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Time course of electrocardiographic changes in transient left ventricular ballooning syndrome

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ABSTRACT

Background: We sought to describe, for the first time, in detail the time course of electrocardiographic (ECG) changes in transient left ventricular ballooning syndrome (TLVBS) from acute onset until 1 year after presentation.
Methods: The serial ECGs of all patients identified with TLVBS who presented to our cardiology department from August 1998 to August 2012 were analyzed, from admission to 1-year follow-up, with respect to time from onset of symptoms.
Results: In total, 145 TLVBS episodes were identified in 139 patients. In 53% of patients, ST segment elevation was present in the first 3 h after symptom onset, after which there was a steady decline with complete resolution in all patients by 1 month. The presence of T wave inversion (TWI), with or without ST segment depression, was most prevalent between day 1 (60%) and day 30 (71%) from symptom onset, with 17% of patients still exhibiting TWI after 6 to 12 months. At 1 year, approximately 80% of patients had no significant residual ST-T wave changes. In 86% of patients, there was prolongation of the corrected QT (QTc) interval in the acute phase, with normalization of all QTc intervals by day 14.
Conclusions: During the early phase, ECG mimics acute ST elevation myocardial infarction with initial regional ST segment elevation progressing to T wave inversion with or without ST depression. In the majority of patients, significant QTc interval prolongation occurs in the early phase, normalizing by day 14.

1. Introduction

Transient left ventricular ballooning syndrome (TLVBS), also known as Tako-Tsubo or stress-induced cardiomyopathy, is a syndrome characterized by acute transient left ventricular dysfunction, frequently occurring after significant emotional or physical stress. It was first described in Japan nearly two decades ago [1] and the first series of TLVBS patients outside of Japan was reported by our group in 2003 [2]. While the original description of Tako-Tsubo cardiomyopathy referred exclusively to apical ballooning, more recently mid-ventricular [3] and basal [4] ballooning have been described, and therefore the term TLVBS is perhaps a more comprehensive terminology. Many aspects of its pathogenesis still remain poorly understood, and prognosis is generally considered good after the treatment of acute phase complications such as hypotension, pulmonary congestion and ventricular arrhythmias. In TLVBS, the early electrocardiographic (ECG) changes include ST segment elevation, deep T wave inversion (TWI) and corrected QT (QTc) interval prolongation. Although these acute ECG changes have been described previously, and have been compared to ECG changes in acute myocardial infarctions [5,6], there have been, to the best of our knowledge, no previous studies documenting the time course of serial ECG changes from acute clinical onset through the early days, and further up until 12 months after initial clinical presentation.

The aim of this study is therefore to characterize precisely the acute to long-term serial electrocardiographic changes in patients presenting with TLVBS.

2. Methods

2.1. Patients

From August 1998 until August 2012, all consecutive patients presenting to our cardiovascular department with TLVBS were identified and prospectively entered into a detailed clinical database. Serial ECGs were performed as per routine clinical practice, at 3–4 months follow-up and at opportunistic occasions. Patients were diagnosed with TLVBS according to the Modified Mayo Clinic criteria [7]. All available ECGs were categorized according to the time from onset of symptoms into the following time intervals; within 3 h, from 3 to 6 h, from 6 to 12 h, from 12 to 24 h; from 24 to 72 h, from 3 to 14 days, from 14 to 30 days, from 1 to 3 months, from 3 to 6 months and from 6 to 12 months.

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2.2. Electrocardiogram analysis

The 12-lead ECG was recorded at a speed of 25 mm/s with a 10 mm/mV amplification scale. The ECG details including cardiac rhythm, the presence of conduction disturbances, ST and T wave changes, the presence of Q/Qs waves, PR interval, QT interval and QTc interval were documented for each ECG. ST segment elevation, measured 80 msec after the J point, was considered present if ST segment elevation was ≥1.0 mm in the precordial leads, and ST segment elevation was ≥0.5 mm in the limb leads. A TWI was considered present if the depth was >1.0 mm in any lead. Q waves were considered pathological if ≥0.02 s (or QS complex) in leads V_2, V_3, and ≥0.03 s and 1.0 mm deep (or QS complex) in leads I, aVL, V_4 to V_6, II, III, aVF [8]. Hard copies and electronic copies of the ECG were analyzed. Each ECG was defined as being: (a) within normal limits (including 1st degree atrio-ventricular block), (b) borderline abnormal (including minor non-specific ST and T wave changes), (c) having TWI with or without ST segment depression, (d) having ST segment elevation with or without the presence of Q/Qs waves, (e) having ST segment elevation and TWI with or without the presence of Q/Qs waves, and (f) having solely ST depression. The QTc interval was calculated by the automated Marquette 550 ECG Machine (GE Healthcare, Waukasha, USA) which employs Bazett's formula. A QTc interval of >450 msec and >460 msec was considered prolonged for males and females, respectively [9].

2.3. Statistical analysis

All data were expressed as mean ± SD or as percentage (number). The Student's t test was used to compare groups. Statistical analyses were performed by SPSS (version 20, SPSS Inc. Chicago, Illinois). A P value of <0.05 was considered significant.

3. Results

3.1. Baseline characteristics (Table 1)

A total of 145 TLVBS episodes were identified in 139 patients; 4 patients had one recurrent episode, with one patient suffering 2 recurrent episodes of TLVBS. The average age at presentation was 67.0 ± 12.2 years and 88.5% (n = 123) of patients were female. Hypertension (53.8%, n = 78) and hyperlipidemia (40.7%, n = 59) were the most common cardiovascular risk factors. Seventy nine percent (n = 115) of patients had classical apical ballooning syndrome and 21% (n = 30) of patients had isolated mid-ventricular ballooning syndrome. Eight patients were admitted following resuscitation after suffering an out-of-hospital cardiac arrest, 5 due to a ventricular arrhythmia and 3 due to pulseless electrical activity. Overall in-hospital mortality was 6.2% (n = 9), with 7 patients dying as a direct result of complications due to TLVBS and 2 patients dying after recovery from the TLVBS episode (one from septic shock; one from post-surgical complications).

3.2. ECG findings

Of the 145 admissions with TLVBS, 77 (53%) patients presented within 3 h of symptom onset. Of these patients, 41 (53%) had ST segment elevation on the ECG, 14 (18%) had TWI only, 3 (5%) had TWI with ST depression, 3 (4%) had only ST depression, 1 (1%) had a borderline abnormal ECG, while 15 (19%) had a normal ECG without ST or T wave changes (Fig. 1).

The examples of typical serial ECG changes are represented in Fig. 2. For all episodes of TLVBS, the serial ECG changes during the early phase throughout long-term follow-up are represented in Fig. 3. The presence of ST segment elevation slowly declined from early after symptom onset, progressing to predominantly ST segment elevation and TWI (30%) or TWI with or without ST depression (50%) at 12 h. After 24 h, TWI (with or without ST segment depression) became the most prevalent pattern (60%), reaching a plateau between day 2 and day 30 (71%). Thereafter TWI remained the most prevalent ECG abnormality up until 3 months (70%). Seventeen percent of patients had residual TWI up until 1 year. In the first 3 h, and from 3 to 6 hour post symptom onset, pathological Q waves were present on 9% and 10% of ECGs, respectively. By 1 month after presentation there was complete resolution of pathological Q waves.

From 1 month after presentation there was a gradual normalization of ECGs with 30%, 75% and 80% at 1–3 months, 3–6 months and 6–12 months respectively, having no significant Q, ST or T wave abnormalities. At 12 months, 80% of ECGs (n = 38) had no significant ST or T wave changes, with 17% having residual TWI.

Table 1
Patient characteristics.

	N = 145
Age (years)	67.0 ± 12.2
Female	88.5% (123)
Hypertension	53.8% (78)
Hyperlipidaemia	40.7% (59)
Family history CAD	24.1% (35)
Current smoker	13.8% (20)
Diabetes mellitus	12.4% (18)
Obesity	9.0% (13)
PVD	4.8% (7)

Values expressed as mean ± SD, or as percentage (number). CAD = Coronary artery disease, PVD = peripheral vascular disease.

3.3. QTc interval

Serial changes in QTc intervals from the acute phase up to 12 months from symptom onset are represented in Fig. 4. Serial ECGs showed QTc interval prolongation at some point in time in 86% (125) of 145 TLVBS episodes. The overall mean peak QTc interval was 515.8 ± 61.1 ms. Of the patients with QTc prolongation, 23 patients were taking potential QT prolonging medication (anti-arrhythmic agents, anti-depressants or anti-histamines), 15 patients had electrolyte/biochemical abnormalities (hypokalaemia, hypocalcaemia, hypomagnesaemia or hypothyroidism) that may predispose to QTc prolongation, and 3 patients had both these potential QTc prolonging risk factors. Of interest, the patients who presented with TLVBS and were taking potential QT prolonging medication or had potential QTc prolonging electrolyte/biochemical abnormalities had a longer peak QTc interval (524.3 ± 48.3 ms) than those TLVBS patients with no known QTc prolonging factors (512.3 ± 65.4 ms) although statistically this was not significant (p = 0.25).

The mean peak QTc interval for male patients (n = 7) presenting within 3 h of symptom onset was slightly prolonged at 463.4 ± 38.8 ms, with a mean peak QTc of 460.0 ± 44.3 ms for female patients (n = 64) presenting during the same time frame. In male patients the mean QTc interval peaked (513.3 ± 64.3 ms) at 3 to 6 h after symptom onset, while in female patients the mean QTc interval reached its maximum (505.9 ± 59.4 ms) later, at 12 to 24 h after symptom onset. In all patients the QTc intervals normalized by 14 days.

Five patients presented following successful resuscitation of an out-of-hospital ventricular fibrillation or ventricular tachycardia cardiac arrest. All 5 patients had prolonged QTc intervals (mean 520.4 ± 36.8 ms) on presentation with none of them on QT prolonging medication and only 1 patient having a predisposing electrolyte abnormality (hypokaelaemia). One other patient had ventricular fibrillation on day 5 after admission during emergency vascular surgery for acute limb ischemia as a result of a displaced angioseal vascular closure device. This was successfully treated with urgent electrical cardioversion. The patient's QTc was significantly prolonged (560 ms) when the arrhythmia occurred. Blood electrolytes were all within normal limits and the patient was not taking QT prolonging medication. However, a general anesthetic was given for this operation which may have included QT prolonging anesthetic agents. In the 6 patients above with documented ventricular arrhythmias the QTc intervals were all prolonged but returned to normal limits within 14 days, suggesting no baseline QTc prolongation.

Of interest, there was no significant difference in the peak QTc interval in patients with typical apical ballooning compared to those presenting with isolated mid-ventricular ballooning (515.9 ± 56.6 ms versus 516.6 ± 75.9 ms, p = 0.97) suggesting that there is no difference in degree of QTc prolongation between these 2 morphologies of TLVBS.