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REVIEW

Short QT syndrome. Update on a recent entity

Le syndrome du QT court : aspects actuels d'une entité récente

Philippe Maury[a,*], Fabrice Extramiana[b], Pascal Sbragia[c], Carla Giustetto[d], Rainer Schimpf[e], Alexandre Duparc[a], Christian Wolpert[e], Isabelle Denjoy[b], Marc Delay[a], Martin Borggrefe[e], Fiorenzo Gaita[d]

[a] *Fédération de cardiologie, hôpital universitaire Rangueil, 31059 Toulouse cedex 09, France*
[b] *Lariboisière University Hospital, Department of Cardiology, 2, rue Ambroise-Paré, 75011 Paris, France*
[c] *Department of Cardiology, CHU Nord, 13915 Marseille cedex 20, France*
[d] *Department of Cardiology, Cardinal Massaia Hospital, Asti, Italy*
[e] *1st Department of Medicine, University Hospital Mannheim, University of Heidelberg, Mannheim, Germany*

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Summary The short QT syndrome, a recently discovered ion channel disorder, combines shortened repolarization, a predisposition to atrial and ventricular fibrillatory arrhythmias, and a risk of sudden death. Few cases have been reported, but the prevalence may be underestimated. This syndrome might account for some cases of unexplained ventricular fibrillation in patients with otherwise healthy hearts. Patients have abnormally short QT intervals and refractory periods, and atrial/ventricular fibrillation can be triggered during investigations. Gain-of-function mutations have been detected in three genes encoding potassium channels. Treatment is based on defibrillator implantation, sometimes as a preventive measure. Quinidine may be beneficial in certain cases.

MOTS CLÉS
Intervalle QT ;

Résumé Nouvelle canalopathie de découverte récente, le syndrome du QT court associe raccourcissement de la repolarisation et propension aux arythmies fibrillatoires atriales et ventriculaires pouvant mener à la mort subite. À ce jour seul un nombre très limité de cas

* Corresponding author.
E-mail address: mauryjphil@hotmail.com (P. Maury).

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Mort subite ;
Canalopathie

a pu être répertorié, mais une sous-estimation de la prévalence réelle est possible, ce syndrome pouvant expliquer un certain nombre de fibrillations ventriculaires inexpliquées sur cœur par ailleurs sain. Les patients présentent des intervalles QT et des périodes réfractaires anormalement courts, et des fibrillations atriales ou ventriculaires sont déclenchables lors des explorations. À ce jour des mutations sur trois gênes codant pour les canaux potassiques et entraînant des gains de fonction ont été découvertes. Le traitement actuel repose sur l'implantation d'un défibrillateur, qui sera même proposé parfois à titre prophylactique. Une alternative médicamenteuse pourrait être représentée par la quinidine dans certains cas.

Introduction

Each year in the United States and Europe, several hundred thousand people are victims of sudden death (SD). The immediate cause is usually ventricular fibrillation (VF) [1,2]. While most patients have a known or unknown underlying arrhythmogenic cardiopathy at the time of the event, the heart is considered ''healthy'' in 5 to 10% of cases [1,3], meaning that no morphological anomalies are detected with the methods routinely used in clinical practice [3,4]. Over the last two decades a number of etiologies have been identified, corresponding to apparently pure electrical disorders related to hereditary disorders affecting certain ion channels that generate cellular action potentials. These ion channel disorders disrupt cardiac rhythms and are capable, when combined with certain environmental factors, of causing malignant ventricular arrhythmias and SD. These disorders comprise, in chronological order of their discovery, long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, and Brugada's syndrome. But some cases of VF in patients with apparently healthy hearts do not correspond to any of these electro-clinical syndromes and are considered ''idiopathic'', reflecting our limited knowledge in this area [4]. Some cases are probably associated with early repolarization, as recently reported.

A few years ago another entity was discovered — associating shortened repolarization with a risk of SD by VF — further reducing the proportion of ''idiopathic'' cases of VF.

Historical background

QT prolongation has long been known to increase the risk of SD and overall cardiac mortality among patients with a variety of underlying etiologies. However, it is only in the early 1990s that Holter recordings of more than 6500 patients suggested that a shorter than normal QT interval could be detrimental: the risk of SD at two years was more than doubled in patients with a mean QT_C below 400 ms or above 440 ms [5]. The princeps description of three familial cases of extremely short QT associated with paroxysmal atrial fibrillation (AF), plus an isolated case with syncope and SD, was reported in 2000 by Ihor Gussak et al. [6]. These authors were the first to postulate the existence of a new syndrome combining consistent shortening of repolarization and electrical instability. Then in 2003, Gaita et al. published a more thorough description of two unrelated families with a history of SD spanning several generations. They found that seven members of these families had a consistently short QT interval associated with syncope, palpitations, AF and documented episodes of VF [7]. These patients had short atrial and ventricular refractory periods, and VF could be induced in most of them. Other cases have since been reported, [8—14] retrospectively validating the existence of this new syndrome of cardiac rhythm disorder.

Diagnosis

The frequency of the QT interval should be between 60 and 85 per min [15] in the lead (often V2) in which the amplitude of the T wave is largest and where the return to the isoelectric line is clearest, from the beginning of the QRS to the junction between the tangent of the maximal descending slope of the T wave and the isoelectric line [16]. QT and QT_C values of 300 ms or less were noted in these initial descriptions of highly selected patients [6,7], associated with a, tall, sharp, fine, positive and symmetrical T wave, especially in the precordial leads (V2 to V4); the ST segment was virtually absent [15,17] and, consequently, the interval between the end of the T wave and the following P wave was prolonged (Fig. 1 and 2). In a review of the first 15 reported cases, the QT_C was found to be below 320 ms, and this value thus became the diagnostic cutoff [18]. In the 29 patients studied to date, the QT interval has always been below 320 ms and the QT_C always below 340 ms, with an acuminate and symmetrical T wave in most cases [16] (Table 1). In some published cases, however, the QT was as high as 340 ms and the QT_C even higher [10,11]. If the upper normal limit of the QT interval is now well known, the lower limit has received far less attention. It can be defined as the mean minus two standard deviations of the QT interval in a normal population. Values of 330 ms (310 ms in children) for the QT [19] and between 360 and 380 ms for the QT_C have been proposed [20]. QT or QT_C intervals below these values can therefore be considered abnormally short. Indeed, other studies show that 99% of the normal population have a QT_C interval greater than 360 ms (men) or greater than 370 ms (women) [21,22] (Table 1). As in this syndrome, the QT interval shows little shortening as heart rate increases [15,17], QT correction with Bazett's formula