

Arrhythmogenic Syncope

Claudia Herrera Siklódy, Patrizio Pascale
Cardiology Department, Centre hospitalier universitaire Vaudois (CHUV), Lausanne, Switzerland

Summary

Syncope is defined as a transient loss of consciousness due to transient cerebral hypoperfusion. It is a frequent cause of consulting in the emergency department, and cardiac arrhythmias play an important role in differential diagnosis. This review article outlines the different arrhythmic causes of syncope and their management, as well as the warning signs that should raise the suspicion of arrhythmia.

Keywords: Syncope; cardiac arrhythmia; bradycardia; tachycardia; cardiac devices

Introduction

Syncope is defined as a complete loss of consciousness characterised by a sudden onset, a short duration and a spontaneous complete recovery [1]. It is a common condition, representing ~1% of all attendances at the emergency unit [2]. Syncope occurs due to transient cerebral hypoperfusion, which can be precipitated by many different causes. Cardiac disease represents the second most common cause [3], representing 5–21% of all syncopes [4, 5], with a significant contribution of arrhythmias [6]. Cardiac syncopes happen due to a transient low cardiac output. Loss of consciousness may be facilitated by other concomitant factors contributing to the decrease in cerebral perfusion, such as valvular heart disease or left ventricular dysfunction. Atherosclerosis of the cerebral arteries might enhance the phenomenon, making arrhythmogenic syncope a frequent event in elderly patients. Thorough anamnesis is a crucial point in the assessment of patients presenting with a syncope. Some findings in the first assessment of patients presenting with a syncope should prompt the clinician to include arrhythmogenic syncope in the diagnostic work-up, such as the occurrence of the syncope while seating or lying, or a syncope preceded by palpitations. Similarly, in patients with structural heart disease (especially in case of a severely depressed left ventricular ejection fraction) or a pathological resting electrocardiogram (ECG), an arrhythmic cause should always be considered. A list of 12-lead ECG red flags which should prompt searching for an arrhythmic cause is presented in table 1.

Arrhythmogenic causes of syncopes can basically be divided into two groups: bradycardia- and tachycardia-related syncope. The list of arrhythmias susceptible of causing syncopes, a summary of the appropriate diagnostic work-up and management is given in table 2.

Bradycardia-Related Syncope

In this group, the syncope is related to a marked decrease in heart rate, which may be transient or persist over time. The decrease in heart rate can be caused by two conditions: sinus node dysfunction or AV conduction disturbances. Bradycardia might be facilitated by many exter-

nal factors such as drugs, electrolyte disorders or acute myocardial ischaemia. These reversible causes must be searched for and corrected, before considering any further therapies.

Bradycardia-related syncope must be suspected in the presence of sinus bradycardia or conduction disturbances on resting ECG. However, these findings do not automatically imply that bradycardia is the cause of the syncope. This point needs careful assessment. In case of an established relationship between the syncope and the bradycardia and in the absence of reversible factors, cardiac pacing is the treatment of choice.

Advanced AV conduction disturbances, such as documented third-degree AV block, second-degree AV block type Mobitz II or alternating bundle branch block represent clear pacing indications. Bifascicular block, with or without associated first-degree AV block and sinus node disease are trickier conditions. Donato et al. performed a study in patients with syncope and bundle branch block [7]. All patients underwent a standardised conventional evaluation of their syncope,

Table 1: Red flags on the resting 12-lead ECG

Sinus bradycardia	Search for sinus node dysfunction
First- or second-degree AVB type I (or Wenckebach) Bifascicular block	Search for AV-block
Second-degree AVB type II (or Mobitz) or third-degree AVB Alternating BBB	Pacemaker implantation
Ventricular pre-excitation	Electrophysiological study
QRS enlargement not fulfilling any bundle branch morphology Presence of pathological Q waves Abnormal repolarisation (ST-segment depression or elevation, T-waves inversion) Frequent and/or polymorphic PVC	Search for structural heart disease Search for ventricular tachycardia
QT interval ≥450 ms in men ≥460 ms in women	Search for reversible causes of QT prolongation Consider congenital long QT syndrome
Abnormal repolarisation in V1-V2 in the absence of complete RBBB	Consider Brugada syndrome

AVB: atrioventricular block; BBB: bundle branch block; RBBB: right bundle branch block; PVC: premature ventricular contraction.

Table 2: Arrhythmias that can potentially cause a syncope

Arrhythmia	When to suspect	Diagnostic arrhythmia work-up	Treatment
Sinus node disease	Sinus bradycardia	Holter Exercise testing to check for chronotropic incompetence Implant event recorder	Correct extrinsic causes Pacemaker
AV conduction disturbances	Bundle branch block AV-block	Search for SHD Holter EPS to measure HV interval Implant event recorder	Correct extrinsic causes Pacemaker
Supraventricular tachycardia	Palpitations preceding syncope Pre-excitation	History of intermittent palpitations Holter	EPS/Catheter ablation AAD
Ventricular tachycardia	Palpitations preceding syncope Syncope during exertion Structural heart disease	Search for SHD Cardiac imaging including cardiac MRI +/- other modalities according to initial work-up EPS (programmed ventricular stimulation)	Consider ICD AAD Catheter ablation
Polymorphic VT/Torsade de pointes	Prolonged QT interval Family history of sudden cardiac death Rest ECG suggesting a channelopathy Syncope during exertion	Ajmaline test (in case of suspicion of Brugada syndrome) Exercise test and other provocative testing Genetic testing if suitable Consider implantation of event recorder in unclear cases	Correct extrinsic causes Pacing in bradycardia-induced torsade de pointes Beta-blocker in some conditions ICD in selected cases

AAD: anti-arrhythmic drugs; AV: atrioventricular; EPS: electrophysiological study; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; SHD: structural heart disease; VT: ventricular tachycardia.

including echocardiography, Holter monitoring and exercise test if the syncope occurred during exercise. They found out that less than half of these patients had a final diagnosis of paroxysmal AV-block syncope and therefore an indication for pacing. Proceeding to pacemaker implantation without having documented the causality of arrhythmias for the syncope (empiric pacing) might end up with implanted patients that present with syncope recurrences. Indeed, implanting patients with undocumented AV block suspicion due to bifascicular block can lead to syncope recurrences in 11–14% of patients over one to two years [8, 9]. These figures are even higher for sinus node dysfunction, with syncope recurrences in up to 25% of patients after two years [10]. This is due to the fact, that sinus node disease is frequently associated with a vasodepressor reflex mechanism, that also contributes to syncopes, but will not be counterbalanced by cardiac pacing. Finally, empiric pacing has not been proven to improve survival.

The diagnostic work-up in case of a syncope in combination with sinus bradycardia should include at least 24 hours of ECG monitoring. In patients with asymptomatic documented sinus pauses >6 seconds, pacing might be indicated, but only after having ruled out other concurrent diagnostic options. Implantable loop recorders are a good option in unclear cases to match symptoms and arrhythmia. In case of bifascicular block without a documented AV block, the recommended

strategy consists in performing an electrophysiological study (EPS) to measure the HV interval and implanting an event recorder if the EPS findings are non-conclusive [11, 12]. Since an intermittent or stable AV block may still be documented later in a significant proportion of these patients, empiric pacing may be considered in elderly patients with unpredictable and recurrent syncopes at high risk of traumatic consequences [12].

An echocardiography must be performed in all patients before implanting a device for choosing the best pacing option. In general, ventricular pacing should be avoided whenever possible, since it may cause a reduction of the left ventricular systolic function, especially if already impaired or borderline. If a high percentage of ventricular pacing is anticipated, patients with a reduced left ventricular ejection fraction <40% should be implanted with a resynchronisation device [12, 13]. As discussed later, it is worth noting that in patients with left ventricular dysfunction and/or structural heart disease, ventricular arrhythmias must be included in the differential diagnosis even if bradycardia is the most prominent finding at initial evaluation.

Finally, atrial arrhythmias with the alternance of fast ventricular rates and bradycardic sinus rhythms (bradycardia-tachycardia syndrome), may be addressed with catheter ablation avoiding a pacemaker implantation. Indeed, in a retrospective analysis, Chen et al. found out that 95% of the patients with tachy-

cardia-bradycardia syndrome who underwent catheter ablation no longer had a pacemaker indication 20.1±9.6 months after the procedure [14]. In these patients, including those with symptomatic sinus pauses after spontaneous atrial fibrillation cardioversion, it is appropriate to consider ablation as first-line therapy.

Tachycardia-Related Syncope

Tachycardia-related syncopes can be divided into supraventricular and ventricular tachyarrhythmias. Differentiating between them is crucial, as it has important therapeutic and prognostic implications. Therefore, it should always be striven to obtain a 12-lead documentation of the tachycardia. Although supraventricular tachycardias are way less often syncopal than ventricular ones, haemodynamic tolerance should not be considered as a reliable diagnostic clue. The treatment options for these tachyarrhythmias are much broader than for bradyarrhythmias, including anti-arrhythmic drugs, catheter ablation and implantable cardiac defibrillators (ICD).

Benign, supraventricular tachycardia can be a cause of rhythmogenic syncopes, especially in elderly patients with concomitant significant valvular heart disease and atherosclerosis of the supra-aortic vessels. The differential diagnoses include AV node reentry tachycardia, atrial flutter or atrial fibrillation and more rarely, orthodromic atrioventricular reentry tachycardia and focal atrial tachycardia. Catheter ablation often represents the

first-line treatment for these arrhythmias, considering the severe clinical repercussions. A ventricular pre-excitation pattern on ECG should raise the suspicion of pre-excited atrial fibrillation as a potential cause of syncope. Catheter ablation would then be first-line therapy, as this condition might result in ventricular fibrillation. Syncope in atrial fibrillation and atrial flutter can be related to fast ventricular rates but are more commonly related to a concomitant sinus node dysfunction. As previously discussed, treatment of the tachyarrhythmia can avoid the need for pacemaker implantation. Anti-arrhythmic drugs can be weighed, considering the patient's concomitant conditions and preferences, but must be carefully selected and monitored, as all anti-arrhythmic drugs can also be pro-arrhythmic and a potential cause of recurrent syncope either through a brady- or tachyarrhythmia.

Regarding ventricular arrhythmias, if documented in a patient with structural heart disease, ICD is indicated for secondary prevention. Whenever a cardiac syncope is suspected based on the anamnesis and/or the resting ECG, a ventricular arrhythmia must always be considered in patients with structural heart disease. Echocardiography therefore has a central role in the initial evaluation. Other cardiac imaging modalities such as cardiac MRI will be required often, complemented or not with other modalities depending on the clinical context, such as 18-FDG positron emission tomography. ICD implantation should always be considered in case of a syncope, when the left ventricular ejection fraction is $\leq 35\%$. Another recognised indication is an induction during EPS of sustained ventricular tachycardia in patients with a history of myocardial infarction and syncope [15].

Patients with monomorphic ventricular tachycardia and a structurally normal heart less commonly present with a syncope. In these patients, the indication for an ICD is weaker, given that a thorough work-up usually including cardiac MRI has ruled out a structural heart disease. ICD will certainly be considered if the arrhythmia cannot be cured with catheter ablation or if anti-arrhythmic drugs fail to avoid arrhythmia recurrences. Arrhythmogenic right ventricular dysplasia should be considered in the differential diagnosis in case of left bundle branch block type premature ventricular contractions.

It is important to keep in mind that an ICD, when indicated, will treat the arrhythmia once present, but is not able to prevent it. Therefore, in case of documented ventricular arrhythmias, catheter ablation and/or anti-arrhythmic drugs should also be used in these patients for arrhythmia prevention.

Finally, arrhythmogenic syncope may be due to polymorphic ventricular tachycardia or torsade de pointes in the setting of congenital or acquired channelopathies. A positive family history or a pathologic 12-lead ECG can point towards an inherited arrhythmogenic heart disease. If suspected, the patients must be referred for a comprehensive work-up, including exercise testing for catecholaminergic polymorphic ventricular tachycardia (CPVT) or an ajmaline test for Brugada syndrome. Genetic testing might also be considered based on the clinical data, in order to complete the examination. Congenital long QT syndrome can be very challenging to diagnose and may require the use of provocative manoeuvres to unmask it (such as an exercise test or a dynamic measurement of the QT interval during heart acceleration in response to brisk standing). Management of CPVT and congenital long QT syndrome includes beta-blockers, with nadolol and propranolol having the best evidence. Patients must be instructed to avoid some drugs and situations, depending on the condition. An ICD implantation may be indicated but should be carefully weighed especially in young patients and depending on the suspected diagnosis.

The most prevalent condition is the acquired form of long QT syndrome, which may lead to torsade de pointes. A severely prolonged QT interval >500 ms confers a two- to threefold risk of developing torsade de pointes. A prolonged QT interval (corrected QT interval of ≥ 450 ms in men or ≥ 460 ms in women) is common and often overseen. In a study published

by Pasquier et al in 2012, 22.3% of patients admitted in internal medicine displayed a prolonged QT interval [16], especially in case of liver diseases or polypharmacy. Moreover, in this study 50.8% of these patients received QT prolonging drugs during their hospitalisation. QT interval should always be assessed on a 12-lead ECG before initiating drugs potentially prolonging the QT interval. A comprehensive list of these drugs can be found online on www.crediblemeds.org. In patients presenting with a prolonged QT interval, reversible factors, such as drugs and electrolyte disorders must be sought and corrected. Bradycardia-induced QT prolongation may also lead to torsade de pointes which can be treated with pacing.

Correspondence

Claudia Herrera-Siklody
Service de cardiologie
Centre Hospitalier Universitaire Vaudois
Rue du Bugnon 46
CH-1011 Lausanne
[claudia.herrera-siklody\[at\]chuv.ch](mailto:claudia.herrera-siklody[at]chuv.ch)

Disclosure Statement

No financial support and no other potential conflict of interest relevant to this article was reported.

Recommended References

- 1 Brignole M, Moya A, de Lange FJ, Deharo JC, Elliott PM, Group ESCSD et al. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39:1883–1948.
- 7 Donato P, Brignole M, Alboni P, Menozzi C, Raviele A, Del Rosso A et al. A standardized conventional evaluation of the mechanism of syncope in patients with bundle branch block. *Europace*. 2002;4:357–60.
- 9 Santini M, Castro A, Giada F, Ricci R, Inama G, Gaggioli G et al. Prevention of syncope through permanent cardiac pacing in patients with bifascicular block and syncope of unexplained origin: the PRESS study. *Circ Arrhythm Electrophysiol*. 2013;6:101–7.
- 11 Moya A, Garcia-Civera R, Croci F, Menozzi C, Brugada J, Ammirati F et al. Bradycardia detection in Bundle Branch Blocks. Diagnosis, management, and outcomes of patients with syncope and bundle branch block. *Eur Heart J*. 2011;32:1535–41.
- 16 Pasquier M, Pantet O, Hugli O, Pruvot E, Buclin T, Waeber G et al. Prevalence and determinants of QT interval prolongation in medical inpatients. *Intern Med J*. 2012;42:933–40.

Keypoints

- Cardiac arrhythmias are a common cause for syncope, representing 5–10% of syncope. They should be suspected when syncope occurs while seating or lying, or if they are preceded by palpitations.
- In case of bradycardia, a careful work-up is needed to ensure the causal role of bradycardia in the syncopal event before implanting a pacemaker.
- Supra-ventricular tachycardia-related syncope are preferentially treated with catheter ablation.
- Implantation of an ICD should always be considered in ventricular arrhythmia to prevent sudden cardiac death. In case of documented ventricular tachycardia, a complementary strategy must be set to prevent the recurrence of arrhythmia.
- In all arrhythmia, reversible factors must be sought and corrected before deciding on the final treatment.



References

You will find the full list of references online at <https://cardiovascmed.ch/article/doi/CVM.2023.02202>.