythmias occur because the refractory period is shortened, many patients develop hypokalaemia and digitalis toxicity is worsened [58].

Electrocardiographic manifestations of hypercalcaemia. The effect of hypercalcaemia on the electrocardiogram is the opposite of hypocalcaemia with the hallmark of abnormal shortening of the QTc interval. Cardiac conduction abnormalities may occur, with bradydysrhythmias being the most common [59]. ECG changes of hypercalcaemia include the following:

- Prolonged PR and QRS intervals
- Shortened QT interval (usually when Ca^{++} is >13 mg/dL)
- Increased QRS voltage with notching of QRS complex
- T wave flattening and widening
- AV block, progressing to complete heart block and to cardiac arrest when serum calcium is >15–20 mg/dL

Hypocalcaemia. Hypocalcaemia is defined as a serum calcium concentration below the normal range of 8.5–10.5 mg/dL (or an ionised calcium below the range of 4.2–4.8 mg/dL). Hypocalcaemia is classically seen with *functional parathyroid hormone deficiency*, either as absolute hormone deficiency (primary hypoparathyroidism), post-parathyroidectomy or related to a pseudo-hypoparathyroid syndrome. Other causes of hypocalcaemia include *vitamin D deficiency, congenital disorders of calcium metabolism, chronic renal failure, acute pancreatitis, rhabdomyolysis and sepsis*. Hypocalcaemia is commonly seen in critically ill patients, with a reported incidence of as high as 50 % [60]. Furthermore, hypocalcaemia is often

associated with hypomagnesaemia. Symptoms usually occur when ionised levels fall *below 2.5 mg/dL.* Neuromuscular irritability is the cardinal feature, with carpal-pedal spasm being the classical physical sign that may progress to tetany, laryngospasm or hyperreflexia and positive Chvostek and Trousseau signs.

Hypocalcaemia prolongs phase 2 of the action potential. *Prolongation of the QTc interval* is associated with early after-repolarisations and triggered dysrhythmias. Torsades de pointes potentially can be triggered by hypocalcaemia but is much less common than with hypokalaemia or hypomagnesaemia.

Severe symptoms and life-threatening dysrhythmias mandate immediate treatment; in addition, associated electrolyte abnormalities, including hypomagnesaemia, phosphate abnormalities and acidemia, may need to be corrected.

Electrocardiographic manifestations of hypocalcaemia. Hypocalcaemia results in *prolonged ST segment and QT interval,* a potential cause of torsades de pointes, although much less commonly than with hypokalaemia or hypomagnesaemia [61]. Whereas electrocardiographic conduction abnormalities are common, serious hypocalcaemia-induced dysrhythmias such as heart block and ventricular dysrhythmias are infrequent.

9.1.2.2 Management of Arrhythmic Complications

Encountering a seriously ill patient with complex metabolic derangement and cardiac, or multi-organ, compromise can be daunting. Firstly, the basic principles of resuscitation provide a means of optimising basic cardiorespiratory physiology whilst giving time to consider the more complex metabolic needs of the patient. Depending on the underlying presentation or disorder, an appropriate initial assessment of electrolytes, acid-base and fluid balance status should be made. The results of this, in addition to the likelihood of rapid changes due to treatment or the natural history of the disorder, should be used to guide timing of repeat assessments. Furthermore, a strategy to normalise the patient's biochemical profile should be planned and regularly updated; addressing the underlying disorder may be all that is required in some cases. Where profound derangement is present, or when treatment of the underlying disease is failing to achieve the goal of physiological normalisation, it may be necessary to provide additional treatment targeted at specific metabolic parameters. This may involve electrolyte correction, rehydration and reduction of other factors, such as hypoxia, which worsens ischaemia. *Manipulation of acid-base status is generally not recommended* [62, 63]; in DKA, or other forms of acidosis, expert consensus suggests sodium bicarbonate therapy results in net harm, perhaps by worsening intracellular acidosis. Bicarbonate is still administered on occasions, but in the most profoundly acidotic patients and often as an act of desperation.

Unfortunately, the evidence base to guide such decisions is limited and so relies upon expert consensus. A 12-lead ECG with continuous recording of the rhythm strip provides invaluable information, but should not be allowed to interfere with emergent treatment where required. If the patient is 'compensating' haemodynamically for their rhythm disturbance, then time is available to classify the rhythm disturbance and manage according to accepted guidance [64]. It is crucial to remember that any 'antiarrhythmic' pharmacotherapy commenced may have unintended pro-arrhythmic consequences, particularly in the setting of metabolic abnormalities

[65]. The principle of never prescribing antiarrhythmic 'cocktails' is even more pertinent in this scenario.

Treatment of Hyperkalaemia

A variety of treatment options are considered for the acute management of hyperkalaemia, including insulin, β2-adrenergic agonists (inhaled, nebulised and intravenous), bicarbonate, resins, fludrocortisone, aminophylline and dialysis.

The treatment of hyperkalaemia is determined by its severity and the patient's clinical condition. First you need to stop the sources of exogenous potassium administration (e.g. consider supplements and maintenance IV fluids) and evaluate drugs that can increase serum potassium (e.g. potassium-sparing diuretics, ACE inhibitors, non-steroidal anti-inflammatory agents). The level of potassium at which treatment should be initiated has not been established by evidence. Several treatment options have been proposed, particularly for shifting potassium into the cells, with differing onset and duration of action [66].

For *mild* elevation *(5.5–6 mEq/L)*, remove potassium from the body with the following:

1. Diuretics—furosemide 1 mg/kg IV slowly
2. Resins—Kayexalate 15–30 g in 50–100 mL of 20 % sorbitol either orally or by retention enema (50 g of Kayexalate)

For *moderate* elevation (*6–7 mEq/L),* shift potassium intracellularly with the following:

1. Sodium bicarbonate—50 mEq IV over 5 min (sodium bicarbonate alone is less effective than glucose plus insulin or nebulised albuterol, particularly for the treatment of patients with renal failure; it is best used in conjunction with these medications) [67, 68]
2. Glucose plus insulin—mix 50 g glucose and 10 U regular insulin and give IV over 15–30 min
3. Nebulised albuterol 10–20 mg nebulised over 15 min

For *severe* elevation *(>7 mEq/L* with toxic ECG changes), you need to shift potassium into the cells and eliminate potassium from the body. Therapies that shift potassium will act rapidly, but they are temporary; if the serum potassium rebounds, you may need to repeat those therapies. In order of priority, treatment includes the following:

- *Shift potassium into cells:*
  1. Calcium chloride (10 %): 500–1000 mg (5–10 mL) IV over 2–5 min to reduce the effects of potassium at the myocardial cell membrane (lowers risk of VF)
  2. Sodium bicarbonate: 50 mEq IV over 5 min (may be less effective for patients with end-stage renal disease)
  3. Glucose plus insulin: mix 25 g (50 mL of D50) glucose and 10 U regular insulin and give IV over 15–30 min

4. Nebulised albuterol: 10–20 mg nebulised over 15 min

- *Promote potassium excretion:*
  5. Diuresis (furosemide 40–80 mg IV)
  6. Kayexalate enema: 15–50 g plus sorbitol PO or per rectum
  7. Dialysis

Treatment of Hypokalaemia

Treatment of hypokalaemia focuses on parenteral and oral potassium supplementation as well as identification and treatment of the source of the electrolyte abnormality. IV administration of potassium is indicated when arrhythmias are present or hypokalaemia is *severe* (*<2.5 mEq/L).* Gradual correction of hypokalaemia is preferable to rapid correction unless the patient is clinically unstable. Acute potassium administration may be empirical in emergent conditions. When indicated, maximum IV K^+ replacement should be 10–20 mEq/h with continuous ECG monitoring during infusion. Central or peripheral IV sites may be used. A more concentrated solution of potassium may be infused if a central line is used, but the catheter tip should not extend into the right atrium.

If cardiac arrest from hypokalaemia is imminent (i.e. malignant ventricular arrhythmias), rapid replacement of potassium is required. Give an initial infusion of 10 mEq IV over 5 min; repeat once if needed. In the patient's chart, document that rapid infusion is intentional in response to life-threatening hypokalaemia. Once the patient is stabilised, reduce the infusion to continue potassium replacement more gradually. Estimates of total body deficit of potassium range from 150 to 400 mEq for every 1 mEq decrease in serum potassium. The lower range of the estimate would be appropriate for an elderly woman with low muscle mass and the higher range for a young, muscular man.

Treatment of Hypermagnesaemia

Hypermagnesaemia is treated with administration of *calcium*, which removes magnesium from serum. Cardiorespiratory support may be needed until magnesium levels are reduced. It is important to eliminate sources of ongoing magnesium intake. Administration of 10 % solution of calcium chloride (5–10 mL [500–1000 mg] IV) will often correct lethal arrhythmias. This dose may be repeated if needed. Dialysis is the treatment of choice for hypermagnesaemia. Until that can be done, if renal function is normal and cardiovascular function adequate, IV saline dieresis (IV normal saline and furosemide) can be used to increase renal excretion of magnesium until dialysis can be performed. However, this diuresis can also increase calcium excretion; the development of hypocalcaemia will deteriorate signs and symptoms of hypermagnesaemia.

Treatment of Hypomagnesaemia

Treatment of hypomagnesaemia depends on its severity and the patient's clinical status. For severe or symptomatic hypomagnesaemia, administer 1–2 g IV MgSO4 over 5–60 min. For torsades de pointes with cardiac arrest, give 1–2 g of MgSO4 IV pushed over 5–20 min. If torsades de pointes is intermittent and not associated with

arrest, administer the magnesium over 5–60 min IV. If seizures are present, administer 2 g IV MgSO4 over 10 min. Calcium gluconate administration (1 g) is usually appropriate because most patients with hypomagnesaemia are also hypocalcaemic [69]. Replace magnesium cautiously in patients with renal insufficiency because there is a real danger of causing life-threatening hypermagnesaemia.

Treatment of Hypercalcaemia

If hypercalcaemia is due to malignancy, careful consideration of the patient's prognosis and wishes is needed. Therapy for hypercalcaemia is generally instituted based on clinical signs more than absolute serum levels, although empiric therapy is often started at levels of 12 mg/dL even in the asymptomatic patient. In patients with hypoalbuminaemia, measured serum calcium levels may mask significant elevations in free ionised extracellular calcium. Treatment is instituted at a level *>15 mg/dL* regardless of symptoms. Immediate therapy is directed at promoting calcium excretion in the urine. The mainstays of treatment are intravenous volume repletion and bisphosphonate agents that inhibit osteoclastic bone resorption. This is accomplished in patients with adequate cardiovascular and renal function with infusion of 0.9 % saline at 300–500 mL/h until any fluid deficit is replaced and diuresis occurs (urine output 200–300 mL/h). Once adequate rehydration has occurred, the saline infusion rate is reduced to 100–200 mL/h. This diuresis will further reduce serum potassium and magnesium concentrations, which may increase the arrhythmogenic potential of the hypercalcaemia. Thus, potassium and magnesium concentrations should be closely monitored and maintained. Hemodialysis is the treatment of choice to rapidly decrease serum calcium in patients with heart failure or renal insufficiency [70]. The use of loop diuretics (furosemide 1 mg/kg IV) to promote calciuresis is often recommended but is problematic in the hypovolemic patient.

Treatment of Hypocalcaemia

Calcium exchange is dependent on concentrations of potassium and magnesium, so treatment depends on replacing all 3 electrolytes.

Treatment of hypocalcaemia requires administration of calcium. Treat acute, symptomatic hypocalcaemia with 10 % calcium gluconate, 90–180 mg of elemental calcium IV over 10 min. Follow this with an IV drip of 540–720 mg of elemental calcium in 500–1000 mL D5W at 0.5–2.0 mg/kg per hour (10–15 mg/kg). Measure serum calcium every 4–6 h. Aim to maintain the total serum calcium concentration between 7 and 9 mg/dL.

Vitamin D and oral calcium supplementation can be administered for chronic hypocalcaemia.

9.1.2.3 When Should Electrolyte Level Be Rechecked?

The studies did not address the frequency and duration of monitoring of patients with ion disturbances; therefore, recommendations regarding ongoing assessment are based on opinion. In the acute management of electrolyte deficiency/excess, the frequency of monitoring depends on the electrolyte level as well as underlying comorbidities. After initial interventions, electrolyte level should be rechecked

within *1–2 h*, to ensure effectiveness of the intervention, following which the frequency of monitoring could be reduced. Subsequent monitoring depends on the electrolyte abnormalities and the potential reversibility of the underlying cause.

We believe the management and treatment of metabolic disorders and ion disturbances that can lead to severe complications, such as life-threatening arrhythmias, should be common knowledge for both the physician working in ED and for the cardiologist. Here, however, we emphasise some peculiarities related to the disorders described that can be particularly useful.

9.2 What Physicians Working in ED Should Know

Profound diarrhoea has the potential to 'waste' large quantities of essential electrolytes, in addition to water and bicarbonate. Without appropriate and timely management, it is possible to develop a highly proarrhythmic situation with metabolic acidosis, increased adrenergic activity, hypokalaemia, hypocalcaemia, hypomagnesaemia and so on. Vomiting can equally result in many of these abnormalities and so in combination with diarrhoea, or when added to other disease states such as DKA, can cause a significant combined cardiac insult. Appropriate identification of these metabolic and fluid balance abnormalities is imperative in order to prevent complications. Thus, regular assessment of hydration, acid-base and electrolyte status is crucial.

Potassium

- Evaluation of serum potassium must consider the effects of changes in serum pH. When serum pH falls, serum potassium rises because potassium shifts from the cellular to the vascular space. When serum pH rises, serum potassium falls because potassium shifts intracellularly. In general, serum K decreases by approximately 0.3 mEq/L for every 0.1 U increase in pH above normal. Effects of pH changes on serum potassium should be anticipated during therapy for hyperkalaemia or hypokalaemia and during any therapy that may cause changes in serum pH (e.g. treatment of diabetic ketoacidosis). Correction of an alkalotic pH will produce an increase in serum potassium even without administration of additional potassium. If serum potassium is 'normal' in the face of acidosis, a fall in serum potassium should be anticipated when the acidosis is corrected, and potassium administration should be planned.
- Hypokalaemia exacerbates digitalis toxicity. Thus, hypokalaemia should be avoided or treated promptly in patients receiving digitalis derivatives.
- The ECG correlates of hypokalaemia can be confused with myocardial ischemia. In addition, it can be difficult to differentiate a U wave from a peaked T wave that is present in hyperkalaemia.
- The use of a beta-agonist appeared to be effective in rapid reduction of hyperkalaemia: salbutamol is effective when given intravenously, in a nebulised form and

as a multi-dose inhaler. IV insulin and glucose is effective and has a rapid onset of action. The evidence for the use of bicarbonate in hyperkalaemia is equivocal, and it is not recommended as monotherapy. If used in conjunction with other treatments, the possible effects on pH and extracellular volume must be carefully considered in the assessment of the risk-benefit ratio for an individual patient.

Combining insulin-glucose with salbutamol (albuterol) probably leads to greater reductions in serum potassium than either alone. In animal and human studies, IV calcium stabilises membranes and reduces the arrhythmic threshold. Though no randomised evidence exists to support its use, it is recommended that calcium chloride be given in the presence of ECG changes or arrhythmia and repeated as needed.

Magnesium

- Abnormalities in magnesium, potassium and pH must be corrected simultaneously.
- Untreated hypomagnesaemia will make hypocalcaemia refractory to therapy.

Calcium

- The concentration of ionised calcium is pH dependent. Alkalosis increases the binding of calcium to albumin and thus reduces ionised calcium. Conversely, the development of acidosis will produce an increase in the ionised calcium level.
- In the presence of hypoalbuminaemia, although total calcium level may be low, the ionised calcium level may be normal.
- Calcium antagonises the effects of both potassium and magnesium at the cell membrane. Therefore, it is extremely useful for treating the effects of hyperkalaemia and hypermagnesaemia.
- Calcium may also be lowered by drugs that reduce bone resorption (e.g. calcitonin, glucocorticoids).

9.3 What Cardiologists Should Know

A diverse array of metabolic disorders is known to precipitate arrhythmia, though their individual proarrhythmic effects can be simplified by considering broad unifying pathophysiological mechanisms.

Metabolic disturbance mediates re-entry because regions of physiologically and pathological conduction (accelerated myocyte repolarisation or reduced myocardial conduction velocity) are both present, although anatomical substrates can interact and so produce complex disturbances of myocardial excitation and conduction.

Acidosis is proarrhythmic through promoting re-entry and triggered activity [71]. It is notable that re-entry on a much larger scale is the cause of certain supraventricular tachycardia, for example, atrioventricular re-entry tachycardia in the Wolff-Parkinson-White syndrome. Metabolic derangement can alter the conduction

properties of the abnormal anatomic pathways in these disorders, promoting re-entry and/or augmenting the maximum heart rate supported by the circuit. More complex re-entry is also a contributory factor to other arrhythmias witnessed in critically ill patients, such as atrial fibrillation and VT. After-depolarisation, or triggered activity, is the other major mechanism through which electrolyte disturbance encourages arrhythmias.

This process may be repeated resulting in tachycardia, and it is through this mechanism in which polymorphic VT, or torsades de pointes, develops. Delayed after-depolarisations are less relevant to proarrhythmia in the context of pure metabolic disarray, though in certain circumstances remain relevant. The classical example is arrhythmia due to digoxin toxicity which is aggravated by hypokalaemia and hypercalcaemia. Catecholamine excess and myocardial ischaemia are also important, and relatively common, precipitants in patients with metabolic disarray.

Potassium

- Interestingly, bypass tracts are more sensitive to delayed conduction from potassium elevation, which can result in the normalisation of the ECG and loss of the delta wave in patients with Wolff-Parkinson-White syndrome.
- With extremely high serum potassium levels, a markedly prolonged and wide QRS complex can fuse with the T wave, producing a slurred, 'sine-wave' appearance on the ECG. This finding is a pre-terminal event unless treatment is initiated immediately. The fatal event is either asystole, as there is complete block in ventricular conduction, or ventricular fibrillation.
- Hyperkalaemia can induce a Brugada-like pattern in the ECG [72]. This usually occurs in critically ill patient with significant hyperkalaemia (serum potassium >7.0 mmol/L) and is associated with pseudo-right bundle branch block and persistent coved ST segment elevation in at least two precordial leads. Prompt recognition of this ECG entity will enable clinicians to identify severe hyperkalaemia, which may result in high mortality.
- The effect of hyperkalaemia on QRS morphology of ventricular paced beats has also been studied [73]: hyperkalaemia is the most common electrolyte abnormality to cause loss of capture. In patients with pacemakers, hyperkalaemia causes two important clinical abnormalities: [1] widening of the paced QRS complex (and paced P wave) on the basis of delayed myocardial conduction; when the K level exceeds 7 mEq/L, the intraventricular conduction velocity is usually decreased and the paced QRS complex widens, [2] and increased atrial and ventricular pacing thresholds with or without increased latency.
- In patients with cardiac resynchronisation therapy, the hyperkalaemia can result in a loss of capture and/or sensing failure of even only one of the two ventricular electrodes, leading to a biventricular activation failure.
- Several cardiac and non-cardiac drugs are known to suppress the HERG K+ channel and hence the IK and, especially in the presence of hypokalaemia, can result in prolonged action potential duration and QT interval, early after-depolarisations and torsades de pointes.

- Hyperkalaemia is a common disorder that can be fatal if unrecognised or untreated. Insulin administered intravenously has the fastest onset of action and is very effective in reducing serum potassium. β2-Adrenergic agonists are as effective as insulin for lowering serum potassium and have a longer duration of action. The combination of β2-agonists and insulin is more effective than either treatment alone. The use of intravenously administered sodium bicarbonate for the management of acute hyperkalaemia is supported only by studies with weak and equivocal results [74] .
- Changes in pH inversely affect serum potassium. Acidosis (low pH) leads to an extracellular shift of potassium, thus raising serum potassium. Conversely, high pH (alkalosis) shifts potassium back into the cell, lowering serum potassium. Metabolic alterations such as alkalosis, hypernatraemia or hypercalcaemia can antagonise the transmembrane effects of hyperkalaemia and result in the blunting of the ECG changes associated with elevated potassium levels.
- Hyperkalaemia inhibits glycoside binding to (Na+, K+) ATPase, decreases the inotropic effect of digitalis and suppresses digitalis-induced ectopic rhythms. Alternatively, hypokalaemia increases glycoside binding to (Na+, K+) ATPase, decreases the rate of digoxin elimination and potentiates the toxic effects of digitalis.

Magnesium

- Low potassium in combination with low magnesium is a risk factor for severe arrhythmias.
- It is well known that both supraventricular and ventricular dysrhythmias can be potentiated if not directly caused by hypomagnesaemia.
- Magnesium has been shown to be efficacious in the management of atrial tachydysrhythmias although there is no correlation between rhythm conversion and plasma concentration.
- Magnesium sulphate is considered first-line therapy by the American Heart Association ACLS Guidelines for torsades de pointes.

Calcium

- The combination of hyperkalaemia and hypocalcaemia has a cumulative effect on the atrioventricular and intraventricular conduction delay and facilitates the development of VF. Hypercalcaemia, through its membrane-stabilising effect, counteracts the effects of hyperkalaemia on AV and intraventricular conduction and averts the development of VF.
- Half of all calcium in the extracellular fluid is bound to albumin; the other half is in the biologically active, ionised form. The ionised form is most active. The serum ionised calcium level must be evaluated in light of serum pH and serum albumin.
- Hypocalcaemia can exacerbate digitalis toxicity Table 9.1.

Table 9.1 Ion disturbances: etiology, diagnosis and treatment

Ione	Disorders	Aetiology	Signs	EKG changes	Treatment
K+	Hyperkalaemia mild (5–6 mEq/L)	Drugs End-stage renal disease Rhabdomyolysis Metabolic acidosis Pseudohyperkalaemia Hemolysis Tumour lysis syndrome Diet Hypoaldosteronism (Addison disease, hyporeninemia) Type 4 renal tubular acidosis Hyperkalaemic periodic paralysis	Weakness Ascending paralysis Respiratory failure	Flattened P waves Prolonged PR interval Widened QRS complex Deepened S waves Merging of S and T waves Sine-wave pattern Idioventricular rhythm Asystolic cardiac arrest	1. Furosemide 1 mg/kg IV slowly 2. Kayexalate 15–30 g in 50–100 mL of 20 % sorbitol
	Hyperkalaemia moderate (6–7 mEq/L)				1. Sodium bicarbonate—50 mEq IV over 5 min 2. Glucose plus insulin—mix 50 g glucose and 10 U regular insulin and give IV over 15–30 min 3. Nebulised albuterol 10–20 mg nebulised over 15 min
	Hyperkalaemia severe (>7 mEq/L)				1. Calcium chloride (10 %): 500–1000 mg (5–10 mL) IV over 2–5 min 2. Sodium bicarbonate: 50 mEq IV over 5 min 3. Glucose plus insulin: mix 25 g (50 mL of D50) glucose and 10 U regular insulin and give IV over 15–30 min 4. Nebulised albuterol: 10–20 mg nebulised over 15 min 5. Furosemide 40–80 mg IV) 6. Kayexalate enema: 15–50 g plus sorbitol PO or per rectum 7. Dialysis
	Hypokalaemia mild (3.5–2.5 mEq/L)	Diarrhoea, Laxatives Hyperaldosteronism Hyperglycaemia Potassium depleting Diuretics Carbenicillin, sodium penicillin, amphotericin B Intracellular shift (alkalosis or a rise in pH) Malnutrition	Weakness Fatigue Paralysis Respiratory difficulty Constipation Paralytic ileus Leg cramps	U waves T wave flattening Ventricular arrhythmias –Pulseless electrical activity (PEA) Asystole	Gradual correction of hypokalaemia is preferable to rapid correction
	Hypokalaemia severe (<2.5 mEq/L)				1. Maximum IV K replacement should be 10 to 20 mEq/h 2. Infusion of 10 mEq IV over 5 min (if cardiac arrest)

(continued)

Table 9.1 (continued)

Ione	Disorders	Aetiology	Signs	EKG changes	Treatment
Mg+	*Hypermagnesaemia* (>2.2 mEq/L)	Renal failure Overuse of mg+ Use of laxatives/antacids containing mg+	Areflexia Muscular weakness Paralysis Ataxia Drowsiness Confusion Respiratory failure Nausea Vomiting Hypotension Hypoventilation	Increased PR and QT Increased QRS Decrease P wave voltage Degree of T wave peaking Complete AV block Asystole	1. 10 % solution of calcium chloride (5–10 mL [500–1000 mg] IV) 2. Dialysis 3. Furosemide [1 mEq/kg]
	Hypomagnesaemia (<1.3 mEq/L)	Bowel resection Pancreatitis Diarrhoea Renal disease Diuretics Pentamidine Gentamicin Digoxin Alcohol Hypothermia Hypercalcaemia Diabetic ketoacidosis Hyperthyroidism Hypothyroidism Phosphate deficiency Burns Sepsis	Seizures Mental status changes Dysrhythmias Vasospasm Hypokalaemia Hypocalcaemia Bronchospasm Muscle weakness	Prolonged QT and PR intervals ST segment depression T wave inversion Flattening P waves Widening of QRS Torsades de pointes VF	1. 1–2 g IV MgSO4 over 5–60 min 2. For torsades de pointes 1 to 2 g of MgSO4 IV over 5–20 min

Ca++	*Hypercalcaemia* > 10.5 mEq/L (or > 4.8 mg/dL ionised calcium)	Hyperparathyroidism Malignancy	Fatigue Lethargy Motor weakness Anorexia Nausea Constipation Abdominal pain Diuresis Hallucinations Disorientation Hypotonicity	Shortened QT interval Prolonged PR and QRS intervals Increased QRS voltage T wave flattening and widening Notching of QRS AV block	1. 0.9 % saline at 300 to 500 mL/h 2. Hemodialysis 3. Chelating agents 4. Furosemide 5. Calcitonin, glucocorticoids
	Hypocalcaemia < 8.5 mg/dL (or < 4.2 mg/dL ionised calcium)	Toxic shock Abnormalities in serum magnesium Tumour lysis syndrome	Neuromuscular irritability Carpal-pedal spasm –Tetany Laryngospasm Paraesthesias of the extremities and face Muscle cramps Hyperreflexia Positive Chvostek and Trousseau signs	QT interval prolongation Terminal T wave inversion Heart blocks Ventricular fibrillation	1. 10 % calcium gluconate, 90–180 mg of calcium IV over 10 min 2. IV drip of 540–720 mg of elemental calcium in 500–1000 mL D_5W at 0.5–2.0 mg/kg per hour (10–15 mg/kg)

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Cardiac Arrhythmias in Drug Abuse and Intoxication

10

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10.1 Focusing on the Issue

Cardiac arrhythmias are common in acute intoxication, although epidemiological data are often restricted to specific substances. A 10 % incidence of cardiac arrhythmias during acute intoxication has been reported by a referral poison center in Germany that analyzed the data of 91,285 patients referred between 1995 and 2003 using the inquiries of physicians and paramedics [1].

A large amount of substances and their association can lead to worsening of preclinical or active cardiovascular diseases and, on occasion, to ex-novo cardiovascular diseases or arrhythmic manifestations. Negative cardiovascular effects are mainly caused by the pharmacokinetics of substances, in particular if drugs are administered or abused in combination, or in cases of concomitant metabolic, renal, or liver diseases; moreover, negative effects can be the result of pharmacodynamics, as in the presence of an interaction between a not otherwise toxic substance and an altered morphofunctional cardiac substrate (e.g., long QT or Brugada syndrome).

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10.2 What Physicians Working in Emergency Departments Should Know

The management of patients with a certain diagnosis or at high risk for "poisoning" or "drug abuse" should be oriented toward the acute handling of symptoms of intoxication and support of hemodynamics (e.g., intubation and respiratory support, electrolyte substitution and hydration, and temporary pacing in the case of bradycardia).

Physicians working in the emergency department (ED) should be aware that people using or abusing illicit drugs are often prone to mix different substances, alcohol being the most abused and coabused substance. Cannabis is the most frequently used illicit drug, followed by cocaine, ecstasy, and amphetamines [2]. Physicians in the ED should be familiar with the telephone number of the local poison control center as well as internal protocols and resources.

When deciding the therapeutic strategy, the medical history of the patient plays a pivotal role, and it is important to follow a systematic approach, starting with the following:

- Habitual medications
- Coexisting diseases
- Which substance or mix was taken, and when
- If a mix of substances was taken, which was the sequela
- Way of substance abuse: pills, sublingual, intravenous, inhalation

It is then important to initiate a treatment as soon as possible in order to achieve a stabilization:

- Cardiopulmonary support including fluids, direct current shock if hemodynamically unstable arrhythmia, or temporary pacing if bradycardia
- Gastrointestinal decontamination of an ingested drug
- Administration of an antidote if available
- Correction of acid–base and electrolyte alterations

10.3 What Physicians Working in the ED and Cardiologists Should Know

In order to offer a pragmatic approach to the management of patients presenting with arrhythmias associated with drug abuse and intoxication, this section focuses firstly on recreational drugs and secondly on the most common prescription drugs.

10.3.1 Recreational Drugs

The use and abuse of recreational drugs is increasing, and every year new "designer drugs" appear on the recreational drug market, such as the novel class of cathinone

derivatives, often proposed as "legal highs" by categorizing them as odorizers, stain removers, potpourri, or most recently the notorious "bath salts" [3].

An updated list of many recreational drugs can be easily found by consulting the web site of the World Anti-Doping Agency [4] (WADA list 2015, updated yearly; www.wada-ama.org). This list comprises all those substances abused by the general population and in particular by athletes with ergogenic scope during their lifetime. Many of these drugs can induce cardiovascular effects, particularly arrhythmias, during short-, mid-, and long-term use [5–8].

10.3.1.1 Stimulants

The heterogeneous group of stimulants includes many classes of drugs, widely used to obtain a performance enhancement, a raise in aggressiveness and competitiveness levels, and a reduction of fatigue perception, or simply for "recreational" purposes.

Among stimulants, amphetamines also are widely used for weight-loss regimens [9–11]. Ephedrine and other similar alkaloids are also contained in the herbal product ephedra, marketed as dietary supplement [12, 13].

The amphetamines are the chemical basis of many designer drugs usually sold as "club drugs": methylenedioxymethamphetamine (MDA) is well known as the "love pill," and 3,4-methylenedioxymethamphetamine (MDMA or Ecstasy) is commonly available under confounding names such as "clarity" or "lover's speed," but many chemical variants are commonly abused. The tablets can contain between 50 and 200 mg, and the toxic effects can be manifest starting from a dose of 50 mg [14, 15].

This class of stimulants (amphetamine or ephedrine derivatives) acts through the release of noradrenaline, dopamine, and serotonin. The symptoms of patients presenting in the ED can include sympathomimetic effects such as arterial hypertension, hyperthermia, mydriasis, dry mouth, and tachycardia. Commonly the patients also present with hyperactivity reactions such as logorrhea, restless syndrome, anxiety, tremors, myoclonus and coma.

Regarding the arrhythmias, patients present commonly with sinus or atrial tachycardia, although atrial flutter, atrial fibrillation, supraventricular reentrant tachycardia, and ventricular tachycardia have also been reported. Re-entry arrhythmias may be due to adrenergic activity during myocardial refractory periods [16, 17]. These patients should be treated with intravenous saline volumes, electrolyte substitution, and a β-blocker can be used through a slow intravenous injection for the management of tachycardia and hypertension.

Several cases of cardiac arrest and sudden death in users were reported to be associated with coronary artery disease, cardiomyopathy and myocarditis, and others with direct myocyte toxicity [14, 16]. In patients with Wolff-Parkinson-White (WPW) syndrome, stimulants can induce rapid atrial fibrillation and ventricular fibrillation [18], increasing atrial and ventricular excitability and shortening accessory pathway refractoriness.

Particular attention should be paid to young patients intoxicated with Ecstasy after physically extreme activity (e.g., "rave parties" or athletes after competitions) presenting with a "serotonin syndrome": the combination of central effects (i.e., hyperthermia) and severe dehydration and electrolyte disorders can lead to

malignant arrhythmias whose management must combine arrhythmia therapy (cardioversion or β-blocker) with cooling, rehydration, and electrolyte replacement.

Physicians in the ED should also keep in mind that patients with amphetamine intoxication commonly present with associated rhabdomyolysis.

In recent years patients taking a new class of recreational designer drugs based on cathinones mixed with amphetamine, so-called bath salts, have been admitted to the ED. 3,4-Methylenedioxypyrovalerone (MDPV), 4-methylmethcathinone (4-MMC or mephedrone), and 4-methylephedrone are some examples. In the USA, MDPV seems to be the primary active ingredient in the majority of bath salts; on the other hand, in the European Union mephedrone is more common [19].

Cathinone is a β-ketone amphetamine analogue naturally present in the leaves of the plant *Catha edulis* (also known as *Khat*) [3]. Cathinone acts as a mild stimulant by inhibiting monoamine transporters for dopamine, serotonin, and norepinephrine within the central nervous system, and is internationally regulated.

Patients who have taken MDPV may present in the ED with sinus tachycardia and other arrhythmias including ventricular tachycardia [3]. Many different symptoms have been reported, particularly related to a dopaminergic mechanism that leads to serotonin syndrome. It is important to be aware of the prolonged psychogenic effects, which may last for up to 1 week [20]. Deaths after the use of bath salts have been reported [3].

Among cathinone derivatives, only bupropion is legally approved for medical purposes as an antidepressant medication.

10.3.1.2 Cocaine

Cocaine is an alkaloid derived from a plant, *Erythroxylum coca*. It can be inhaled or smoked, only rarely being injected [21, 22]. On the illicit drugs market it can be found as a salt (hydrochloride or sulfate) or a free Base ("crack"). Indeed, this alkaloid may cause different kinds of focal or re-entry supraventricular and ventricular arrhythmias, such as ectopic beats, atrial fibrillation, atrioventricular node re-entry tachycardia, WPW arrhythmias, and nonsustained and sustained ventricular tachycardia and ventricular fibrillation. Arrhythmias are frequently associated with physical effort, which can induce a sympathomimetic effect synergic with cocaine addiction [23].

Regarding electrocardiographic (ECG) alterations and arrhythmias, experimental animal studies on the effects of cocaine showed prolongation of PR, QT, and QTc intervals, a wider QRS, supraventricular and ventricular ectopic activity, ventricular tachycardia, and ventricular fibrillation [21, 24–26].

Cocaine can lead to cardiac side effects through multiple arrhythmogenic mechanisms:

- Local anesthetic effect with block of both sodium and potassium channels
- Sympathomimetic effect with α- and β-receptor stimulation, and consequent increase in heart rate and atrial and ventricular excitability
- Intracellular calcium overload (afterdepolarization arrhythmias)
- Arrhythmias due to ischemia/reperfusion mechanisms
- Increase in heart rate through vagolytic effect
- Inhibitor of generations and conduction of the action potential, with prolongation of QRS caused by sodium channel-blocking effects [27].

Arrhythmias may be also "secondary" to systemic effects of the drug such as hyperthermia, acidosis, stroke or subarachnoid haemorrhage or in Crack-smokers also to pneumotorax.The ability of cocaine to cause myocardial infarction, frequently with severe complications, is well known [22, 23, 28, 29], with the risk in the first hour after use increasing by up to 24-fold [30].

Myocardial infarction as well as various arrhythmias can occur even after the first administration of cocaine, regardless of dose.

In the ED the patients who have used/abused cocaine may present with many different types of arrhythmias whether in the setting of ischemic/reperfusion events or not. "Chaotic atrial arrhythmia," similar to that observed in severe respiratory insufficiency or acute myocarditis, is considered a typical toxic cocaine-related arrhythmia (Fig. 10.1). Moreover, supraventricular tachycardia, atrial fibrillation, ventricular tachycardia/fibrillation, torsade des pointes due to secondary long QT syndrome frequently related to hERG potassium channel blockade [25, 31], asystole (sporadic reports of asystole treated with emergent cardiac pacing), and cardiac arrest [18] have also been reported. Cocaine-induced wide complex ventricular tachycardia may be considered a typical toxic arrhythmia, frequently caused by high doses of the drug [22], and the treatment is based on administration of sodium bicarbonate [32].

Cocaine can also induce ECG modifications such as a V1–V3 ST elevation (coved type) typical for Brugada syndrome, due to a selective block of myocardial sodium channels in subjects with latent arrhythmic disease [33].

Moreover, patients abusing cocaine also commonly mix it with different substances such as hallucinogens, strychnine ("dead hit"), heroin ("speedball"), and alcohol ("liquid lady"): in case of associated intake of alcohol and cocaine the risk of sudden death has been found to be higher probably because of the additive effects of a metabolite, coca-ethylene, which can block the dopamine reuptake, enhancing the toxic effect of the cocaine used alone [34].

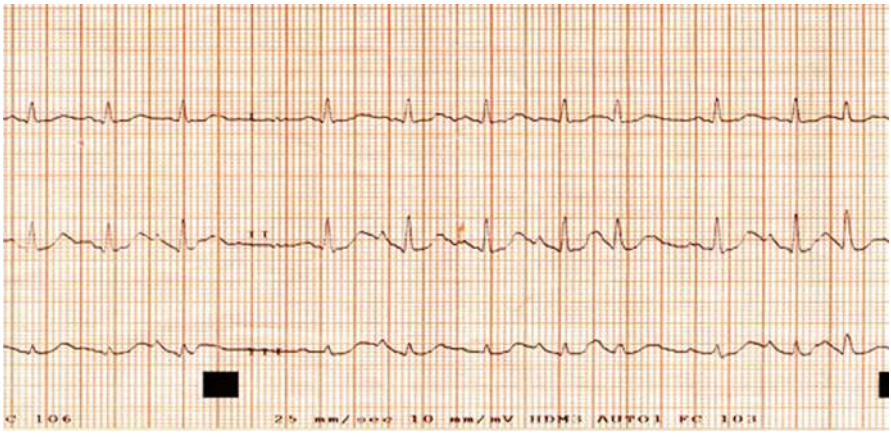

Fig. 10.1 Amateur football player, 17 years old, suspected cocaine intoxication and "chaotic atrial arrhythmia," i.e., sinus rhythm and polymorphic supraventricular ectopic beats

10.3.1.3 Cannabinoids

Many patients can present to the ED after consumption of cannabinoids, including marijuana and hashish, with different arrhythmic disorders: exercise-related sinus tachycardia, atrial fibrillation, paroxysmal supraventricular tachycardia, supraventricular and/or ventricular ectopic beats, and severe ventricular arrhythmias [35, 36], which can be mediated by catecholamines (Fig. 10.2).

The onset of arrhythmias is usually 30 or 60 min after smoking, and the arrhythmic disorders are related to the dose. At low and moderate doses there is an increase in sympathetic activity and a decrease in parasympathetic activity, and patients commonly present with sinus tachycardia, ectopic beats, or paroxysmal supraventricular tachycardia. At higher doses, there is a decrease in sympathetic activity and an increase in parasympathetic activity that can favour atrial fibrillation [37].

10.3.2 Prescription Drugs

Different common prescription drugs can induce arrhythmic complications in cases of involuntary abuse, suicidality, or in case of multiple interactions. Rather than providing an exhaustive list of all possible arrhythmias related to the use or abuse of prescription drugs, this section aims to help physicians working in the ED to get

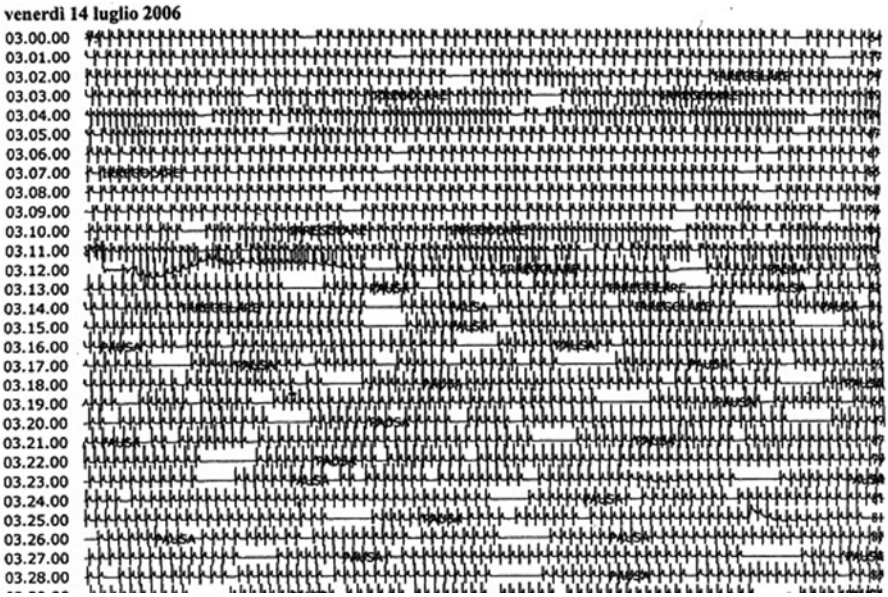

Fig. 10.2 ECG-Holter monitoring of a young male athlete (soccer player), 22 years old. Chronic use of cannabinoids and sporadic use of cocaine. This ECG-Holter tracing taken overnight shows a sick sinus syndrome with sinus arrest, sinus tachycardia, and nonsustained atrial tachycardia

used to a comprehensive attitude on managing not only the arrhythmias but also the whole pathologic affections.

Here, the most common prescription drugs whose abuse or misuse can present with arrhythmias are reviewed.

10.3.2.1 β-Blockers

Abuse of β-blockers can induce bradyarrhythmias with atrio-ventricular blocks of various degrees, sinus bradycardia, junctional and ventricular escape rhythms, bradycardia-dependent ventricular ectopic beats, and asystole, especially in patients with underlying structural and electrical disorders. Among the β-blockers, sotalol is associated with a high rate of cardiac dysrhythmias [1] and related QT prolongation. Other symptoms can be associated as hypotension, syncope, muscular contractions, mydriasis, bronchial obstruction and often hypoglycaemia especially in children.

The doctors in the ER should perform a gastrointestinal decontamination with activated charcoal and a correction of the hypoglicemia and other electrolyte disorders if present. Intravenous dopamine or adrenaline may be necessary, and the cardiologist should prepare a central venous access for a promt temporary pacing if required.

10.3.2.2 Digitalis

Patients presenting in the ED with symptoms of digitalis intoxication, mainly gastrointestinal in nature, such as anorexia, nausea, and vomiting, may suffer from many different dysrhythmias involving almost any rhythm or conduction disturbance [38–40]. The most common disorders are first-degree AV block or more advanced AV block degree and premature ventricular contractions.

Digoxin has two main actions in the cardiac myocyte: inhibition of the Na^+-K^+ Adenosinetryphosphate pump, interfering with AV conduction and increase in calcium concentrations, enhancing automaticity [41].

It is therefore important to recognize associated electrolyte disturbances, acid-base alterations, and renal or hepatic failure. In digoxin intoxication, hyperkalemia can be also sustained via a toxic mechanism of the Na^+-K^+ pump, which can be difficult to treat and can result after the treatment in hypokalemia.

In the presence of bradyarrhythmias, both atropine and cardiac pacing are usually effective. The most effective treatment for digitalis overdose is the administration of antidigitalis immunoglobulin IgG. The administration of magnesium and lidocaine often successfully treats premature ventricular contractions.

10.3.2.3 Antiarrhythmic Drugs

A patient with a history of atrial fibrillation treated with an antiarrhythmic drug such as flecainide or propafenone can present at the ED with an atrial flutter with a 2:1 or 1:1 atrioventricular conduction, or, in cases of drug abuse, also with a wide complex tachycardia related to class I effects on Na channels and QRS prolongation (Fig. 10.3).

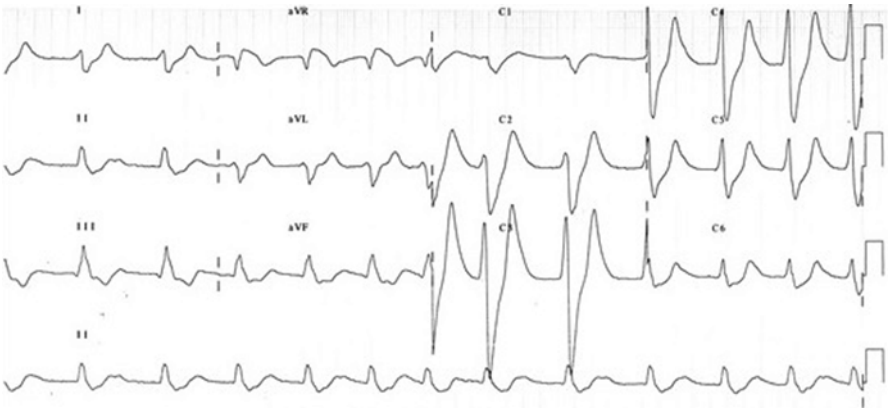

Fig. 10.3 A 60-year-old woman, 60 kg, with a history of paroxysmal atrial fibrillation; intake of 300 mg flecainide per os

10.3.2.4 Benzodiazepine

When a patient with a history of anxiety presents at the ED with palpitations, the medical history plays, as usual, an important role; in fact, discontinuation of benzodiazepine (BDZ) can cause a withdrawal syndrome with reactions that vary in severity and duration. Withdrawal syndrome is more common with triazolam and BDZs with a short to intermediate half-life, in particular if taken in repeated doses during the day, whereas the syndrome is rare with long-half-life BDZs and virtually absent with BDZ analogues such as zolpidem and zopiclone.

Arrhythmias during withdrawal syndrome are induced by autonomic arousal caused by sympathetic hyperactivity, and include mainly sinus tachycardia and ectopic beats, often associated with blood pressure imbalance (orthostatic hypotension and mild systolic hypertension). The administration of β-blockers or clonidine can help in managing reactions resulting from sympathetic hyperactivity [42].

10.3.2.5 Antidepressant Agents

Depressed patients seem to be predisposed to cardiac arrhythmias, one of the proposed mechanisms involves a reduced parasympathetic nervous system activity, that can be often present as a decreased heart rate variability [43].

In patients with depression presenting with dysrhythmias in the ED, it is important to recognize the different classes of drugs.

- *Tricyclic antidepressant agents* (TCA), such as imipramine, amitriptyline, and clomipramine, act as nonselective monoamine reuptake inhibitors. TCAs induce quinidine-like effects that are frequently encountered in older patients and children. On surface ECG it's often recognizable an intraventricular block and atrio-ventricular conduction block of different degrees with an increase in QRS width and PR interval; moreover, there are repolarization abnormalities with QT interval prolongation and negative T waves: therefore these patients present with

a higher risk of ventricular arrhythmias, in particular torsade de pointes. TCA can also induce sinus tachycardia (5–20 % of patients treated), with a mean increase of 15–20 bpm, probably caused by peripheral anticholinergic activity. Patients with cardiac diseases treated with class IC antiarrhythmic drugs (flecainide, propafenone) or quinidine should be closely monitored because the interaction between these drugs can lead to an increase in TCA blood concentration.

- *Selective serotonin reuptake inhibitors* (SSRI) include fluoxetine, sertraline, paroxetine, and citalopram, among others. A sinus tachycardia can be frequently recorded and, rarely, palpitations. In older patients SSRI can lead to sinus bradycardia and, rarely, syncope. In the case of drug overdose rhythm disorders, both bradyarrhythmia and tachyarrhythmia, as well as hypotension, are frequently present [44]. SSRI inhibits hepatic CYP3A4 and it is important to avoid or administer with reduced doses antiarrhythmic drugs as amiodarone, flecainide, propafenone, and lidocaine (i.v.) or sildenafil. [44, 45].
- *Monoamine oxidase inhibitors* (MAOI), such as phenelzine, tranylcypromine, and isocarboxazid, comprise the third main group of drugs used in clinical practice. A patient taking MAOI and presenting at the ED with palpitations and either tachycardia or bradycardia should be evaluated for a hypertensive surge, which has sometimes been reported as fatal. The anamnesis plays a pivotal role; in fact if the patient has ingested cheese or other foods with a high tyramine content, the arrhythmias could be due to norepinephrine release and an exaggerated adrenergic reaction induced by high tyramine blood levels [46–48].

10.3.2.6 Antibiotics

Patients treated with antibiotics can often present at the ED with sinus tachycardia or palpitations related to ectopic beats or to high rate atrial fibrillation; both dysrhythmias are probably related to the underlying condition (usually an infection) and subsequent fever and electrolyte disturbances.

In any event, a 12-lead ECG is mandatory to exclude a QTc prolongation and the risk of ventricular arrhythmias, in particular torsade de pointes.

These arrhythmias can be due to the following classes of antibiotics:

- *Macrolides* such as erythromycin, clarithromycin, and azithromycin. The risk of QT prolongation is higher if an H1 antagonist (e.g., terfenadine, astemizole) is administered at the same time. QT prolongation has been described with erythromycin, spiramycin and, less frequently, clarithromycin and azithromycin. Moreover, palpitations have been reported in patients taking azithromycin. An increase in digoxin levels has been reported in patients receiving erythromycin attributable to killing of digoxin-metabolizing bacteria [49].
- *Fluoroquinolones* such as levofloxacin and ciprofloxacin. Rarely, ventricular arrhythmias resulting from QT prolongation have been described during fluoroquinolone therapy.

10.4 A Suggested Algorithm/Pathway for Diagnosis and Treatment

All patients with bradyarrhythmia or tachyarrhythmia and suspected drug abuse or intoxication	What to do	How to do it
	Medical history and identification of suspected drug/s	Habitual medications Coexisting diseases Which substance or mix was taken (! alcohol) When the substance/mix was taken If a mix of substances was taken, which was the sequela Route of substance abuse: tablets, intravenous, inhalation, transdermal, sublingual
	Search for antidote	Contact local poison control center (the telephone number should be available in every ED)
	Medical management	Cardiopulmonary support including fluids DC shock if hemodynamically unstable arrhythmias or temporary pacing if bradycardia Gastrointestinal decontamination of an ingested drug Administration of an antidote if available Correction of acid–base and electrolyte alterations

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Pacemaker Malfunction: Myth or Reality?

11

Roberto Verlato, Maria Stella Baccillieri, and Pietro Turrini

11.1 Focusing on the Issue

Pacemaker (PM) and implantable cardiac defibrillator (ICD) malfunction is a serious and frequent finding in clinical setting. Depending on baseline rhythm and the type of malfunction, symptoms with different severity can occur, from no symptoms to syncope and sudden death due to asystole or ventricular fibrillation. Unfortunately, symptoms, such as asthenia, dizziness, dyspnea, and palpitations, are often vague, and this can lead to a dangerous delay in cardiac implantable electronic device (CIED) malfunction detection. An ECG recording and careful device and lead evaluation by means of telemetry are necessary for the diagnosis. A great help to early detection of CIED malfunctions is coming from remote control, allowing therapeutic interventions within 24 h since the malfunction occurs in most cases.

CIED malfunctions include two main categories: problems with sensing and problems with pacing. Problems with sensing are made of failure to sense, or *undersensing*, and excessive sensing of noncardiac or cardiac signals, called *oversensing*. Undersensing causes asynchronous inappropriate and not necessary pacing, which in turn can precipitate ventricular arrhythmias due to pacing during the ventricular refractory period (R-on-T phenomenon). Oversensing of spurious signals will lead to lack of stimulation and asystole in PM-dependent patients. In ICDs, inappropriate shocks are frequently caused by oversensing. Undersensing and oversensing are mostly due to lead-related problems, either insulation failure or conductor fractures. A connection defect must be considered as differential diagnosis. The problems with pacing have a common final result: PM spikes ineffective to capture the myocardium. If such malfunction is of minor importance in the atrium, it is a life-threatening emergency in PM-dependent patients, which can exit in sudden death.

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In patients with an implanted biventricular PM or ICD for cardiac resynchronization therapy (CRT), the loss of left ventricular capture is associated with recurrence of heart failure symptoms.

Battery depletion can lead to asynchronous pacing and other functional abnormalities mimicking either under- and oversensing.

11.2 What Physicians Working in Emergency Department Should Know

11.2.1 About Basic Function of Pacemakers and ECG Interpretation

The basics of PM are illustrated in Fig. 11.1, showing the normal function of a dual chamber (DDD) PM. These systems are preferred by cardiologists as they reproduce the normal atrioventricular (AV) conduction and physiology. They can sense and pace both the atrium and the ventricle. When they sense an atrial signal, a ventricular impulse is delivered at the end of the programmed AV delay. If no atrial signal is detected at the end of the programmed escape interval, the atrium is paced. If a ventricular spontaneous signal is sensed within the AV delay, no ventricular impulse is delivered to the ventricle [1].

The basics of single chamber (SSI), more often ventricular (VVI) PM, are more simple: the ventricle is paced at the end of the programmed escape interval, or basic rate, when nonsensed signal occurs within this time. In rate-responsive PM, either VVI or DDD, the stimulation rate is increased during effort according with sensors [1].

11.2.2 Most Important, Basic Programmable Functions in a Pacemaker

(a) *Lower rate*: it is the rate below which the pacemaker will stimulate the heart. If spontaneous activity is higher than the programmed lower rate, pacemaker output is inhibited. If programmed rate is higher than spontaneous rate and PM spikes are not visible, a malfunction is present, usually oversensing. The only exception is the presence of a "hysteresis" algorithm programmed on.

(b) *Hysteresis*: if this function is activated, the lower heart rate below which the PM will start the stimulation is different from the programmed pacing lower rate. For example, if hysteresis is programmed at 40/min and lower rate at 70/min, the PM will start the stimulation only if spontaneous heart rate drops below 40/min, but stimulation rate will be 70/min. The PM will check periodically the presence of spontaneous rate between 40 and 70/min.

(c) *Rate-responsive pacing*: the stimulation rate is increased when activity sensors detect patient movements (accelerometers). Respiratory activity sensors or other algorithms are also able to increase the basic pacing rate.

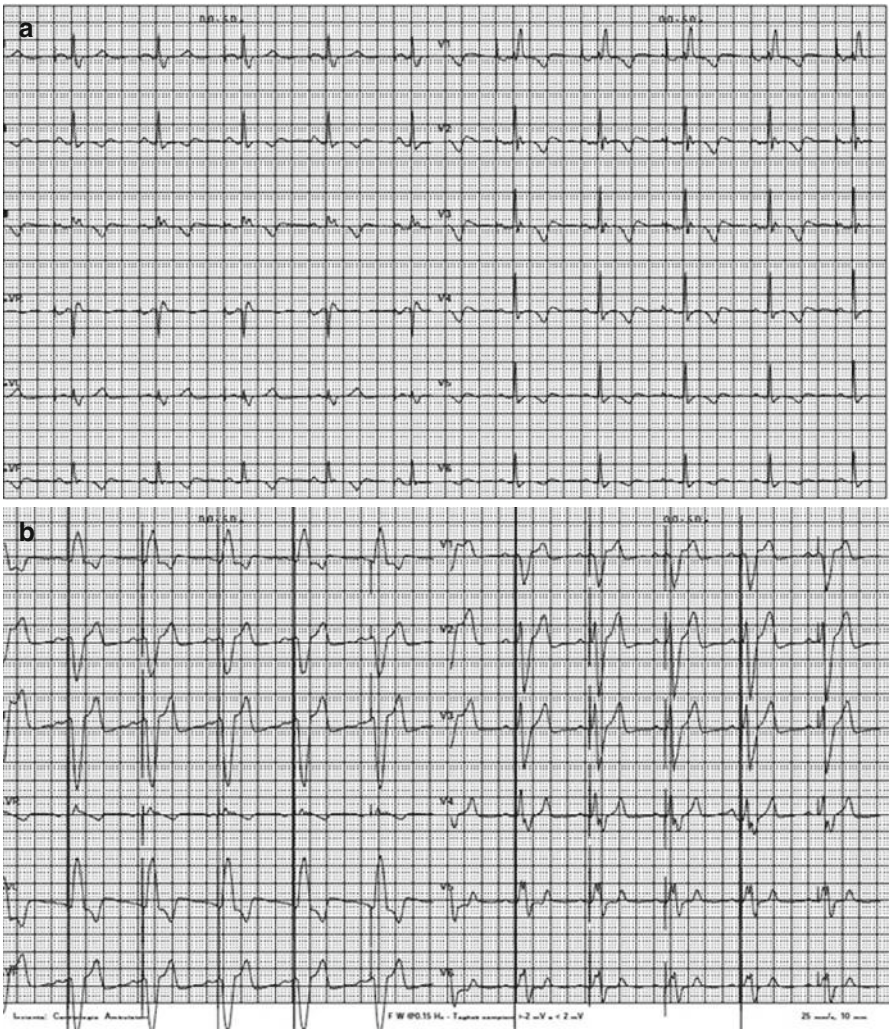

Fig. 11.1 *Top panel* (**a**). DDD pacemaker. Atrial rhythm is paced at 60 bpm. Spontaneous QRS with right bundle branch morphology occurs after 180 ms that inhibits ventricular pacing. This is called atrial-driven rhythm. *Bottom panel* (**b**): spontaneous sinus rhythm is present; each P wave is followed by a ventricular stimulus at the end of the programmed AV delay (120 ms) that captures the ventricular myocardium. The QRS morphology is left bundle branch block with superior axis, typical of right ventricular apical pacing

(d) *Upper rate*: it is the maximum stimulation rate either in case of atrial-driven or sensor-driven stimulation. If the PM stimulates at a rate higher than the programmed upper rate, a hardware/software malfunction is present. This can happen in case of unprotected exposition to strong electromagnetic fields, such as magnetic resonance imaging.

(e) *Algorithms to reduce ventricular pacing:* in order to reduce unnecessary ventricular pacing, several algorithms are present in modern dual chamber PM. Most commonly, only the atrium is stimulated (AAI mode) if atrioventricular conduction is preserved; when one or two (depending on the model and device programming) consecutive A-V blocks occur, the mode of stimulation automatically changes to atrioventricular pacing (DDD mode). Other algorithms prolong the programmed A-V interval up to 400 ms to detect if spontaneous A-V conduction is present. When these algorithms are activated, it is sometimes difficult to understand if the PM is working normally or not, for example, in case of single atrial beats without any ventricular activity; this can be a normal behavior of the device, when followed by DDD pacing, but can be expression of ventricular oversensing. Knowledge of the device programming, PM interrogation, or real-time telemetry can be necessary for the diagnosis.
(f) *Pacing voltage*: this is the voltage of PM stimulus. If it is programmed below the ventricular pacing threshold, spikes will be ineffective leading to an *exit block*.
(g) *Pulse duration*: this is the duration of PM stimulus. If it is programmed too short, spikes could be ineffective leading to an exit block.
(h) *Autocapture*: this algorithms automatically reduce PM output energy to values just above the ventricular pacing threshold. In case the delivered stimulus doesn't capture the ventricle, a second high-energy stimulus is provided: this is a normal behavior of modern PM and not a malfunction.
(i) *Mode switch*: when this algorithms are activated in dual chamber PM, the mode of stimulation automatically switches from DDD(R) to VDI(R) when an atrial tachycardia/fibrillation is detected. If atrial arrhythmia terminates, the mode of stimulation will return from VDI to DDD [1].

11.3 What Cardiologists Should Know

Cardiologists must be familiar with basic PM functions, mode of stimulation, PM algorithms, and interpretation of ECG recordings in PM patients. Modern PMs are very complex, fully programmable devices, with a lot of therapeutic and diagnostic capabilities. PM interrogation, evaluation of battery and lead data, analysis of real-time telemetry, and stored data are necessary for the final evaluation of PM functions. It would be desirable that cardiologists were trained and capable to use at least basic functions of PM programmers and the meaning and utilization of the following:

(a) *Magnet*: the application of a magnet above the PM pocket induces asynchronous pacing (VOO or DOO in single chamber or dual chamber PM, respectively). In case a PM is apparently not working (because spikes are not evident) but bradycardia (below lower rate, including hysteresis) is present, it is useful to apply a magnet on the PM. If PM spikes appear and capture the ventricle, oversensing inhibiting PM stimulation is likely. When necessary, in this cases magnet function is also useful for emergency treatment of the bradycardia.

(b) *ERI*: this is a message of "low battery charge" (Elective Replacement Indicator), meaning that the device will soon (usually after about 3 months) reaches the complete battery depletion, or EOL (End Of Life); ERT (Elective Replacement Time) and EOS (End Of Service) are synonymous of ERI and EOL, respectively, used by some manufacturers.
(c) *Pacing impedance*: this value is normally in the range between 350 and 900 Ω. Pacing impedance is influenced by the integrity of pacing circuit (conductors and insulation), by the lead model (i.e., active or passive fixation, steroid eluting or normal electrodes), and by electrode endocardial contact surface. When pacing impedance drops below 250 Ω, an insulation failure of the lead is likely. When pacing impedance is above 1500–2000 Ω (depending on the lead model), a conductor fracture or a connection defect is possibly present. In case of an abnormal pacing impedance in bipolar pacing and sensing configuration, PM reprogramming to unipolar pacing and sensing is recommended.

All cardiologists involved in emergency evaluation of PM patients should be trained to recognize the most commonly PM malfunctions, i.e., undersensing, oversensing, and exit block [1–3].

11.3.1 Undersensing in Cardiac Pacemakers

Undersensing occurs when the PM fails to sense the spontaneous atrial or ventricular activity. In this case the PM will ignore the spontaneous activity and pace the heart at the programmed rate as if the patient had no rhythm. This results in the so-called "asynchronous" pacing, that is, pacing competitive with spontaneous cardiac activity. Ventricular pacing during the vulnerable period of cardiac cycle (T wave) can occur, triggering ventricular arrhythmias including ventricular fibrillation [1–3].

An example of ventricular undersensing is illustrated in Fig. 11.2.

11.3.1.1 Causes of Undersensing

Causes of undersensing include lead failure, pacemaker failure, and environmental and physiologic changes. Lead failure is the most frequent cause of under- and oversensing in current CIEDs. Both insulation failure and lead fracture are able to induce undersensing, so it is pivotal to interrogate the pacemaker to evaluate pacing impedance. An increase of pacing impedance > 2000 Ω is diagnostic of conductor damage. A decrease of pacing impedance below 250 Ω is diagnostic of insulation failure. A connection defect is usually associated with a high pacing impedance, >3000 Ω, and this must be distinguished from conduction fracture in the presence of high pacing impedances. To identify a connection defect, chest X-ray is useful, as it can show the lead connector incompletely inserted into the PM head. An example of connection defect is illustrated in Fig. 11.3.

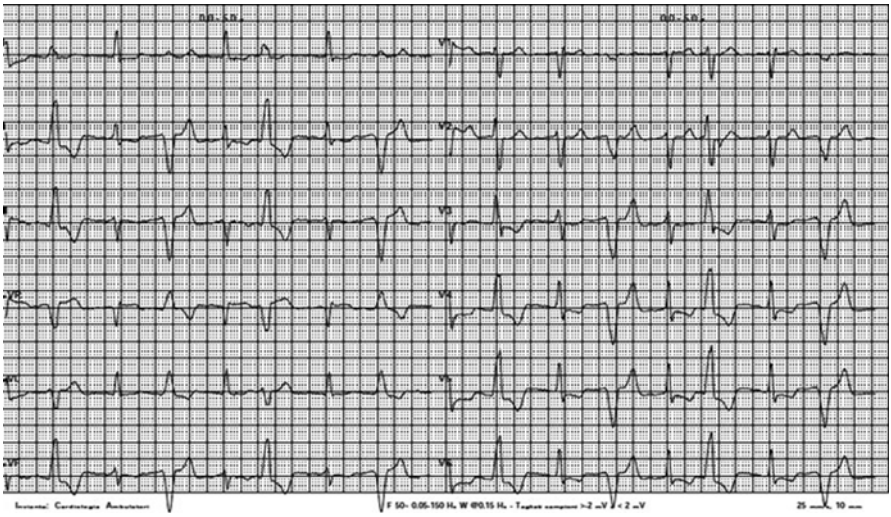

Fig. 11.2 VVI pacemaker. Spontaneous rhythm is present interrupted by premature beats of different morphology. At careful ECG inspection, small pacemaker spikes (bipolar) precede the QRS with left bundle branch morphology and left axis deviation. Other spikes follow spontaneous QRS in random sequence (asynchronous pacing). Undersensing of ventricular activity is present

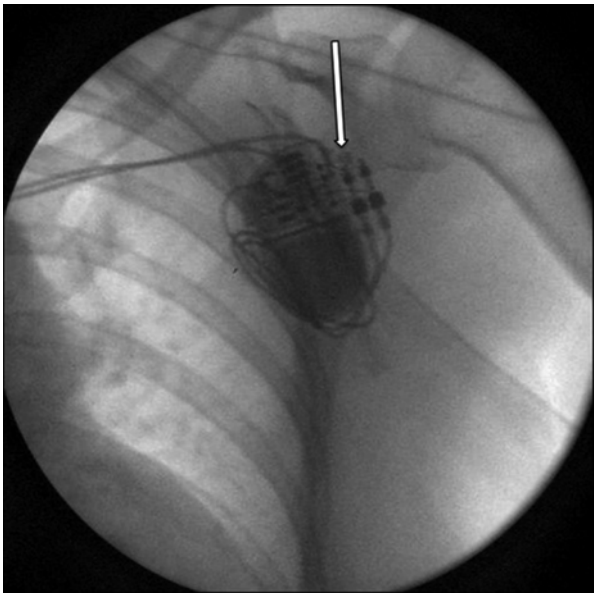

Fig. 11.3 Chest X-ray showing a close-up of pacemaker pocket. Patient had undergone to device replacement 1 week before and presented with high pacing impedance (>3000 Ω), under- and oversensing. The connector of the atrial lead, the lateral one, is completely inserted into the head of pacemaker, and its terminal pin is visible outside the electrode ring. The ventricular connector (*arrow*) is incompletely inserted and its terminal end is not visible

Chest X-ray is less useful to detect lead failure as leads seem apparently intact in most cases.

Pacemaker failure can cause undersensing. The most frequent situation is battery depletion (end of service, or EOL message at telemetry interrogation is displayed): this switches the mode of stimulation to asynchronous pacing.

Environmental causes of undersensing are strong magnetic fields, such as anti-theft devices, great motor engines, the application of a magnet on the pacemaker pocket, and magnetic resonance imaging. A frequent environment cause of undersensing is cardiac defibrillation. In this case undersensing but also an exit block with lack of ventricular capture can occur due to tissue damage at the myocardium-tip electrode interface.

Physiologic cardiac and noncardiac changes can facilitate undersensing, reducing the amplitude of cardiac sensed signals. New bundle branch block, myocardial infarction, hypokalemia and other ionic abnormalities, and old age of the implanted lead, associated with fibrous tissue growing around the electrode tip, are all situations associated with PM undersensing.

11.3.1.2 Treatment of PM Undersensing

In the case of reduced amplitude of sensed signals (measured by telemetry), it's possible to increase the PM sensing function by reprogramming, even if this in turn increases the risk of oversensing, in particular for unipolar leads. PM or lead replacement is the only way to correct the malfunction when battery depletion or lead failure is present [1–3].

11.3.2 Undersensing in ICDs

Undersensing in ICDs recognizes the same causes as in cardiac PM. Lead failure, either insulation or conductor defects, is the most dangerous situation in ICD patients, and it must be excluded in the presence of undersensing or oversensing. In ICDs either lead-related undersensing or oversensing may be intermittent, making diagnosis more difficult. A "physiologic" degree of undersensing is frequently observed in ICDs due to low voltages of cardiac signals during ventricular tachycardia and fibrillation, but this is rarely a clinical problem. Otherwise, prolonged ventricular undersensing during ventricular fibrillation (VF) could result in patient death, and the only possible treatment is an external rescue shock. However, in ICDs the most frequent cause of ventricular tachycardia (VT) undersensing is a programming "error," that is, the cutoff detection rate set at values above the rate of spontaneous VT. Reprogramming of VT detection rate will correct the problem [1].

11.3.3 Oversensing in Cardiac Pacemakers

Oversensing occurs when a PM senses noise, artifacts, or physiologic cardiac or noncardiac signals different from the atrial or ventricular depolarization and classifies such signals as atrial or ventricular depolarizations. The result will be inhibition of ventricular pacing when oversensing occurs at ventricular level or unnecessary ventricular pacing when oversensing occurs at atrial level. Pacing during oversensing is erratic, irregular, and completely unrelated with the programmed lower rate. In the case of prolonged pacing inhibition in PM-dependent patients, asystole will occur [1–3].

11.3.3.1 Causes of Oversensing

Lead failure is by far the most frequent cause of oversensing. Insulation failure, conductor fracture, and lead dislodgement are all able to induce oversensing of noise. Lead problems are identified by means of pacing impedance measurements, as described for undersensing. High pacing impedance is diagnostic of conductor problems, low impedance of insulation defect. Lead dislodgement and connection defect are often visible on X-ray imaging.

Environmental electromagnetic interferences (EMI) are the second more frequent cause of oversensing. They can reach the distal dipole of PM leads because electromagnetic currents flow through the patient's body, which acts as a volume conductor. Electrocautery, extracorporeal shock lithotripsy, and MRI (when CIED presence is ignored) are frequent causes of oversensing in the hospital setting. Noise signals can also originate from metal to metal friction in patients with multiple implanted pacemaker or defibrillation leads.

Myopotential oversensing can occur at pocket level (pectoral muscle oversensing), especially when programmed unipolar sensing, but more frequently the PM can sense the diaphragmatic respiratory activity.

T wave oversensing is the most common situation of oversensing of cardiac physiologic signals; it leads to a decrease of pacing rate as the escape interval is reset by the T wave sensing [1–3].

11.3.3.2 Treatment of Oversensing

The application of a magnet on the pocket will immediately induce (in PM, not in ICDs) atrial and ventricular asynchronous pacing. In the emergency setting this is the only maneuver that must be immediately applied to the patient, especially if symptomatic bradycardia is present.

If the PM programmer is available, sensing function must be reprogrammed to decrease PM sensitivity. In the case of unipolar sensing, the change of sensing configuration to bipolar, if a bipolar lead is implanted, will reduce or even could completely correct the oversensing of muscle potentials. In case T wave oversensing is present, longer ventricular refractory periods must be programmed.

The switch of pacing mode to VOO, or asynchronous, is the safest option in PM-dependent patients with oversensing due to lead problems to correct the bradycardia. In this case replacement of the failing lead is mandatory [1–3].

11.3.4 Oversensing in ICDs

Oversensing is the second leading cause of inappropriate detection and therapy of arrhythmias, including inappropriate shocks after atrial tachyarrhythmias. Lead failure must be suspected in any case of inappropriate shocks and noise stored in device memories. Several algorithms have been developed for early detection of lead failure based on the presence of very short intervals between sensed signals. The presence of a connection defect must always be considered as an alternative source of noise oversensing. Failing ICD leads must be replaced, with or without lead extraction based on careful evaluation of individual risk/benefit profile of lead extraction.

When noise oversensing is due to interference between implanted leads, lead extraction is mandatory [1–4].

11.3.5 Problems with Pacing

The most frequent situation is the presence of pacemaker spikes visible on monitor screens or ECG recordings, not followed by ventricular or atrial depolarizations (exit block). The failure to capture must be immediately recognized as it is a life-threatening malfunction.

In Fig. 11.4 an example of failure to capture is shown. PM spikes are delivered by pulse generator, not followed by ventricular depolarization [1–3].

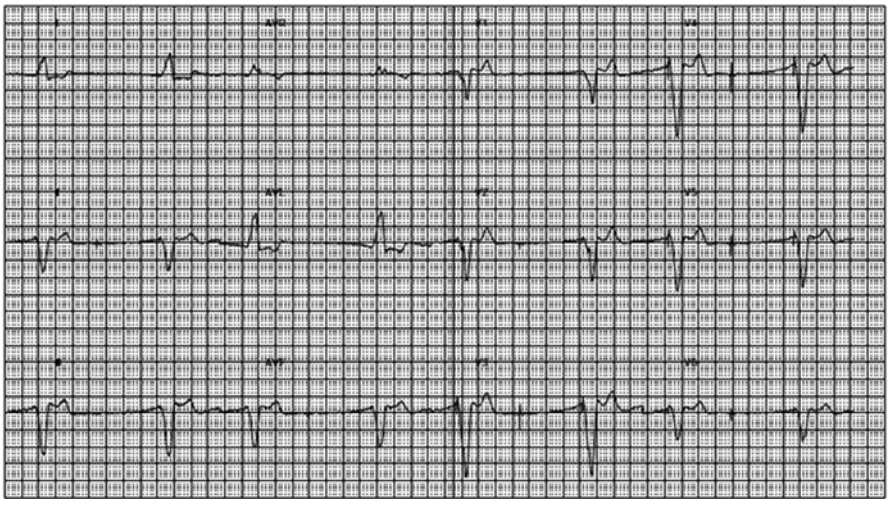

Fig. 11.4 Patient with PM presenting to the emergency room after a syncope. 12-lead ECG shows several pacemaker spikes not followed by ventricular depolarization (exit block). A failure to capture is certainly present. Real-time telemetry showed high pacing impedance (2500 Ω). Combining the two findings of exit block plus high pacing impedance, the diagnosis of lead fracture was made. Lead replacement was necessary in this case

11.3.5.1 Causes of Failure to Capture

In the period just following pacemaker implantation, lead dislodgement and cardiac perforation are the most common causes of failure to capture. Chest X-ray is necessary for the diagnosis, and reintervention for lead repositioning must be performed as soon as possible. Sometimes perforation is subtle, and a CT scan can be helpful to identify the relationship and exact position of the electrocatheter tip and the pericardium.

If the exit block occurs several weeks after implantation (the most frequent situation), it is usually due to an increase in stimulation threshold because of fibrosis maturation close and around to the electrode tip. Steroid-eluting leads are less frequently involved, while the risk is higher for active fixation leads, where an increase of pacing threshold frequently occurs during the first weeks after implantation. Such increase is usually transient, although it can rarely persist or even worsen (especially in young people) during follow-up.

Failure to capture can be also caused by too low voltage and/or duration of the stimulus emitted by the pacemaker in proximity of battery end of life or in the case of battery failure, but usually it depends by an inappropriate PM programming. Autocapture algorithms in modern pacemaker ensure ventricular capture.

Cardiac defibrillation and strong electromagnetic fields emitted by MRI can cause exit block due to tissue damage by current flow through the lead up to the electrodes, a sort of inadvertent tissue ablation, in particular when insulation failure is present.

Lead failure, in PM and especially in ICDs, is very often associated with deterioration of pacing and sensing thresholds, in addition with under- and oversensing [1–3].

11.3.5.2 Treatment of Failure to Capture

Acute perforation usually presents as an emergency in operating room. It requires pericardiocentesis and immediate lead repositioning.

Subacute and chronic perforation may be difficult to recognize. Symptoms may be minor; pericarditis, chest pain, diaphragmatic stimulation, and sometimes pneumothorax may be present. Perforation may occur at both atrial and ventricular levels. Loss of capture is almost always present together with sensing problems. Device reprogramming can transiently be useful to correct sensing and pacing abnormalities, but again lead revision/repositioning is absolutely required to solve the problem once the diagnosis is made.

When failure to capture occurs due to increased pacing thresholds, device reprogramming and selection of higher energy output, in terms of pulse voltage and duration, are the solutions in the acute setting. However, in current pacemaker technologies, the programmation of high pacing energies, i.e., voltage amplitude of 5–6 V and pulse duration of 1–2 ms, is associated with a marked reduction of battery longevity, up to less than two years. Lead revision, reposition, or replacement must be considered in pacemaker-dependent and/or young people with high pacing threshold.

Failure to capture occurring after MRI or cardiac defibrillation requires lead revision.

11.4 False Malfunctions

In modern devices, the complexity of some algorithms can sometimes make the ECG interpretation and the distinction between normal behavior and malfunctions quite difficult.

For this reason, to reach a correct ECG interpretation, it is necessary to know the model and the programming of the device, because what can be considered a normal behavior in some models and with some programming can be a malfunction in other cases [5].

- For example, a spontaneous rate below the lower rate programmed can be normal when a hysteresis is programmed, but a marker of oversensing in the absence of this function.
- In order to prevent sudden changes of the heart rate, an algorithm called "rate smoothing", "flywheel" or "ventricular rate stabilization," according to the manufacturer, can be enabled. In this case, stimulation can transiently occur beyond the lower rate, even if a rate response function is not present, just after a spontaneous fast activity, allowing a "smooth" reduction of heart rate. This can frequently happen during atrial fibrillation with very irregular rate, after ectopic ventricular beats or at the end of a tachycardia.
- Convincing data have shown that stimulation of the right ventricle is hemodynamically unfavorable and can sometimes cause or worsen congestive heart failure. In some devices, algorithms for minimizing ventricular pacing are enabled. In this case it is possible to observe an extremely long PQ interval, or even two consecutive P waves (spontaneous or stimulated) not followed by any ventricular activity, before the automatic switch from AAI (or ADI) to DDD mode occurs (Fig. 11.5).

Finally, a very short paced AV interval (about 100 ms) can sometimes be observed.

This is due to a function called "ventricular safety pacing," which consists in the delivery of a ventricular stimulus when a signal is detected in the ventricular channel immediately after an atrial stimulation. As in practice, the device is not able to distinguish whether the signal is derived by the artifact of atrial pacing detected at ventricular level (crosstalk) or a real ventricular beat (as an ectopic ventricular beat), so it immediately delivers a ventricular stimulus ensuring stimulation (in the presence of crosstalk) but with an interval short enough to fall, in the presence of a beat of ventricular origin, in its refractory period, avoiding the risk of triggering dangerous arrhythmias. Ventricular safety pacing can be present even in case of a lack of atrial sensing, when the atrial stimulus coincides with the spontaneous QRS complex, as in the course of sinus rhythm and normal AV conduction.

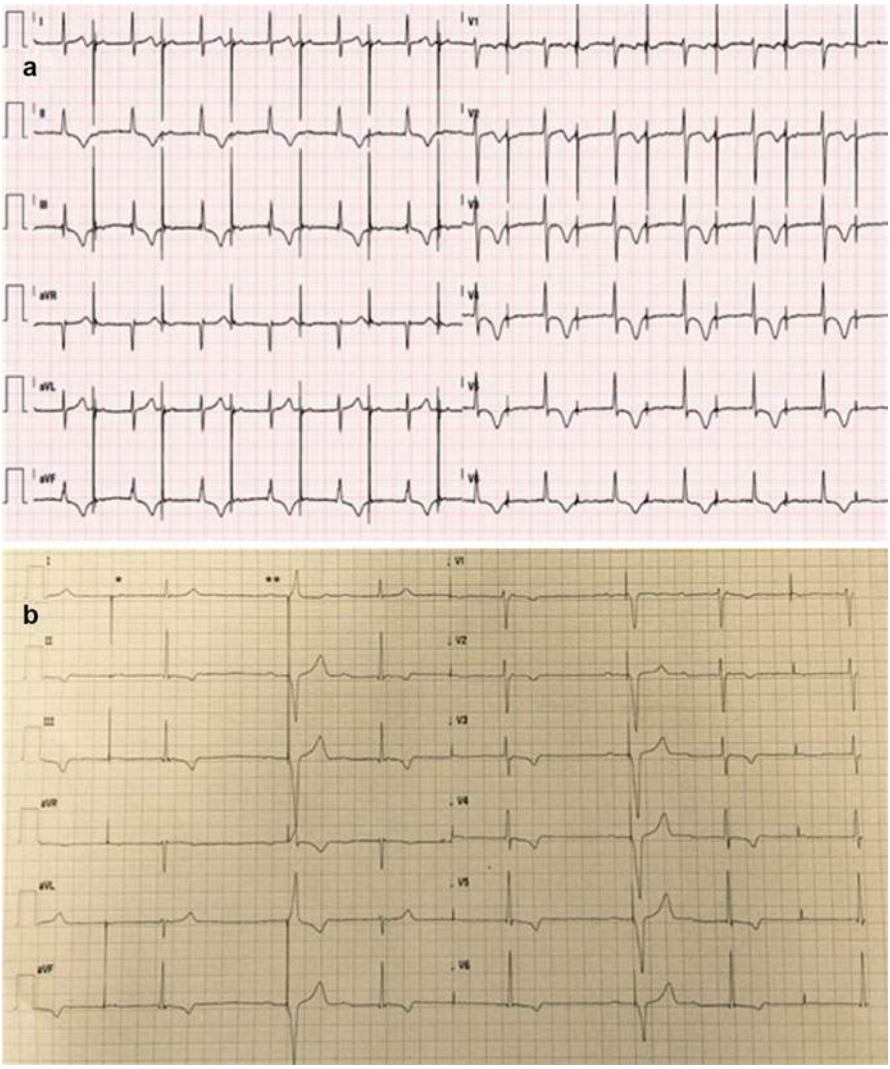

Fig. 11.5 Apparent malfunctions due to algorithm for reduction of ventricular pacing. (**a**) Atrial stimulation with spontaneous AV conduction with very long (440 ms) PQ interval. (**b**) Alternation of AAI (*) and DDD (**) mode, resulting in excessively low ventricular rate

11.5 What to Do in Case a Pacemaker Malfunction Is Suspected

If a PM malfunction is suspected, the patient must be immediately monitored and a complete standard 12-lead ECG obtained.

If artifacts of stimulation are not visible on ECG recording, a magnet must be applied on the device pocket. This will induce asynchronous pacing in both the

atrium and ventricle (VOO, DOO). If pacemaker stimuli become visible, it will be possible to evaluate if they capture the heart (paced P waves and QRS).

If the bradycardia is corrected by magnet application, oversensing is present and lead failure must be considered the most likely cause. The main differential diagnosis is with the presence of a connection defect, especially if the patient has recently undergone PM replacement.

If PM artifacts are visible but fail to capture, either constantly or intermittently even with magnet application, lead dislodgment, cardiac perforation, lead failure, high pacing thresholds, tissue ablation, and programmation errors are the possible causes of the exit block.

Device control by means of real-time telemetry is essential for the final diagnosis. Pacing impedance instant value and trends must be examined. High or low pacing impedances (>2000 or <250 Ω) are diagnostics of lead failure. As they can be intermittent, the temporal impedance trends must be obtained as well. The presence of even only one out-of-range value allows the diagnosis of lead failure. Pacing and sensing thresholds may be evaluated in real time and temporal trends examined.

Battery level is immediately displayed on programmer screen after interrogation, and a message of alert is displayed if battery level is low (ERI, EOS, EOL messages).

Chest X-ray must be obtained to check for connection defects or visible lead fracture, in particular in ICDs recipients. If cardiac perforation is suspected, an echocardiogram and CT scan are recommended.

If a malfunction of the generator is present, like battery exhaustion, PM replacement is necessary. Lead revision/replacement reposition is necessary in most of the other cases as discussed above.

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Management of the Electrical Storm in Patients with ICD

12

Daniele Muser, Domenico Facchin, Luca Rebellato, and Alessandro Proclemer

12.1 Focusing on the Issue

Current definition of electrical storm (ES) is the occurrence of three or more episodes of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) within 24 h requiring appropriate medical intervention. The same definition applies in implantable cardioverter-defibrillator (ICD) carriers in which ES is defined by three or more appropriate and separate (at least 5 min) device interventions in 24 h, either with antitachycardia pacing (ATP) or shock [1].

Current guidelines recommend ICD implantation for secondary prevention of sudden cardiac death (SCD) in survivors of cardiac arrest with no correctable causes and in patients with sustained symptomatic VT of different etiology. They also recommend ICD implantation for primary prevention in patients with ischemic or non-ischemic dilated cardiomyopathy and ejection fraction equal or lower than 35 % after at least 3 months of optimized medical therapy [2] and in other less frequent inherited arrhythmogenic syndromes.

Considering that approximately 1–2 % of the adult population in developed countries suffer from heart failure (HF) and that at least half of these patients have a low ejection fraction [3], the number of ICD carriers is wide spreading. Moreover, the improving therapies of HF ensure a long survival of patients making them older and affected by more comorbidities. For these reasons, ES is an increasingly

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frequent cause of access to emergency department (ED). It is estimated that about 25 % of ICD carriers experience at least one ES episode per year follow-up [4]. ES is definitely a medical emergency requiring a multidisciplinary approach.

12.2 What Physicians Working in ED and Anesthesiologists Should Know

12.2.1 How Is an ICD Made and How Does It Work?

The ICD is a subcutaneous implantable device able to monitor cardiac rhythm and terminate potentially life-threatening arrhythmias. It consists of two main components:

- The *generator* that contains the battery, all the circuits that run the device, and the operator communicating system. It is implanted in a subcutaneous pocket, usually under the left clavicle.
- The *leads* that reach heart chambers through the venous system and allow the device to either monitor heart electrical activity and deliver therapies. The ICDs have a lead implanted in the right ventricle apex able both to record ventricular activity and release therapies like pacing and/or direct current shock. In adjunct some ICDs have another lead implanted in the right atrium to record atrial electrical activity, improving discrimination between supraventricular arrhythmias (SVA) and ventricular ones and to pace the atrium (ICD-DR). ICDs with cardiac resynchronization therapy (CRT-D) have a third lead that paces the left ventricle, through the coronary venous system, synchronously to the right ventricle improving contractility. Some recent devices are implanted entirely subcutaneously, leads included (subcutaneous ICD), and can deliver high-energy shocks only (without long-term pacing capabilities) without a direct contact with the heart chambers and no leads inserted in the venous system.

ICDs use mathematical algorithms defined by the manufacturer to discriminate life-threatening ventricular arrhythmias from SVA and deliver appropriate therapy. Sometimes correct recognition fails, and in this case the therapy delivered is defined *inappropriate*. In other cases the delivered therapy may not be able to terminate the ventricular arrhythmia, and in this case it is called *ineffective*:

- The operator interfaces with the ICD through a programmer able to communicate with the device. Each manufacturer uses a different programmer, so it is imperative *to know the manufacturer and use the right equipment*. The programmer establishes an initial connection with the device through a head which must be positioned on the skin above the ICD. Usually green lights turn on to indicate the head is in the right place. At this point, depending on the features of the device, it may be necessary to maintain the head above the ICD throughout the query to allow communication, or, in some devices, the head can be removed since the communication continues via Wi-Fi.

The programmer allows the operator to visualize all the data stored in the device such as:

- *Arrhythmic events*: the device registers all arrhythmic events recognized as such on the basis of user-defined criteria. Each event provides endocavitary (or external for subcutaneous ICDs) electrocardiogram lead recording and therapies delivered.
- *Battery status*.
- Information about *lead integrity*.

On the basis of stored data, the operator may decide to change some settings such as:

- Arrhythmia recognition criteria (heart rate, time before treatment, algorithms for SVT recognition, etc.) and intervention criteria
- Type and characteristics of therapies delivered

12.2.2 How Does the ICD Recognize and Treat Arrhythmias (Appropriate Therapies)?

VT recognition is primarily based upon tachycardia cycle length (to distinguish from normal sinus rhythm) and duration (to detect non-sustained episodes). Both of these parameters are tailored on the patient's characteristics. Thus, ICD uses ventricular rate zones for rhythm classification. The boundaries between zones are defined by two main principles:

- The recognition of unstable fast VT/VF must be highly sensitive even at the cost of inappropriate rapid SVA treatment.
- The recognition of slower VT (generally better tolerated) has to be more specific to avoid inappropriate therapies even at the cost of some delay in detection.

The ICDs treat ventricular tachyarrhythmias by:

- *Antitachycardia pacing* (*ATP*): it is a brief ventricular pacing (6–8 beats) with a cycle length slightly lower (thus at a faster rate) of the arrhythmia (usually 81–88 %), in the attempt of resetting the reentrant circuit and interrupting the arrhythmia. Sometimes the paced cycle shortens from beat to beat, and in this case it is referred as ATP ramp.
- *Direct current shock* (*DC shock*): it is a biphasic electrical shock provided between the generator case and the coil localized on the right ventricular lead. The energy released may vary, reaching up to 40 J with the latest generation high-energy devices.

Basing on several studies [5–7], ICD programming should empirically involve the use of three rate zones:

- A slow VT zone up to 320 ms cycle length (<188 bpm)
- A fast VT zone from 320 to 240 ms (188–250 bpm)
- A VF zone from 240 ms (>250 bpm)

In both VT zones, a variable number of ATP attempts precede shocks delivery. In the slow VT zone, a greater number than in fast VT zone are usually programmed (e.g., 3 ATPs followed by 3 ATP ramps), as fast arrhythmias are usually less tolerated.

In the VF zone, the hemodynamic instability of the arrhythmia and its high life-threatening potential require an immediate shock delivery (usually at the maximum energy from the beginning). In modern devices an ATP during capacitor charging (usually requiring less than 10 s) is delivered, avoiding the shock in the case of arrhythmic interruption.

VT/VF detection not only is based upon ventricular rate but also requires a programmable duration of the arrhythmia to avoid detection of non-sustained episodes. Usually a VT/VF is detected when a certain percentage of ventricular sensed beats meets cycle length criteria. The type of counting used varies between detection zones and among manufacturers. In order to improve sensibility, according to some manufacturers, the arrhythmia is detected when a certain percentage of beats (not necessarily consecutive) falls in VF zone, while consecutive interval counting is required in the VT zone, increasing specificity. The time to detection in the VT zone should be longer enough to allow spontaneous termination of non-sustained episodes [6, 8].

12.2.3 Inappropriate Therapies

Inappropriate therapies (especially shocks) are one of the main issues to be avoided as they cause patient discomfort, are potentially proarrhythmic, and reduce battery life.

The two main causes of inappropriate shock are failure in discriminating SVA and signal misinterpretation.

Frequently SVA is associated with a fast ventricular response leading ventricular rate to fall into VT/VF detection zone causing inappropriate therapy release. This problem occurs more frequently with single-chamber ICDs that do not have atrial sensing capabilities. Dual-chamber devices can compare atrial and ventricular rates to set the origin of the. ICDs use a variety of algorithms to discriminate SVA from VT; major ones are listed below:

- *Atrioventricular rate comparison*: applies only in dual-chamber ICDs; when the ventricular rate is faster, the diagnosis is VT. When atrial and ventricular rates are equal, additional criteria are required for discrimination.
- *Onset*: useful for discrimination of gradually accelerating sinus tachycardia from sudden-onset VT. It applies when the RR interval shortens by a programmed percentage if compared with the average number of preceding beats. May fail in case of VT occurring during sinus tachycardia.
- *Stability*: useful for discrimination of fast response AF. It evaluates RR variability; when greater than a programmed percentage (e.g., 20 %), AF is supposed. It may fail in the case of very fast AF in which there is a pseudo-regularization of ventricular rate, in atrial flutter or in irregular VT.

- *Morphology*: it compares endocavitary electrocardiograms recorded during sinus rhythm and during VT. It is useful in single-chamber ICDs lacking of atrial information but may fail in intraventricular conduction delays and in rate-dependent conduction delays.
- *Rate duration*: it is an extreme lifesaving measure. It results in shock delivery after a programmable time interval even if the episode is classified as SVA; this algorithm is usually activated when there is a high risk of undertreatment of VT erroneously recognized as SVA, but it increases the risk of overtreatment.

Signal misinterpretation is the other big deal leading to inappropriate shocks. It may depend on some programmed variables; easily editable, external, and far-field interferences; or device/lead failure that usually requires an interventional approach. Main causes of signal misinterpretation are listed below:

- *T wave oversensing*: it happens when a high amplitude T wave is erroneously recognized as an R wave. It may happen because of the low ventricular sensing threshold necessary to recognize even low-amplitude VF. This problem can be solved by increasing sensing threshold, lengthening refractory period, or changing sensing decay parameters to suppress T wave detection.
- *Electromagnetic external interference*: external electromagnetic fields can be mistaken for intracardiac signals resulting in inappropriate arrhythmic detection and therapy. Common household appliances are not generally a problem, but some high-intensity fields such as high-voltage power lines, electric motors, magnetic resonance imaging, TENS units, electrocautery during surgery, neurostimulators, and radiotherapy should be avoided.
- *Myopotentials*: far-field myopotential recording may lead to inappropriate arrhythmic detection. This problem occurred in the past with unipolar leads using large sensing fields (from the lead tip to the generator case) and is now largely avoided with the modern bipolar leads, recording more localized signals only.
- *Lead failure*: lead fracture or insulation loss of continuity may cause external noise recording and inappropriate detection. In these cases lead extraction and/or new lead insertion is the only choice. Modern devices usually provide alerts for lead integrity.

12.2.4 Electrical Storm

12.2.4.1 Incidence and Clinical Predictors

Several studies examined the incidence of ES in ICD recipients, although ES definition was not standardized and the inclusion criteria and follow-up period were not homogeneous. Considering current definition, the incidence varies from 4 to 28 % in a follow-up period between 1 and 3 years [9]. In the sub-analysis of the AVID trial [10], including 499 patients treated for secondary prevention, the rate

of ES was 20 % at 3-year follow-up. Of note, the incidence of ES in primary prevention trials appears lower (4 % in MADIT II), and in our experience [11], after a mean 2-year follow-up, only 13 patients (2 %) experienced an ICD treatment configuring an ES.

A recent meta-analysis [9] evaluated the real weight of ES as a risk factor and its clinical predictors. On the basis of 13 studies, a trend toward an increased prevalence of ES was associated with advanced age and male gender. Other factors related to ES in ICD carriers were heart failure-related clinical variables (as lower ejection fraction), an ICD implant for secondary prevention, the presence of monomorphic VT as triggering arrhythmias instead of polymorphic VTs and VF, and the treatment with class I antiarrhythmic drugs but not with amiodarone and beta-blockers. On the contrary, no significant differences between patients with ischemic or nonischemic dilated cardiomyopathy were reported. After meta-regression analysis, no significant interaction between any of the examined clinical variables and the increased risk of ES was confirmed.

The main clinical characteristics and clinical predictors of ES in the group of patients treated with a CRT-D have been considered in a multicenter experience including 631 patients, with a mean follow-up of 19 ± 11 months. In this study VT or VF episodes were detected and treated in 141 patients (22 %), and ES occurred in 45 (7 %). At univariate analysis, the only predictors of ES were the nonischemic etiology of cardiomyopathy and secondary prevention indication, while other common variables such as age, male gender, ejection fraction lower than 25 %, and advanced NYHA class did not correlate.

Our experience included 62 patients (mean age 66 years, 90 % male) admitted for ES during the period 2006–2012. The mean interval from implant to ES was 47 months. Ischemic heart disease was present in 30, nonischemic cardiomyopathy in 11, and other etiologies in 14, and 60 % of patients had been treated with ICD for secondary prevention. Mean ejection fraction was 35 %. In 23 patients the arrhythmia at admittance was incessant VT, while the remaining 39 experienced several VT/VF episodes, with a mean number of 6 shocks per patient. In more than half of patients (31), there wasn't a clear trigger and the ES rises from a primitive electrical instability. In the remaining the most frequent triggers were worsening heart failure, electrolyte imbalances, myocardial ischemia, and proarrhythmic drug side effects.

12.2.4.2 Prognosis

The majority of papers evaluating the role of ES as a mortality risk factor showed that it was associated with a threefold risk of death. ES maintained a significant value as risk factor even when compared with unclustered sustained VT/VF [9]. For the composite end point of all cause mortality, heart transplantation and hospitalization for heart failure ES was associated with a 3.39-fold increased risk.

The reported mortality among large series [12] of patients with ES treated by catheter ablation appeared extremely variable between 15 and 29 % during a follow-up ranging from 1 to 2.5 years. In our series, including patients treated not exclusively by catheter ablation, the overall survival of patients experiencing their first ES episode was 60 %, 50 %, and 44 % after 1, 2, and 3 years, respectively.

Considering that ES is associated with increased SCD and non-sudden cardiac mortality, Guerra et al. evaluated the association between ES and heart failure in patients with chronic heart failure and ICD. They reported that during 5-year follow-up, the survival estimates were not significantly different between patients with ES and HF worsening (36.4 vs. 38.5 months), while it was significantly lower in comparison to survival of patients with unclustered VT/VF episodes (49.2 months). The primary mortality cause in ES group was refractory heart failure (59 %), followed by noncardiac conditions and by SCD in only two patients. Even hospitalization-free rate was lower in both ES and HF worsening groups in comparison to patients with unclustered VT/VF episodes (15.4 vs. 20.1 vs. 36.1 months), while the hospitalization rates were not significantly different between ES and HF worsening groups. The conclusions of the authors were that heart failure patients admitted for ES show important outcome analogies with patients admitted for acute heart failure and that ES should be identified as an important clinical consequence of heart failure decompensation.

12.3 What the Cardiologist Should Know

ES is a medical emergency potentially leading to acute cardiac failure and cardiogenic shock and requiring a multidisciplinary approach.

Initial diagnostic workup includes physical examination, electrocardiogram (ECG), chest X-ray, echocardiogram, blood gas analysis, electrolytes, serum creatinine evaluation, and ICD interrogation.

The first issue to assess in a patient with multiple ICD shocks is to seek ICD intervention causes.

In case of appropriate therapies due to VT/VF, it is necessary first of all to rule out reversible causes of ES including electrolyte imbalances, acute ischemia, worsening heart failure, infective state, hyperthyroidism, and proarrhythmic drugs. In a large series reversible causes of ES account for no more than 10 % of cases referred to EP labs [4].

Following initial evaluation, an accurate patient's risk stratification should be made according to hemodynamic tolerance of the clinical VT and comorbidities [13]. Hemodynamic decompensation defined as sustained hypotension (i.e., systolic blood pressure <80–90 mmHg) despite increasing doses of vasopressors and requiring mechanical hemodynamic support (i.e., intra-aortic balloon pump, left ventricular assist devices, or extracorporeal membrane oxygenation) [14] makes the patient at high risk by itself and in some cases even at the temporary restoration of sinus rhythm. In case of hemodynamically tolerated VT, the presence of at least one comorbidity such as left ventricular ejection fraction less than 30 %, serum creatinine level >1.5 mg/dl, chronic occlusion of left anterior descending coronary artery, and severe chronic lung disease makes the patient particularly high risk [13]. All high-risk patients should be admitted to intensive care unit (ICU) and, if necessary, undergo circulatory and/or ventilatory support and/or hemodialysis.

All the efforts should be made to reduce VT/VF episodes to avoid further shocks considering even in combination of a complex strategic approach including antiarrhythmic drug therapy, device reprogramming, deep sedation/mechanical assistance, and catheter ablation.

12.3.1 Antiarrhythmic Drugs

Initial treatment of ES usually involves the use of antiarrhythmic drugs, weighing their proarrhythmic risk and negative inotropic effect, to prevent arrhythmic recurrences.

The cornerstone of antiarrhythmic therapy still remains sympathetic blockade with *beta-blockers* to suppress the adrenergic drive to VT recurrence [15]. Although all beta-blockers are able to reduce susceptibility to VT/VF as class action, most of the studies analyzed *propranolol*. In patients with HF, propranolol resulted to be more effective than *metoprolol* in reducing sympathetic tone due to its capability of blocking both β1 and β2 receptors and to its lipophilic nature that enables penetration within the central nervous system blocking also presynaptic adrenergic receptors [16, 17]. Sympathetic blockade is able not only to suppress ES [18] but also to improve short-term survival more than the combined antiarrhythmic therapy with lidocaine, procainamide, and bretylium [15]. In severely compromised patients, intravenous short-acting drugs like *esmolol* should be preferred [19]. The first-choice antiarrhythmic drug should be *amiodarone*, even in combination with propranolol that effectively controlled ES and improved survival [15, 18]. When amiodarone is administered intravenously, it reduces adrenergic tone, blocks sodium and L-calcium channels without prolonging ventricular refractoriness, and, when administered, orally prolongs ventricular refractory period [20, 21]. When ineffective alone or in combination with beta-blockers, amiodarone may be helpful even in adjunct to other agents [22]. Even patients who previously keep amiodarone may beneficiate from a reloading dose/therapy adjustment if serum levels of amiodarone/desethil-amiodarone are under therapeutic levels. The acute administration is relatively safe even in patients with depressed ejection fraction due to its low inotropic negative effect. It can increase the defibrillation threshold, making potentially ineffective ICD therapy; consequently ICD defibrillation energy should be re-tested or re-evaluated. Long-term amiodarone assumption is burdened by several side effects like thyroid, liver, and lung toxicity, sometimes forcing to therapy discontinuation. In case of amiodarone failure, other additionally drugs may be considered such as procainamide both orally or intravenously. The use of multiple antiarrhythmic drugs makes the drug-to-drug interaction unpredictable, potentially increasing the side effect occurrence. The use of *lidocaine* is limited by its relatively incapacity to terminate scar-related VT [23]. Lidocaine is a sodium rapid channel blocker that binds to channels in a use-dependent way. During ischemic VT, the altered membrane potential as the pH reduction [24] increases the rate of drug binding, making lidocaine effective in terminating arrhythmias. The pharmacodynamic proprieties

make lidocaine not so effective in settings different from ischemic arrhythmias, maintaining a role only for the treatment of polymorphic VT associated with ischemia (IIb recommendation according to the American College of Cardiology/American Heart Association guidelines [25]).

Procainamide (not available in all countries) is another IC class antiarrhythmic drug commonly used as second- or third- line therapy in refractory VTs. Procainamide acts as fast sodium channel blocker, while its active metabolite N-acetylprocainamide blocks potassium channels and accounts for much of the antiarrhythmic effect in vivo as well as side effects like QT interval prolongation. Care must be taken in administering the drug in patients with low ejection fraction due to the high risk of hypotension.

12.3.2 Device Reprogramming

Several studies demonstrated that repeated ICD shocks are associated with increased mortality as well as with a reduction of quality of life [10]. For these reasons optimization of ICD programming in order to avoid unnecessary shock is mandatory in patients experiencing ES. As stated above, arrhythmic detection and treatment by ICD is a step process including several variables such as heart rate threshold, number of intervals to detect, discrimination of SVA, and type and number of therapies released. Each of these steps can be tailored upon patient characteristics to avoid unnecessary treatment.

12.3.2.1 Higher Heart Rate Threshold

Usually patients treated with ICD for primary prevention tend to develop fast VT, while patients treated for secondary prevention usually have slower VT with a wider overlap with SVA [26]. On this basis, the first may benefit from higher rate detection zones, while the latter needs slower rate detection zones and improved SVA discriminating algorithms. Even better, rate detection zones can be tailored upon patient's clinical history when previous arrhythmia episodes occurred. In three trials (PREPARE, MADIT-RIT, and PROVIDE), higher rate detection zones demonstrated reduce ICD shocks without increasing both syncope and death risk.

12.3.2.2 Longer Detection Period

The effect of prolonging arrhythmic detection time is well studied especially in the primary prevention setting with lower data available in the setting of secondary prevention.

The REVELANT study showed that a higher number of intervals for arrhythmic detection (30/40 vs. 12/16) significantly reduced the incidence of ICD intervention without increasing syncope or death in patients with ICD for primary prevention and nonischemic cardiomyopathy. MADIT-RIT trial showed a reduction of both inappropriate therapy and all-cause mortality with a 60-s delay at 170–199 bpm, a

12-s delay at 200–249 bpm, and a 2.5-s delay at ≥250 bpm vs. conventional programming. These results were recently confirmed by ADVANCE III trial [27] in which the combination of a higher number of intervals to detection (30/40 vs. 18/24) with ATP therapy during charge significantly reduced either appropriate or inappropriate therapies regardless of ICD type and indication. Even in the PROVIDE trial, multi-parametric programming including higher detection rate, longer detection intervals, and optimized SVA discriminating algorithms was associated with better overall survival and reduction of ICD shocks without increasing arrhythmic syncope risk, and the PainFree SST trial confirmed that longer detection intervals are safe in terms of risk of syncope. Of all these studies, only ADVANCE III and the PainFree SST included patients with both primary and secondary preventions for ICD, while the remaining trials focused only on patients treated for primary prevention.

12.3.2.3 Improving ATP Programming

ATP therapy demonstrated to be highly effective in terminating VTs, reducing unnecessary shocks and consequently improving survival, quality of life, and generator life. In several studies 85–90 % of "slow" VTs (<188–200 bpm) [28] and 54–72 % of "fast" VTs (188–250 bpm) [29, 27] were terminated by ATP. As stated before, ATP therapy can be administered as *bursts or ramps* on the basis of the pacing cycle length variations. Bursts and ramps proved similar efficacy in treating slower VTs [28], while fast VTs (>200 bpm) were best treated by bursts that also showed a lower risk of arrhythmic acceleration than ramps. Due to less efficacy of ATP in terminating fast VTs (>200 bpm) and the negative hemodynamic consequences of such arrhythmias, usually in the fast VT and VF zone, *ATP is delivered during capacitor charge* to avoid any delay in shock therapy. The majority of VTs were effectively interrupted by one or two ATP attempts with only a minority of patients responsive to more than three attempts [30, 31], and for this reason programming more than three ATP attempts should be discouraged. In CRT-D recipients, biventricular ATP should be preferred to right ventricular ATP due to its higher efficacy and safety [32, 33]. The last key point in ATP programming is burst cycle length that can be empirically programmed at 85–90 % of the arrhythmic cycle length for fast VTs and at 70–80 % for slower ones. When ATP appears ineffective in VT termination, the analysis of the post pacing interval can allow tailoring ATP programming upon patient characteristics, for example, by shortening drive cycle length or by increasing the number of paced beats [34].

Accordingly to all these data, the increase of detection time and threshold rate in patients experiencing ES helps to prevent both inappropriate and unnecessary shocks, making ICD reprogramming a mandatory step in the clinical workup of ES.

In case of inappropriate therapies, specific measures must be taken: e.g., change ICD detection parameters, enhance drug therapy, or consider catheter ablation in case of SVA; temporarily turn off the device before lead replacement in case of lead fracture/failure.

12.3.3 Sedation, General Anesthesia/Mechanical Ventilation, and Mechanical Hemodynamic Support

The sympathetic adrenergic activation in patients experiencing multiple shocks due to ES may perpetuate VT/VF [35] and render the arrhythmias life threatening and refractory to several maneuvers. Therefore, some patients with ES should be sedated or even undergo general anesthesia to reduce sympathetic tone and suppress ventricular electrical instability. *Propofol* has been reported to suppress ES [36, 37], but this beneficial effect may be offset by the inotropic negative effect. In this regard, only few data are available in literature about the effect of deep sedation/general anesthesia on the prognosis of ES patients, and most of them are extrapolated from patients undergoing catheter ablation to treat ES. Drugs inducing general anesthesia should be considered with attention because they can exacerbate hypotension and depress cardiac function [14]. Deep sedation with *remifentanil* even in association with a *benzodiazepine* like midazolam should be preferred as it is able to reduce sympathetic hypertone and provide analgesia avoiding dangerous negative inotropic effects [38–40]. A valuable alternative may be *dexmedetomidine* [41], an α2 presynaptic adrenergic receptor agonist able to markedly reduce sympathetic tone by both enhancing central vagal tone [42] and inhibiting presynaptical adrenaline release [43]. However, it has important side effects like hypotension and bradycardia [44] that should be rigorously monitored during its usage.

General anesthesia and mechanical ventilation should be reserved only to patients with hemodynamically non-tolerated arrhythmias refractory to all therapies. Such patients may benefit from hemodynamic mechanical support like *intra-aortic-balloon pump* (IABP), *left ventricular assistance devices* such as the Impella (Abiomed Inc., Danvers, MA) [45–47], and even *extracorporeal membrane oxygenation* (ECMO) [48, 49]. These devices can not only suppress ischemic VTs by increasing coronary perfusion but can be effective in suppressing ES reducing LV afterload and wall tension [50] as well as prevent multiple organ failure sustaining organ perfusion. Last but not least, they have a key role in mapping and ablating unstable VTs. Some patients experiencing refractory unstable arrhythmias should also be carefully evaluated for urgent check for cardiac transplantation.

12.3.4 Neuraxial Modulation (Thoracic Epidural Anesthesia, Cardiac Sympathetic Denervation)

Given the importance of the autonomic nervous system in triggering and maintaining ventricular arrhythmias, sympathetic neuromodulation through thoracic epidural anesthesia [51], cardiac sympathetic denervation (CSD), and spinal cord stimulation may help in reducing arrhythmic burden in selected patient with ES refractory to multiple antiarrhythmic drugs and catheter ablation. CSD is usually performed via video-assisted thoracic surgery and consists of removal

the lower third of the stellate ganglia (to avoid Claude-Bernard-Horner syndrome) as well as T2–T4 thoracic ganglia. The resection is usually performed on the left side, reserving bilateral CSD for selected cases. The procedure should be performed in referral centers only, due to special anesthesiology skills required such as selective bronchus intubation management. Most of what we know about the results of the procedure results from case reports [52, 51, 53], but in a prospective study of 41 patients with ES refractory to medical therapy and catheter ablation, CDS demonstrated to be effective in prolonging ICD shock-free survival at 1-year follow-up with greater effect of bilateral CDS compared to left CDS only [54].

12.3.5 Catheter Ablation

Currently, radiofrequency catheter (RF) ablation represents the mainstay treatment of recurrent VTs and even of ES. Several studies demonstrated how catheter ablation may prevent VT recurrence as well as improve survival of ES patients with a growing effectiveness due to technological improvement and deeper knowledge of arrhythmogenic substrate [14]. In the past, RF ablation was considered as the last chance treatment in patients refractory to multiple antiarrhythmic drugs, but in the last decade there has been a growing evidence for early referral to RF ablation in case of recurrent ICD therapies or even prophylactically [55–57]. RF ablation showed to be highly effective in suppressing refractory VTs in the acute management of ES, reaching an acute success rate of 80 % in the largest series [40, 12, 58, 59], especially when the end point of non-inducibility of all clinical VTs was reached [12]. As stated before, patients with unstable hemodynamic VTs should be referred for mechanical assistance in order to allow mapping and ablation but also those with apparently stable arrhythmia may develop acute hemodynamic decompensation during RF ablation procedure. In a preliminary study, a simple score named PAINESD taking in account patient's baseline comorbidities (Pulmonary chronic obstructive disease, Age older than 60, Ischemic cardiomyopathy, NYHA class III or IV, Ejection fraction lower than 25 %, Storm at presentation, and Diabetes mellitus) was tested to predict acute decompensation during VT catheter ablation in order to select patients who may benefit prophylactic mechanical support [14] (Fig. 12.1).

12.4 Indication for Follow-Up and Referral

All patients who experienced an ES episode remain at high risk of recurrences even if effectively treated with catheter ablation and multiple antiarrhythmic drug prophylaxis. Often ES is the expression of worsening of the underling heart disease. For these reasons all patients who developed at least one episode of ES

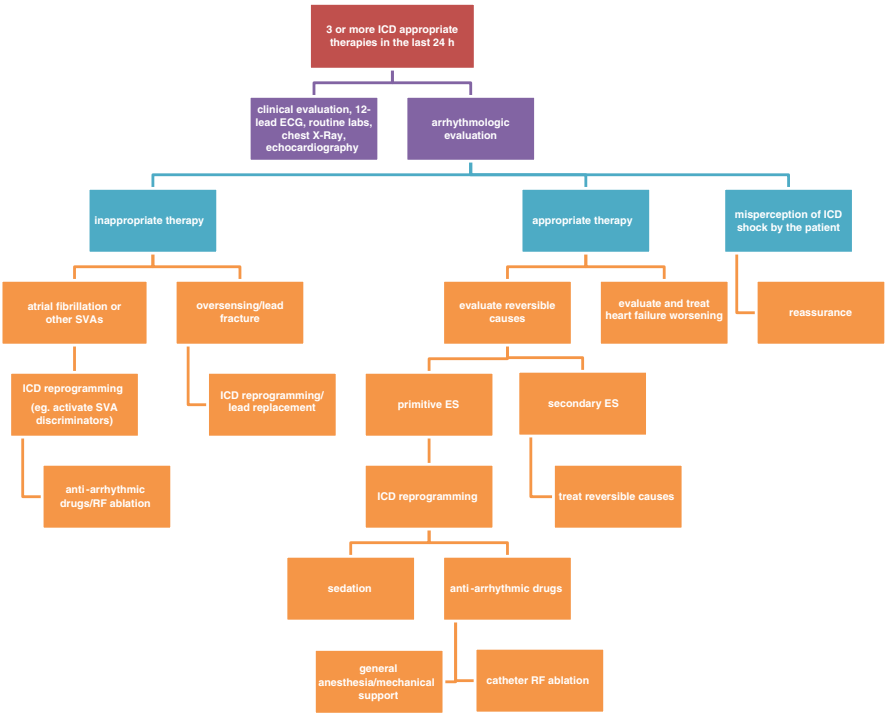

Fig. 12.1 A suggested algorithm/pathway for diagnosis and treatment of ES

should be referred both to a heart failure specialist and proper electrophysiological management in order to optimize the heart failure therapy and evaluate indication to heart transplantation or left ventricular assistance devices both as a bridge to transplant and as destination therapy. Arrhythmic follow-up may be best done with home monitoring of the ICD that allows a prompt evaluation of arrhythmic events.

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Emergency Surgery and Cardiac Devices

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13.1 Focusing on the Issue

The number of patients with CIED (Cardiac Implantable Electric Devices) who need emergency surgery has been increasing in the last decades, considering the spread of ICD (Implantable Cardiovetrer-Defibrillator) and CRT (Cardiac Resynchronization Therapy) implantations for sudden death prevention and heart failure treatment.

It is estimated that about three million patients worldwide have a pacemaker (PM) and about 500,000 patients have an ICD [1]. According to EUCOMED data, in Europe nearly 1000 PM and 170 ICD new implantations were performed every million inhabitants in 2012. Although the implant rate of PMs has not significantly changed, there has been an increase of ICD and CRT implantations in the last decade, after the publication of several trials proving their efficacy. Despite some regional differences, this trend can be observed in most western countries.

In case of urgent surgical intervention, patients with CIED (especially ICD) can be considered at high risk for many reasons, mostly due to the underlying cardiac disease, hemodynamic impairment/left ventricular dysfunction (in particular those with ICDs), and the advanced age (in particular those with PMs) [2].

In addition, during surgical interventions, transient or even permanent malfunctions of the device, because of electromagnetic interferences or mechanical damages, are possible [3].

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Electromagnetic fields can potentially cause several malfunctions: damage to the CIED circuitry, pacemaker inhibition, noise tracking, asynchronous pacing, communication failure, etc. [4].

An electromagnetic field is characterized by a wavelength, a frequency, and a field strength. The range of frequency emitted by sources such as magnetic resonance imaging (MRI) and electrosurgery is between 0 Hz and 450 MHz. The electric field strength is measured in volts per meter, while the magnetic field intensity components of electromagnetic fields are measured in amperes per meter. Electromagnetic field energy decreases as an inverse squared function of distance from the source, so the risk of exposure is fourfold lower just doubling the distance from the source.

Even static magnetic fields can be a possible cause of CIED malfunction; sterile magnetic drapes, frequently used during surgery to hold metal instruments, can potentially interfere with the function of PM and ICDs if positioned at a distance less than 15 cm [5].

Electrocautery is associated with tissue heating. However, conductive devices and leads, particularly when placed in a loop configuration, can increase the risk of burns due to the inductive heating of the lead conductor from radiofrequency fields.

In recent years, a great effort to minimize CIED has been performed. Generators are shielded by hermetically sealed titanium or stainless steel cases. The extent of shielding varies depending on the manufacturer, weight of the device, and dimensions and usually rejects electric fields >2 MHz.

EMI are also reduced by the use of bipolar sensing and low-pass filters. However, frequencies between 0 and 60 Hz overlaps the cardiac signal range so a "noise reversion feature" is activated when signals are detected in the noise-sampling period of the atrial and ventricular refractory periods, programming the device in asynchronous pacing.

Additionally, lead design was modified to improve shielding from radiofrequency and time-varying gradient magnetic fields.

13.2 What Physicians Working in ED, Anesthesiologists, and Surgeons Should Know

The PM is a pulse generator, generally placed in the left (less frequently right) subclavian region, usually subcutaneously or under the pectoral muscle. It is connected with the heart across the cephalic, axillary, or subclavian vein by one or two leads reaching the right ventricle, the right atrium, or both; in patients with cardiac resynchronization therapy (CRT), another lead is positioned in a branch of the coronary sinus for left ventricular pacing. Depending on the needs of an individual patient and model of the PM, programming and pacing function will differ from one device to another.

The ICDs differ from PMs for their antitachycardia properties, as they can recognize and automatically interrupt (by overdrive pacing or high-voltage DC shock) potentially fatal arrhythmias, as sustained ventricular tachycardias or ventricular fibrillation, the leading causes of sudden death. In patients with left ventricular dysfunction of any origin, as well as in those with other cardiac conditions at high risk of sudden death, treatment with ICD is associated with an improved survival even in

Table 13.1 NASPE code for pacing modalities

I	II	III	IV	V
Chamber (s) paced	Chamber (s) sensed	Response to sensing	Rate modulation	Multisite pacing
O → none A → atrium V → ventricle D → dual (A + V)	O → none A → atrium V → ventricle D → dual (A + V)	O → none T → triggered I → inhibited D → dual (A + V)	O → none R → rate modulation	O → none A → atrium V → ventricle D → dual (A + V)
S → single (A or V)	S → single (A or V)			

the absence of previous history of ventricular arrhythmias. With the exception of some newly released entirely subcutaneous ICD, without intravascular leads (s-ICD), all ICDs have PM properties. In addition, it is possible to program the minimum rate and duration of arrhythmias required to be recognized and treated, to avoid unnecessary therapies in the case of slow and/or brief self-terminating tachycardias.

13.2.1 PM Programming Modes

Pacing modalities are expressed according to the North American Society of Pacing and Electrophysiology/British Pacing and Electrophysiology Group (NASPE/BPEG) revised code (see Table 13.1) [6]. The first letter indicates the chamber in which pacing occurs, while the second indicates the chamber with sensing capabilities. The third letter indicates the effect of sensing on the triggering or inhibition of subsequent pacing stimuli. The fourth and the fifth letter, not always used in clinical practice, respectively indicate the presence (R) or absence (O) of an adaptive-rate mechanism and whether multisite pacing (as in CRT) is present.

13.2.2 Unipolar Versus Bipolar Leads

Artifacts during electrocauterization can be erroneously considered by the CIED as spontaneous fast electrical activity of the heart (oversensing) [7]. Nearly all leads implanted in the last decade are bipolar, meaning that both the cathode and the anode are on the tip of the catheter, reducing the inter-electrode distance and the likelihood of external interferences. However, in some patients, especially with less recent implantations, unipolar leads can still be present. In these patients, the risk of oversensing is particularly high, as the sensed field is included between the tip of the lead (functioning as a cathode) and the generator (anode).

13.2.3 Unipolar Versus Bipolar Electrocautery

Electrosurgery current usually occurs in the frequency range between 100 and 5000 kHz and is typically delivered in a unipolar configuration between the

cauterizing instrument and ground electrode. Bipolar electrosurgery involves the use of an electrical forceps where each limb is an electrode; it is used far less commonly because it is useful only for coagulation and not dissection. Bipolar systems deliver the current between two electrodes at the tip of the instrument, reducing the likelihood for EMI with CIEDs. Therefore, malfunctions are associated with unipolar electrocautery only, while bipolar electrosurgery does not cause EMI when not directly applied to CIED.

EMI usually occur when electrosurgery is performed within 8–15 cm from the device. Electrosurgery below the umbilicus with the grounding pad placed on the thigh is therefore unlikely to result in EMI with thoracic CIEDs.

EMI are more likely with the cutting mode rather than with the coagulation mode of surgical electrocautery, probably because of the higher power and the longer period of time applied for tissue cutting than coagulating a bleeding vessel.

The use of a harmonic scalpel, an ultrasonic cutting and coagulating instrument, can avoid surgical diathermy, according to some data [8].

13.2.4 Effects of EMI on CIED: General Considerations

Depending on the type of devices and lead, the programming of the devices and the type of surgery, different malfunctions can be found.

The possible effects of EMI can be transient (due to oversensing) or permanent (initiation of noise reversion, electrical reset mode, or increase of pacing thresholds).

Permanent damages are extremely rare, unless the energy is applied directly to the pulse generator or system electrode. There are some old reports of various serious effects, such as failure to pace, system malfunction, and even inappropriate life-threatening uncontrolled pacing activity [3]. However, because of the advances in lead and generator technology, most recent reports suggest that nowadays these effects infrequently occur.

13.2.4.1 Reset

Resetting of PMs has been reported in presence of energy coursing through the pulse generator (i.e., when the electrocautery touches, or is very close to, the generator) and simulates the initial connection of the power source at the time of manufacture. During reset, pacing parameters are automatically programmed in VVI mode with a lower rate from 60 to 70/min (depending on the manufacturer) and high output energy. For ICD, beside a VVI 60–70/min pacing mode, a fixed antitachycardia therapy (with lower rate cutoff ranging from 146 to 190/min according to the manufacturer) is programmed.

13.2.4.2 Generator Damages

The application of electrosurgery either in immediate close proximity or directly to the pulse generator can cause failure or permanent damage to a CIED, especially to older pacemakers (with voltage-controlled oscillators, no longer manufactured).

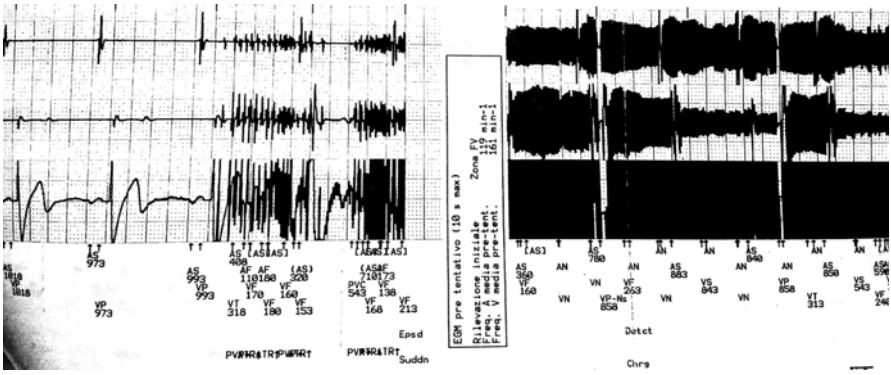

Fig. 13.1 Ventricular oversensing during thoracic surgery leading to ICD charge

ICDs may be more resistant, but energy can still enter the pulse generator in presence of breaches of lead insulation.

13.2.4.3 Lead-Tissue Interface Damage

Damage to the lead-myocardial interface is unlikely to occur with modern devices, but monopolar electrosurgery pathways crossing a pulse generator can produce enough voltage to create a unipolar current from the pulse generator case to a pacing electrode in contact with myocardium. This can result in a localized tissue damage with an increase in pacing threshold and possible loss of capture [9].

13.2.4.4 Oversensing

The most frequent CIED interaction with EMI is oversensing, leading inappropriate inhibition of pacing output and false detection of a tachyarrhythmia, with possible inappropriate CIED therapy (Fig. 13.1).

Electrosurgery applied below the umbilicus is much less likely to cause PM or ICD interference than when applied above the umbilicus. However, endoscopic gastrointestinal procedures that use electrosurgery may result in interference (Fig. 13.2). In a recent analysis on 71 subjects with ICD, EMI were recorded in 50 % of thoracic and head or neck procedures, 22 % of upper extremity procedures, 7 % of abdominal/pelvic procedures (laparoscopic cholecystectomies only), and 0 % of lower extremity procedures. No EMI in any lower abdominal procedures were recorded [10].

13.2.4.5 Pacemaker Response to EMI

When programmed in inhibited pacing modes (AAI, VVI, or DDI), pacing inhibition can occur in presence of EMI, with consequent bradycardia or asystole in PM-dependent patients. When programmed in tracking mode (DDD), sensing of EMI in the atrial channel (more likely to occur, because of the higher sensitivity necessary to detect atrial signals) could result in increased rate of ventricular pacing or false atrial arrhythmia detection and consequent "mode-switch" to inhibited pacing modes (VDI, VVI, or DDI).

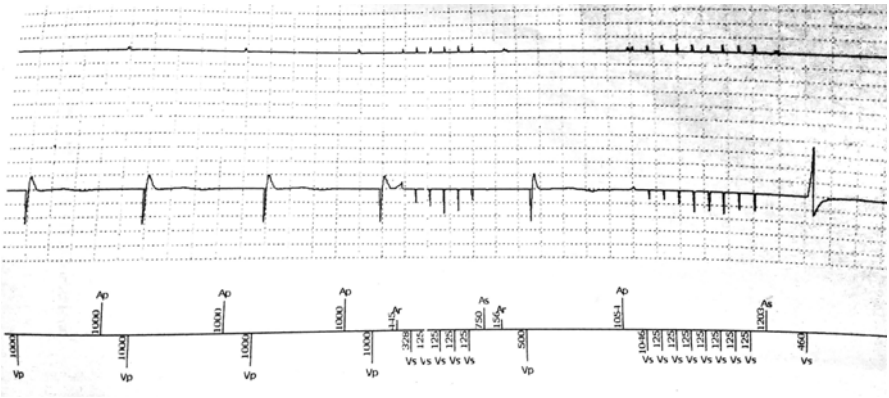

Fig. 13.2 EMI during polypectomy

For a patient with spontaneous underlying rhythm, pacing inhibition does not have any consequences, while in PM-dependent patients, a prolonged (>4–5 s) pacing inhibition can result in significant hemodynamic compromise. Therefore, *limiting electrosurgery usage to shorter bursts* is desirable and may be a safer approach than either reprogramming the CIED or placement of a magnet over the pulse generator [3].

In patients with cardiac resynchronization therapy (CRT), ventricular stimulation is, or should be, always present at surface ECG; however, these patients are not usually pacemaker dependent, so will not experience hemodynamic difficulties if biventricular pacing is transiently interrupted, with the exception of patients with advanced spontaneous AV block and those treated with AV node ablation ("ablate and pace").

13.2.4.6 ICD Response to EMI

The ICDs require a certain duration (several seconds) of continuous high-rate sensing to satisfy arrhythmia detection criteria and consequently start the treatment (antitachycardia pacing or DC shock). Therefore, short bursts (<5 s) of electrosurgery alternating with pauses lasting some seconds are unlikely to result in false tachyarrhythmia detection and inappropriate antitachycardia therapies.

Inappropriate ICD shocks, although painful in nonsedated patients, should not be necessarily considered a serious danger for both the patient (apart from skeletal muscle contraction even if the patient is paralyzed by curare) and the people surrounding, who will not experience any shock. There is, however, a rare but possible proarrhythmic effect of DC shocks, which can initiate ventricular fibrillation.

13.2.5 Effects of the Magnet

A simple magnet (typically 90 G) should always be present in the operating room when a patient with a CIED undergoes a procedure potentially causing EMI. However, the effect of the magnet positioned on the skin just above the device (Fig. 13.3) differs between pacemakers and ICDs.

Fig. 13.3 A magnet placed on the CIED pocket

13.2.5.1 Pacemakers

When a magnet is applied on a pacemaker, it usually causes "asynchronous pacing" (generally VOO or DOO), meaning that pacing at a fixed rate is provided, independently from any sensed activity, ensuring cardiac stimulation (or avoiding inappropriate triggered activity) even in the presence of persistent artifacts. The pacing rate in the presence of a magnet is CIED characteristic and varies according to the battery charge.

If spontaneous ventricular activity is adequate, asynchronous pacing (provided by the magnet or by CIED reprogramming) can be unnecessary or even inappropriate and potentially dangerous, as the magnet rate may compete with the patient's rate; however, the risk that asynchronous pacing in patients with intrinsic rhythm can potentially induce atrial or ventricular arrhythmias, although widely feared, is very low [11].

13.2.5.2 Implantable Defibrillators

In ICDs, arrhythmias detection or tachycardia therapy can be disabled by magnet application and is automatically re-enabled when the magnetic field is removed. In some elderly Boston Scientific (former Guidant) ICDs, antitachycardia therapy may be permanently, and not transiently, deactivated by magnet application, necessitating reprogramming of the device or magnet repositioning to restore prior function. For this reason, and because it is possible to turn off magnet response in some devices, careful monitoring is required during the procedure to determine the effects of cauterization.

If inappropriate antitachycardia therapies (shock or antitachycardia pacing) should be delivered despite the magnet, shorter bursts (<5 s) with pauses between bursts, or bipolar cautery, are mandatory. On the other side, when true sustained

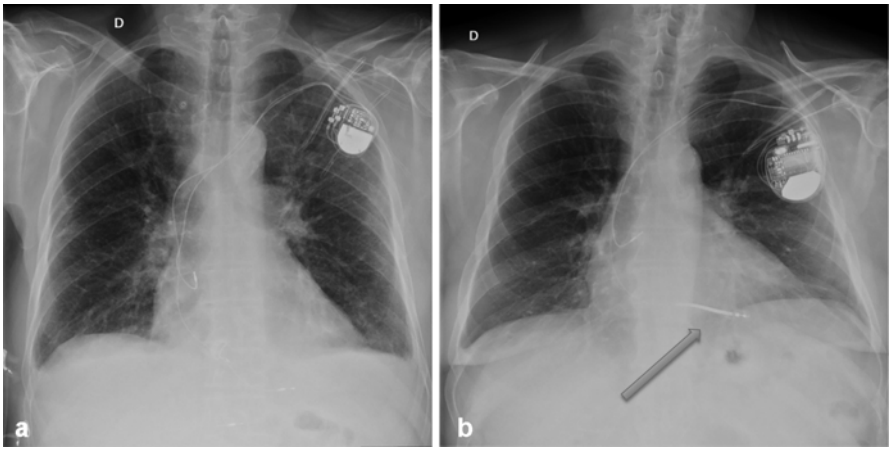

Fig. 13.4 Posterior anterior thoracic X-ray in a patient with a pacemaker (**a**) and an ICD (**b**). The shocking coil along the right ventricular lead in the ICD patient is indicated by the *arrow*

ventricular arrhythmias occur, appropriate antitachycardia therapies can be delivered by the device by just removing the magnet or by using an external defibrillator. In this case, external pads should be placed in the anteroposterior rather than anterolateral position, ensuring the anterior (apical) pad is at least 5 cm away from the device.

Differently from PM, the *magnet does not affect ICD antibradycardia pacing functions*. As a consequence, *in PM-dependent patients with ICD, reprogramming is more desirable* to avoid pacing inhibition when EMI are expected to be significant.

13.2.6 How to Recognize that a Patient Has a CIED and if Is PM Dependent

When data from medical history or files are not available, a CIED can be easily recognized by the presence of the wound in the infraclavicular region, more frequently on the left side. In less skinny patients, some devices, as some recent PMs, cannot be always detected because of the small dimensions and the position, sometimes several centimeters away from the original site under the wound.

All patients should always carry a device identification card, necessary to understand the type (PM, ICD, or CRT) and devices' manufacturer; these information are particularly important, as every device can be interrogated by the programmer from its manufacturer only. In emergency situations, chest radiograph is useful to distinguish a PM from an ICD, as the latter presents a shocking coil (section of the lead which are wider and more radiodense) along the right ventricular lead, close to the tip (Fig. 13.4). Sometimes another coil is present along the same lead, more proximally, in the superior vena cava. In addition, chest X-ray often allows the recognition of the model and even the device's serial number.

A patient with spontaneous activity is not, by definition, PM dependent. Even if the risk of bradyarrhythmias can be present, the occurrence of pauses contemporary to the inhibition of pacing during EMI is very unlikely. Therefore, PM reprogramming or magnet positioning is usually unnecessary in these patients, when the CIED is not an ICD.

When feasible, in paced patients, the PM dependence should be evaluated by the cardiologist during a preoperative PM evaluation, reprogramming the device at a low (usually 30 or 40/min) rate to detect spontaneous activity. This is particularly important in patients with CRT, where 100 % biventricular pacing is usually present, even in the absence of bradyarrhythmias. When interrogation cannot be performed before the operation, all patents with constant paced rhythm should be considered as PM dependent.

Routine PM check is usually performed every 6–12 months (3–6 for ICD). Therefore, most patients should have been evaluated in the past year; in addition, an increasing number of devices are regularly followed by "remote monitoring": using a base unit (similar to a modem), connected to the internet (via a standard phone line connection or a cell phone communication technology) and communicating wirelessly with the CIED, most information available during routing ambulatory evaluation are transmitted to designed servers and can be viewed by authorized personnel whenever desired. Data are automatically sent according to fixed intervals, in the presence of significant events (as arrhythmias or malfunctioning) or manually by the patient. Current systems, however, do not permit remote device reprogramming.

13.2.7 How to Minimize the Risk

The risk of EMI is greatest when the current field crosses the CIED or the leads or is closer than 15 cm from the CIED. During electrosurgical application, the return electrode should be placed on the ipsilateral heel or flank; however, for operations involving the ipsilateral arm of the CIED, the return electrode should be placed on the same arm to avoid the full exposure to the electrosurgical energy.

The umbilicus can be not a precise anatomical landmark especially in obese patients and many abdominal laparoscopic surgical procedures go through the umbilicus. Therefore, *iliac crest as the landmark below which no magnet or reprogramming need to be performed should be recommended. Utilization of the magnet, rather than turning off the ICDs, significantly reduces the time of exposure to the risk of untreated life-threatening arrhythmias* [10].

In addition, there is a potential risk of not re-enabling tachycardia therapies after the surgical intervention, leaving the patient unprotected in the case of ventricular arrhythmias, as demonstrated by a report on 67,410 remote follow-up patients in which the most common "red alert" was that detections and therapies for ventricular fibrillaton were "off".

Equipment for urgent cardioversion, defibrillation, and emergent pacing should be immediately available. It is important to remember, however, that artifacts can be also present at surface ECG, and arrhythmias can be difficult to detect by

electrocardiographic monitoring during electrosurgical application. Therefore, cardiac activity should be monitored with other modalities, like invasive or noninvasive continuous arterial pressure monitoring or pulse oxymeter.

Therefore, *application of short burst of electrocautery (<5 s), with some seconds of pause, is the best mode to minimize the risk* of both significant bradyarryhythmias in PM-dependent patients and inappropriate antitachycardia therapy in patients with an ICD.

13.3 What the Cardiologist Should Know

When an urgent or emergent surgical intervention is needed, a cardiologist may not be immediately available, and not all cardiologists are practical with CIED programming. However, whenever possible, the cardiologist or, better, an electrophysiologist should be involved in the management of the patient, especially in case of thorax, head, or upper limbs surgery.

Clearly, the cardiologist should be aware of the patient's cardiac problems, including the reason for CIED implantation, whether the patient is PM dependent, and the model, the manufacturer, and the programming of the CIED, as responses to EMI and to magnet application vary among different CIED and according to the programming. For example, in impedance-based rate responsive systems (as in minute-ventilate sensors), EMI may result in pacing at the sensor-triggered upper rate limit if rate response is activated.

In the presence of significant EMI, a "noise reversion" may occur, during which time the CIED paces asynchronously and tachyarrhythmia therapy is suspended. Noise reversion mode is an algorithm designed to minimize the effects of EMI, and, differently from reset, it is automatically disabled once the noise is no longer present. However, noise reversion algorithms are manufacturer specific and can be useful mainly in the presence of persistent EMI; they may not provide an adequate protection in presence of sporadic and/or transient EMI, as encountered in the operating room; therefore, transient inhibition of pacing or inappropriate pacing at the programmed upper rate is more likely in this context.

13.3.1 Magnet Responses

Magnet responses vary according to different manufacturers, and different models continuously change as manufacturers release new devices. In addition, pacing rate is different at beginning of life (BOL) and at elective replace indicator (ERI).

13.3.2 Pacemakers

In PM, the magnet generally causes asynchronous pacing by closing a magnetic switch.

At BOL, VOO or DOO pacing rate vary from 85/min (Medtronic) to 100/min (Boston Scientific and S. Jude. At ERI, it decreases to lower values (Medtronic 65/min, Sorin and Biotronik 80/min, S. Jude 85–86.3/min). Other different responses can be found when magnet response is programmable (Biotronik, Boston, S. Jude).

In some devices with atrial antitachycardia therapies (Medtronic AT500), antitachycardia pacing only is suspended, but there is no conversion to an asynchronous pacing mode.

Rate response is always suspended.

In some devices (Biotronik, Boston Scientific and Medtronic), pacing amplitude remains unchanged as programmed, while if autocapture algorithm is operating, the output is usually reset above the autocapture threshold value.

13.3.3 ICD

In all ICDs, antitachy-therapy is suspended while PM functions are usually unchanged; only in Sorin devices pacing rate changes (96/min at and 80/min at ERI), continuing in demand mode (therefore, not switching in asynchronous pacing).

In some models (Boston and S. Jude), it is possible to disable magnet response to ICD.

When placing the magnet on the device, tones can be audible in some models (R wave-synchronized beep in Boston devices, steady tone in Medronic devices). However, if the device continues to emit a tone after magnet removal, it should be interrogated because of a possible fault.

13.4 A Suggested Algorithm/Pathway for Diagnosis and Treatment

13.4.1 Preoperative/Preanesthesia Assessment

In urgent/emergent setting, a preoperative assessment, as required in elective procedures, may be difficult to achieve. However, information available in the patient's records should be sufficient to generate most perioperative prescriptions, as most patients are regularly followed by ambulatory or remote evaluations.

If such evaluation has not been performed in the appropriate time frame (12 months for PM, 6 months for ICD/CRT), a consultation with an available CIED team is desirable prior to the procedure, when feasible.

13.4.2 Before Surgery

See Table 13.2

13.4.3 During Surgery

See Table 13.3

Table 13.2 Before Surgery

	What to do	How to do
All patients	Identify CIED patient	Check medical records, physical examination
	Identify the device (PM, ICD, CRT), manufacturer, and model (always)	Check medical records, patient card, or chest X-ray
	Verify CIED indications (whenever possible)	Check medical records or patient card
	Verify PM dependency (whenever possible)	Preoperatory ECG; in absence of evident spontaneous activity at surface ECG, check medical records or assume PM dependency when preoperatory interrogation and programming is not feasible
Patients with pacemaker		
PM-dependent patients *and* procedures *above* the umbilicus or iliac crest, unipolar cautery necessary	Verify underlying rhythm and spontaneous heart rate (whenever possible)	Preoperatory interrogation and transient programming at the lower rate (if not recently performed during PM routine evaluation)
	Heart rate monitoring (always)	Monitor patient with plethysmography or arterial line rather than ECG only
	Verify response to magnet placement (always)	Verify heart rate during magnet placement
	Alternative stimulation mode available (whenever possible)	Transcutaneous pacing available
Patients with ICD		
All procedures	Heart rate monitoring (always)	Monitor patient with pulse oxymeter or arterial line rather than ECG only
Procedures *under* the umbilicus or iliac crest; bipolar cautery	No reprogramming required	
Procedures *above* the umbilicus or iliac crest, unipolar cautery necessary		
Magnet available and device accessible during the operation (non PM-dependent patients)	Disable antitachycardia therapies (always)	Position a magnet over the device
Magnet unavailable/device *not accessible* during the operation (but CIED personnel readily available)	Disable antitachycardia therapies (always)	Disable tachyarrhythmia therapies by programming and *ensure postoperative reprogramming*

(continued)

Table 13.2 (continued)

	What to do	How to do
PM-dependent patients (and CIED personnel readily available)	Ensure adequate heart rate	Preoperatory reprogramming in asynchronous mode (VOO or DOO) at appropriate rate and *ensure postoperative reprogramming*
PM-dependent patients; magnet unavailable/device *not accessible* during the operation; *no CIED personnel readily available*	Extreme attention to minimize EMI during electrocautery (always)	Electrosurgical return electrode placed on the ipsilateral heel or flank (or the same arm for operations involving the ipsilateral arm)

Table 13.3 During Surgery

	What to do	How to do
All procedures	Heart rate monitoring (always)	Monitor patient with pulse oxymeter or arterial line rather than ECG only
	Avoid magnetic fields (if possible)	Position sterile magnetic drapes >15 cm far from the CIED
Procedures *under* the umbilicus or iliac crest or bipolar cautery	No reprogramming required	
Procedures *above* the umbilicus or iliac crest, unipolar cautery necessary		
All patients, but particularly PM-dependent ICD patients (even with the magnet applied) ICD patients, no magnet applied PM-dependent PM patients, no magnet applied (*and* CIED personnel not readily available)	Minimize EMI during electrocautery (always)	Short electrosurgical bursts (<5 consecutive sec) with pauses >5 s
PM-dependent PM patients (magnet applied)	Verify response to magnet (always)	Verify heart rate during cauterization (with and without magnet placement)
ICD patients (therapies disabled by the magnet)	Ensure proper treatment in the case of intra-procedure ventricular arrhythmias (always)	Remove the magnet to enable tachycardia therapies
ICD patients (therapies disabled by reprogramming)		External DC shock

13.4.4 After Surgery

After surgery, CIED personnel should be contacted as soon as possible when:

- Reset of the CIED occurred during surgery.
- Reprogramming (asynchronous pacing in PM-dependent patients, disabling of antitachycardia therapy in ICD patients) before surgery was performed.
- Significant brady- or tachyarrhythmias occurred during the operation.

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