Scientific Research Publishing

Open Journal of Endocrine and Metabolic Diseases, 2023, 13, 107-135
https://www.scirp.org/journal/ojemd
ISSN Online: 2165-7432
ISSN Print: 2165-7424

Electrocardiographic Manifestations of Endocrine and Metabolic Disorders

Masoud Amini, Nasim Golchin, Monica Kharat, Abdullah Mahmood, Issac Sachmechi

Department of Medicine, Icahn School of Medicine at Mount Sinai, Queens Hospital Center, New York, USA
Email: drmasoud624@gmail.com

How to cite this paper: Amini, M., Golchin, N., Kharat, M., Mahmood, A. and Sachmechi, I. (2023) Electrocardiographic Manifestations of Endocrine and Metabolic Disorders. *Open Journal of Endocrine and Metabolic Diseases*, **13**, 107-135.
https://doi.org/10.4236/ojemd.2023.137010

Received: June 6, 2023
Accepted: July 28, 2023
Published: July 31, 2023

Abstract

Endocrine dysfunction has an adverse impact on the cardiovascular system that may be due to an endocrine abnormality that leads to electrocardiogram (EKG) changes. The EKG changes due to endocrine disorder can be reversible and irreversible and treating underlying disease can reverse EKG changes in some cases. In this article, we review the electrocardiogram manifestations of various endocrine disorders.

Keywords

Endocrinology, EKG, Cardiovascular, Thyroid, Cushing Syndrome, Electrocardiographic

1. Introduction

Specific Electrocardiographic changes occur in different endocrine disorders. This paper aims to document these changes in review articles and to make physicians aware of these changes. Occasionally, these electrocardiographic changes may raise suspicion of the presence of endocrine disorders.

2. Growth Hormone Hypersecretion

Acromegaly in most cases is caused by pituitary tumors that secret growth hormone (GH) and is characterized by increasing levels of GH and serum insulin-like growth factor-1 (IGF-1). Both GH and IGF-1 play a role in the function of the cardiovascular system. In acromegaly patients, adverse cardiovascular events are considered leading causes of increased the mortality [1]. According to mortality analysis, cardiovascular disease is the cause of death in 60% of acromegalic patients. Arrhythmia can be detected in 40% of patients with acromegaly [1].

Some common observable rhythm disturbances for these patients, which are

most pronounced during periods of physical exertion, include atrial and ventricular ectopic beats, paroxysmal atrial fibrillation, paroxysmal supraventricular tachycardia, sick sinus syndrome, bundle branch block, and ventricular tachycardia [1]. The detection of pathological electrocardiography findings in patients with acromegaly in remission can imply the presence of anatomically permanent arrhythmogenic pathways caused by the irreversible fibrotic process.

QT intervals and QT dispersion specifically reflect the duration of ventricular repolarization and homogeneity [2]. Ventricular repolarization is an important period for developing ventricular arrhythmias. QT dispersion is the difference between the longest (QT max) and shortest QT (QT min) intervals in 12-derivation-electrocardiography (ECG). Corrected QT (QTc) and QTc dispersion can be beneficial in the estimation of morbidity and mortality in certain pathological conditions (**Figure 1**) [3] [4]. And play a role in the determination of potential proarrhythmia. Increased QT dispersion is correlated with increased risk of arrhythmia. QT intervals, especially QTc, are presumed as the markers of increased cardiovascular risk and provide important prognostic information in clinical practice and beneficial in the prediction and evaluation of ventricular arrhythmia [3] [4]. Studies showing lengthened QT intervals in patients with acromegaly are uncommon [2] [5] [6] [7] [8]. In BASER *et al.* [8], the study was constructed from individuals with similar comorbidities (DM, HT) to the patients with acromegaly to exclude the effects of such conditions on QT intervals. The results of the thyroid function test were within normal limits in both groups, and baseline QT max, QT dispersion, QTc max and QTc dispersion were longer, compared to controls. Lengthening of QT intervals in patients with acromegaly can be explained by the direct effects of GH and IGF-1 on myocardium or left ventricular hypertrophy due to DM, HT, and similar disorders [8]. Malignant ventricular tachyarrhythmia might account for some instances of recurrent syncope and sudden cardiac death in patients with acromegaly [9]. Additionally, cardiac autonomic functions are also reported to be impaired in patients with acromegaly [10]. Myocardial interstitial fibrous tissue proliferation due to GH and IGF-1 excess is thought to be the most important factor in arrhythmia in patients with acromegaly (**Figure 2**) [11]. Pathological ECGs may be a sign of irreversible fibrotic processes and permanent arrhythmogenic pathways, including patients

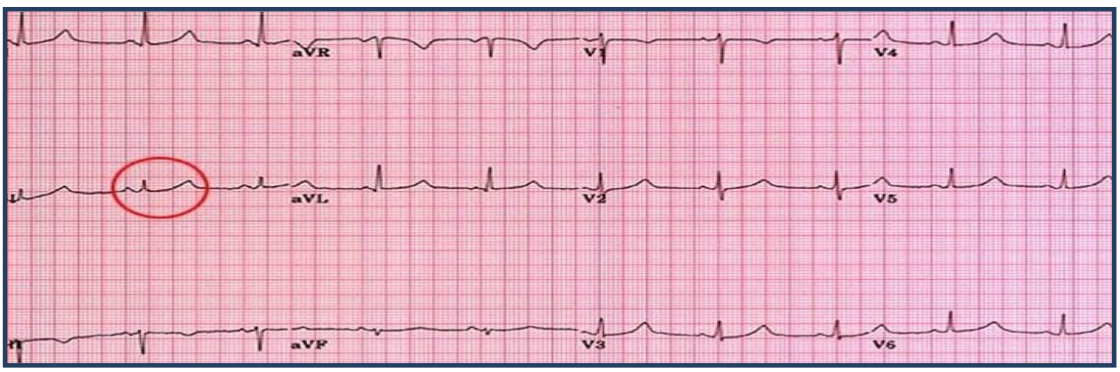


Figure 1. The QT interval represents the time between the beginning of the Q wave until the end of the T wave.

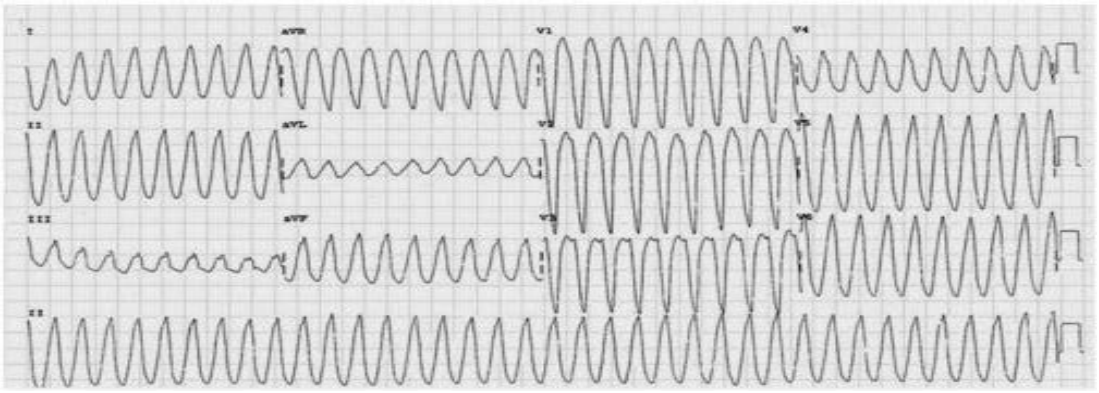


Figure 2. 12 lead EKG in acromegaly patient showing ventricular tachycardia [11].

in remission [12]. However, somatostatin analogs can reduce QT intervals, thereby improving the arrhythmic profile of patients with Acromegaly [13]. On the other hand, a significant association was found between low IGF-I and IGFBP-3 serum levels and AF. This association was independent of age, gender, beta-blocker use, hypertension, history of stroke or TIA, and chronic heart failure [14].

This interval is best measured in lead II and represents both the depolarization and repolarization phases of the ventricles. QTc can be calculated by the modified version of Bazett's formula. This formula states that the QTc = QT + 1.75(ventricular rate - 60). Normal values for this corrected QT interval are found to approximate 0.41 seconds, although this value is slightly longer in females and in patients of increasing age. If this calculation is applied to the ECG demonstrated above, the QTc is measured as 0.52 seconds [QTc = 0.52 + 1.75 (60 -60)].

(image is originally taken from
https://elentra.healthsci.queensu.ca/assets/modules/ECG/prolonged_qt_interval.html)

3. Cushing Disease (CD) EKG Findings

Hypercortisolemia is associated with an increased risk of cardiovascular disease (CVD), either by the direct impact of excessive cortisol on the myocardium or by increased traditional cardiovascular risk factors [15] [16]. There are a couple of electrocardiographic manifestations in patients with Cushing's syndrome. One of the specific ECG features of CD is Prolonged QTcd (dispersion of corrected QT interval) in association with ECG evidence of left ventricular hypertrophy (LVH) (**Figure 3**) [17]. In an ECG analysis of 79 patients that were diagnosed with CD, they found that QTcd but not QTc (corrected QT interval) was strongly associated with CD along with the well-established association of LVH with QTcd. Additionally, the sensitivity, the specificity, the positive predictive value (PPV), and the negative predictive value of QTcd > 50 ms to identify a patient with CD were 50.6%, 95.2, 95.6%, and 53.3%, respectively [17]. As CD is associated with an increased risk of CVD and mortality, ECG features might represent an easily assessable CV-risk marker present early in the natural history of CD, this may be relevant in the choice of medical therapy for CD [17]. Considering what was searched on the database for the cause of LVH in patient with Cushing's syndrome patients, the increase in relative wall thickness (RWT) and higher prevalence of concentric remodeling and LVH are relatively independent of the blood pressure overload and the pressure profile (dipping/non-dipping) [18].

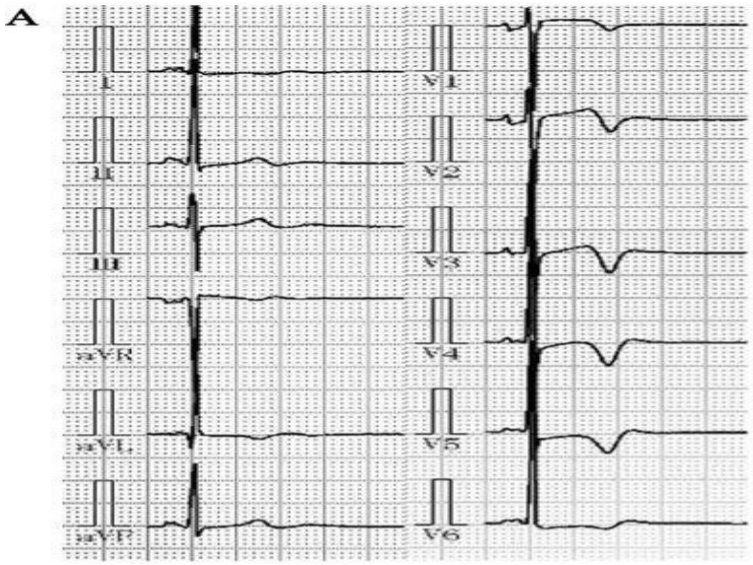


Figure 3. ECG showing high voltage QRS complexes, impaired ST segments and T wave inversion in the broad leads [19].

Whether this indicates a direct effect of cortisol, or more tightly related to disease duration than, is an interesting hypothesis that will will need further investigation. Another general EKG finding can be noticed because of hypokalemia as a short-coupled variant of torsade de pointes [20].

4. Hyperaldosteronism

Primary hyperaldosteronism due to hyperplasia of the adrenal cortex has the EKG abnormalities characteristic of hypokalemia and left ventricular hypertrophy [21]. The High levels of aldosterone could be associated with a pressure-independent remodeling of the left ventricle. Compared to patients with similar levels of hypertension, patients with primary aldosteronism have greater left ventricular hypertrophy (LVH) and an increased rate of cardiovascular complications [22] [23]. Primary hyperaldosteronism also contributes to the prolongation of the QT interval [24], in an attempt to assess gender difference in the QT interval in patient with primary hyperaldosteronism Kurisu *et al.* suggested that QTc interval was inversely associated with serum potassium level in male patients, but not in female patients (**Figure 4**) [25].

In 2007 Yu-Shien Ko *et al.* investigated the relationship between QT duration and its dispersion in patients with primary hyperaldosteronism, they concluded that QTmax correlates with aldosterone levels; however, QTd is maintained in patients with primary hyperaldosteronism. The relatively unchanged QTd which indicates the maintenance of repolarization homogeneity, may be related to the rare presentation of ventricular tachydysrhythmia in hyperaldosteronism patients [26]. In an attempt to assess the role of the autonomic nervous system in hypertension due to hyperaldosteronism, Munakata performed an analysis, which showed Supine respiratory-related power spectrum (RRP) of the RR interval, an index of cardiac parasympathetic tone, was significantly greater in patients

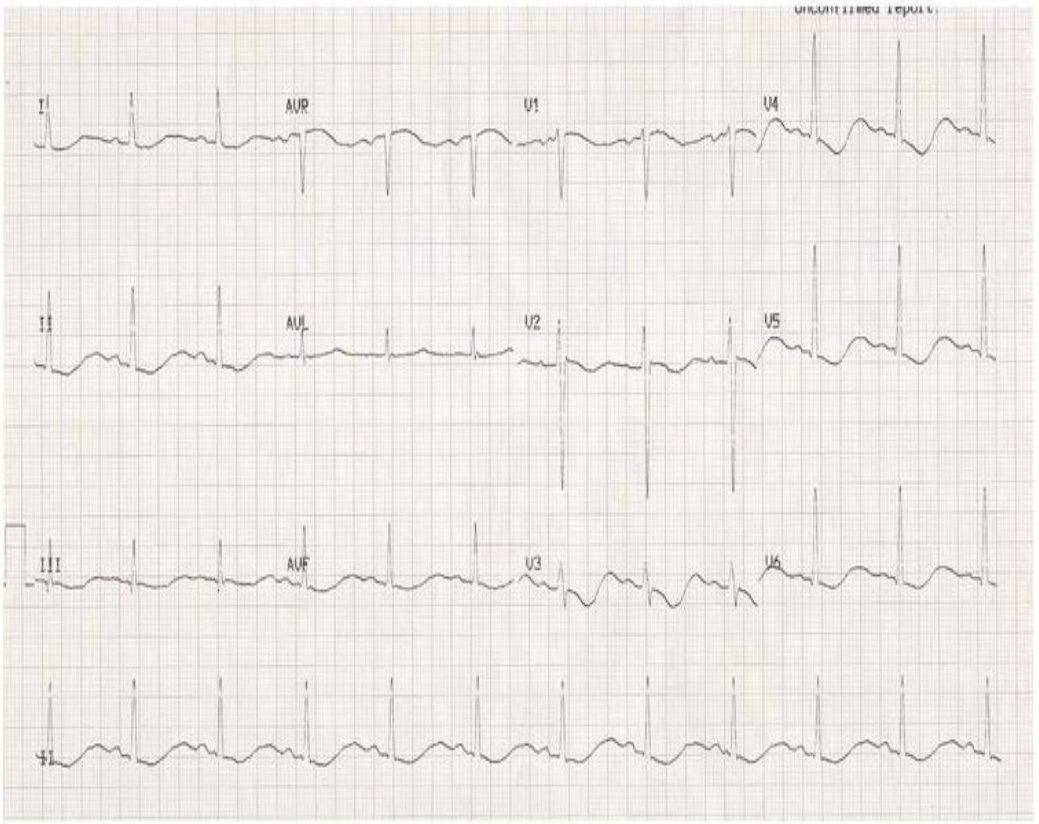


Figure 4. ECG of a hypokalemic patient showing ST depression, T wave inversion, prominent U waves and long QU interval (image originally taken from https://litfl.com/hypokalaemia-ecg-library).

with Primary hyperaldosteronism than in patients with Essential Hypertension, also the RRP of the RR interval decreased dramatically (−75%, $P < 0.01$) following adrenalectomy [27]. In 2015, Yen-Hung Lin *et al.* performed a cohort study and showed impairment of heart rhythm complexity in patients with aldosterone-producing adenoma compared to patients with essential hypertension, which is reversible by adrenalectomy. The finding was independent of blood pressure [28]. In 2015, Kurisu *et al.* stated that ECG indexes that are routinely used for LVH had high specificity, but low sensitivity in patients with primary hyperaldosteronism. Four indexes that are usually used for LVH included: Sokolow-Lyon index (SV1 + RV5), Cornell voltage index (RaVL + SV3), Cornell product index (men: (RaVL + SV3) × QRS duration, women: (RaVL + SV3 + 8) × QRS duration) and Gubner index (RI + SIII). Based on the above-mentioned study findings, Cornell voltage index and Cornell product index had a better diagnostic value for LVH in patients with primary hyperaldosteronism [29]. Atrial fibrillation [30] [31] and Ventricular fibrillation [32] [33] can be associated with hyperaldosteronism, however more studies should be performed to demonstrate the causality, in terms of direct effect of aldosterone or altered hemodynamics consequence. Hence, all the above information points out the importance of early and proper diagnosis of secondary hypertension before it gives leads to serious sequelae.

5. Addison Disease

There is some suggestion that the abnormally tall T waves found in Addison's disease are characteristically similar to those observed in hyperkalemia. However, when potassium levels are restored to normal, T wave amplitudes diminish, but EKGs remain abnormal (**Figure 5**) [34]. For more chronic cases of adrenal insufficiency, commonly encountered EKG abnormalities include abnormal T-waves or prolonged PR or QT intervals (**Figure 6**) [35].

6. Addison Crisis

EKG abnormalities related to the Addisonian crisis may present with ST depression and inverted T waves. The Addison crisis may also cause ECG changes similar to ischemia, although the mechanism of inducing ST depression and negative

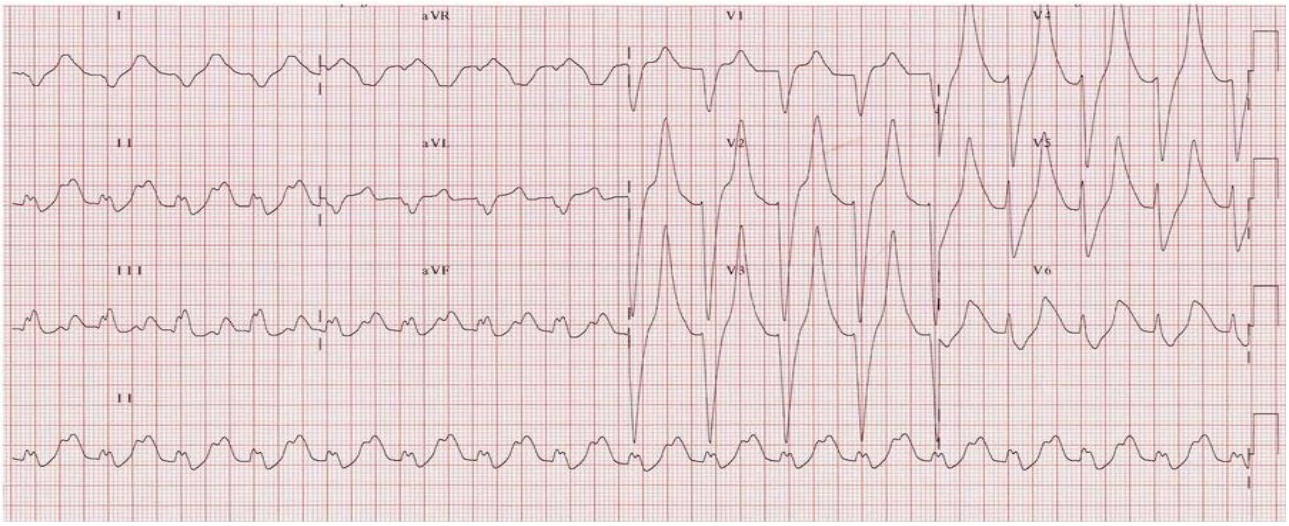


Figure 5. This patient had a serum K+ of 9.2. ECG shows prolonged PR intervals, broad bizarre QRS complexes, these merges with both the preceding P wave and subsequent T waves and Peaked T waves (https://static1.squarespace.com/static/5121177ae4b06840010a00c1/t/51239a68e4b068400110f062/1361287784417/Hyperkalemia.jpg).

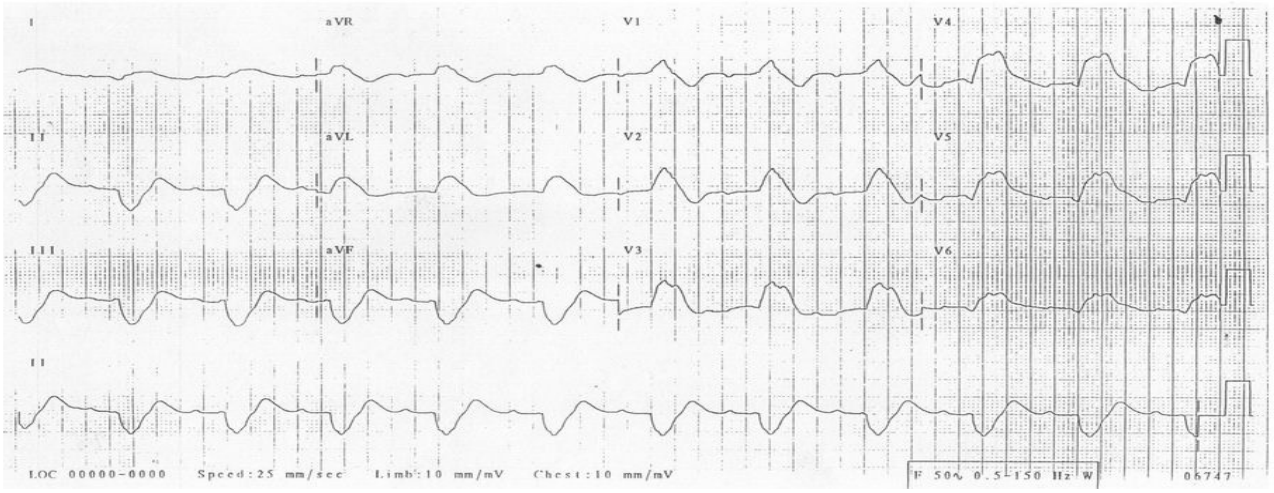


Figure 6. Long PR segment and bizarre QRS complex (https://litfl.com/hyperkalaemia-ecg-library).

T waves are currently unknown (**Figure 7**) [36]. In a few studies, a Type-1 Brugada-like ECG pattern induced by adrenal crisis has been reported [37] [38]. Brugada syndrome characterized by coved type ST-segment elevation on the right precordial leads (V1 - V3), inverted T waves, J point elevation, and broad P wave with some PQ prolongation. In 2015, Singh *et al.* [39] reported a case of Addisonian Crisis in a clinical setting of pituitary macroadenoma with persistent hypotension refractory to resuscitation, and ECG findings of ST elevation and T-wave inversion in lateral leads. Transthoracic echocardiography was suggestive of Takotsubo's cardiomyopathy with severe regional wall motion abnormalities (RWMAs) involving the left anterior descending territory and low ejection fraction (EF). It is important for clinicians to early recognize the association of ECG changes in a neurologic setting with a possible underlying endocrinology condition since, in can be lifesaving through rapid resuscitation, and supportive care to have a favorable outcome. In 2018, Manthri *et al.* [40] presented a case with ECG characteristics of sinus tachycardia, low voltage, PR suppression, and ST changes consistent with acute pericarditis as a presentation of adrenal insufficiency. The above finding shows that rare presentations in adrenal crisis through ECG changes, should be early recognized since prompt treatment can be critical to preventing morbidity and mortality.

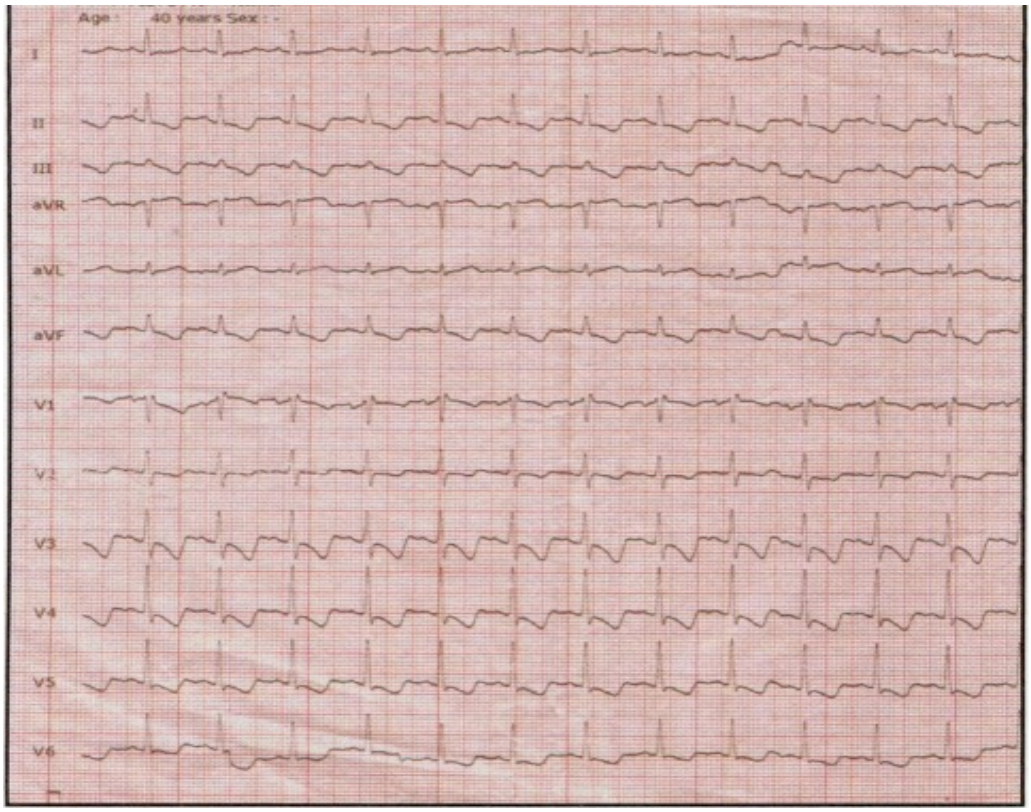


Figure 7. ST depression and negative T waves on inferior and V4 - 6 leads during the adrenal crisis. The image is taken from journal of the national medical association (https://www.researchgate.net/figure/ST-depression-and-negative-T-waves-on-inferior-and-V4-6-leads-during-adrenal-crisis_fig1_7434184).

7. Hyperthyroidism

In approximately 40% of overt hyperthyroidism cases, sinus tachycardia is observed and generally resolves after the restoration of euthyroidism [41]. This is in line with subclinical hyperthyroidism being typically associated with an increased heart rate (**Figure 8**) [42]. The second most common arrhythmia in overt hyperthyroidism is atrial fibrillation, which occurs in 10% - 15% of patients with its prevalence increasing with age (**Figure 9**) [41]. Additionally, patients with subclinical hyperthyroidism are also at an increased risk of atrial fibrillation [42] [43]. Factors that include increasing age, history of heart failure, diabetes, elevated blood pressure and left ventricular hypertrophy on ECG are independently associated with atrial fibrillation in overtly hyperthyroid patient. [44]. Although the sinus rhythm of up to two-thirds of patients with overt hyperthyroidism can be restored, increased age and duration of atrial fibrillation correspond with higher rates of persistent arrhythmia. Furthermore, there is limited evidence that treatment of subclinical hyperthyroidism aids in the reversion of atrial fibrillation to normal sinus rhythm [45]. In more recent studies, the corrected QT prolongation has been detected in patients with hyperthyroidism, and there was a correlation between the fT4 levels and the QTc intervals [46].

Example 1 - Sinus tachycardia

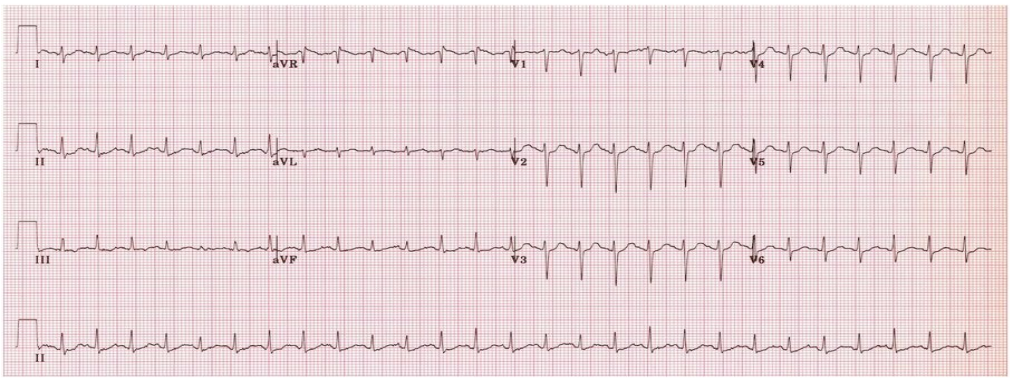


Figure 8. Image originally taken from lifeinthefastlane.

Example 2 - Rapid atrial fibrillation with high left ventricular voltage

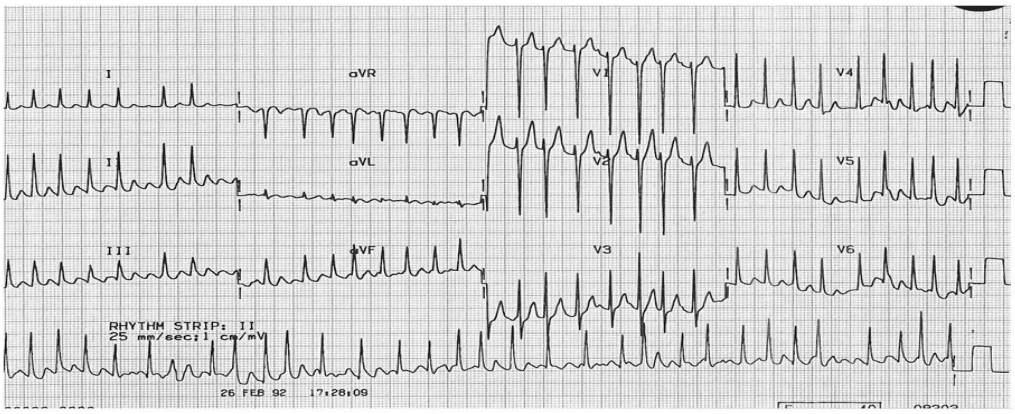


Figure 9. Image originally taken from lifeinthefastlane.

For uncommon cardiac complications of Graves' disease, acute pericarditis [47], recurrent ventricular fibrillation, and acute St segment elevation myocardial infarction [48] has been mentioned in studies.

8. Hypothyroidism

Hypothyroidism, which can be associated with congenital heart block, can show ECG changes like bradycardia, low voltage QRS complexes or small P waves, prolonged PR and QT intervals, and flattened T wave or T wave inversions (**Figure 10**) [49]. In some cases, ventricular conduction abnormalities were also associated with hypothyroidism, and could be related to QT interval prolongation (**Figure 11**, **Figure 12**) [19], which might lead to torsades de pointes [50].

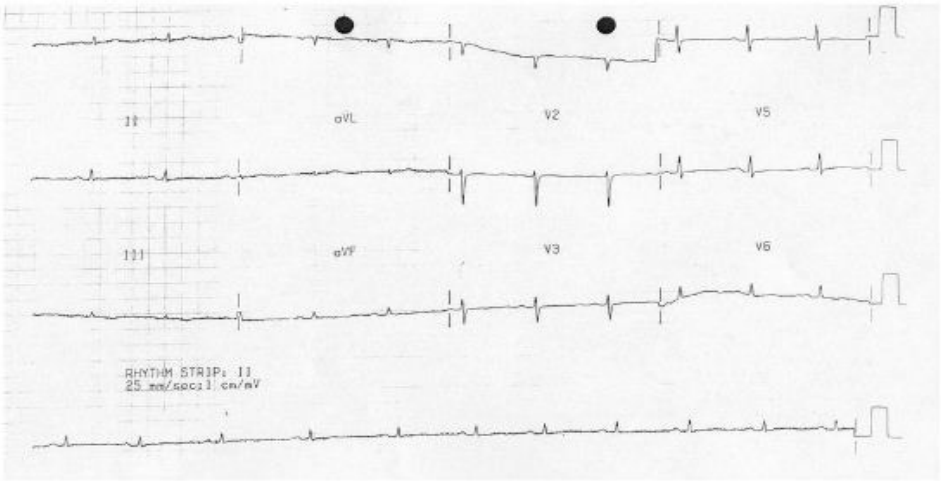


Figure 10. Low QRS complex due to myxoedema. The image is taken from life in the fast line (https://litfl.com/low-qrs-voltage-ecg-library/).

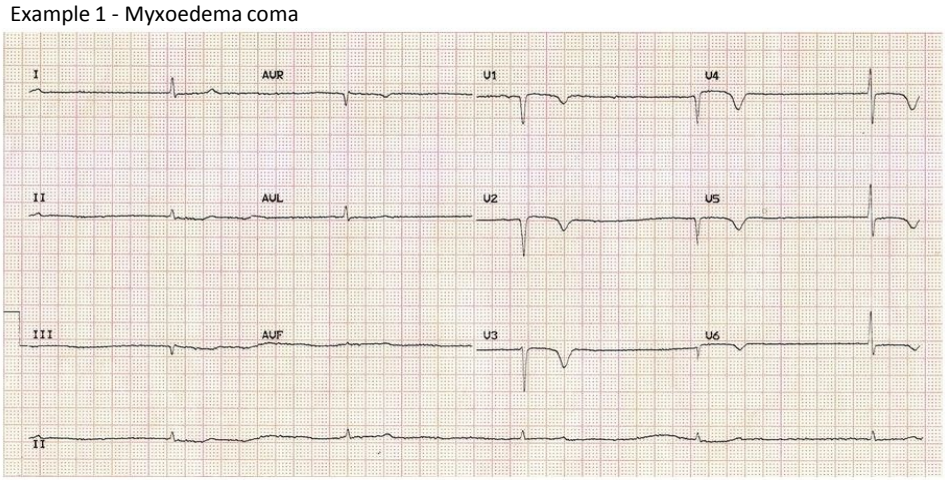


Figure 11. This is the admission ECG of 79-year-old man who was referred to the ICU with Coma, hypothermia, severe bradycardia, and hypotension refractory to inotropes. TSH was markedly elevated with an undetectable T4. The ECG shows marked bradycardia (30 bpm) with low QRS voltages (esp.in the limb leads) and widespread T-wave inversions, typical of severe myxedema (image originally taken from Life in the Fast Lane).

Example 2 - Myxoedema coma (after treatment)

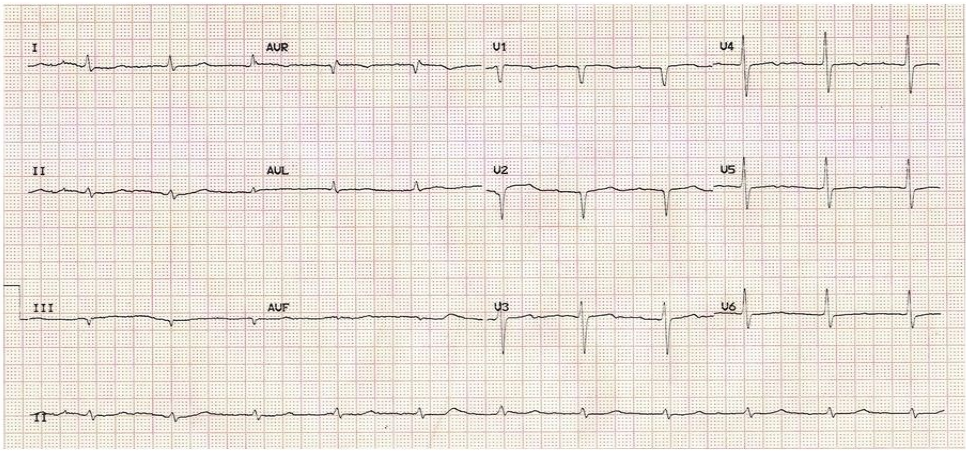


Figure 12. An ECG of the same patient shortly after initiation of thyroid replacement with intravenous T3 and T4. The heart rate has normalized and the T-wave inversion has corrected. Low voltage in the limb leads persists and is likely due to myxoedematous infiltration of the myocardium (image originally taken from Life in the Fast Lane).

Complete AV block has also been described in several case reports to be secondary to severe hypothyroidism [51].

9. Hyperparathyroidism

Primary hyperparathyroidism causes hypercalcemia, which shortens the plateau phase of the cardiac action potential and decreases the effective refractory period. This results in a shortening of the ST segment. ECG findings in significant hypercalcemia include shortened intervals of QT and QTc, increased amplitude of QRS complex, early peak, and a gradual down slope at the descending limb of the T wave. In severe hypercalcemia (serum calcium > 16 mg/dl), the duration of the T wave can increase potentially resulting in the QT interval seeming normal even though the ST segment remains shortened. Other ECG abnormalities in severe hypercalcemia include increased amplitudes of the QRS complex, ST segment elevation, diphasic T waves, prominent U waves, and J waves may also occur (**Figure 13**) [52]. However, whether hyperparathyroidism and hypercalcemia result in clinically relevant cardiac conduction abnormalities remains uncertain [53].

10. Hypoparathyroidism

Hypoparathyroidism causes hypocalcemia, which prolongs the duration of the plateau of the cardiac action potential. The distinguishing EKG manifestation of hypocalcemia is a prolongation of the QT interval due to the lengthening of the ST segment. Because hypocalcemia does not affect phase 3 of an action potential, T waves are generally uncommon. However, in some cases of severe hypocalcemia, decreased T-wave voltage, T-wave flattening, terminal T-wave inversion, and deeply inverted T waves have been described (**Figure 14**) [52]. ST segment elevation has also been associated, though rarely, with hypocalcemia [54].

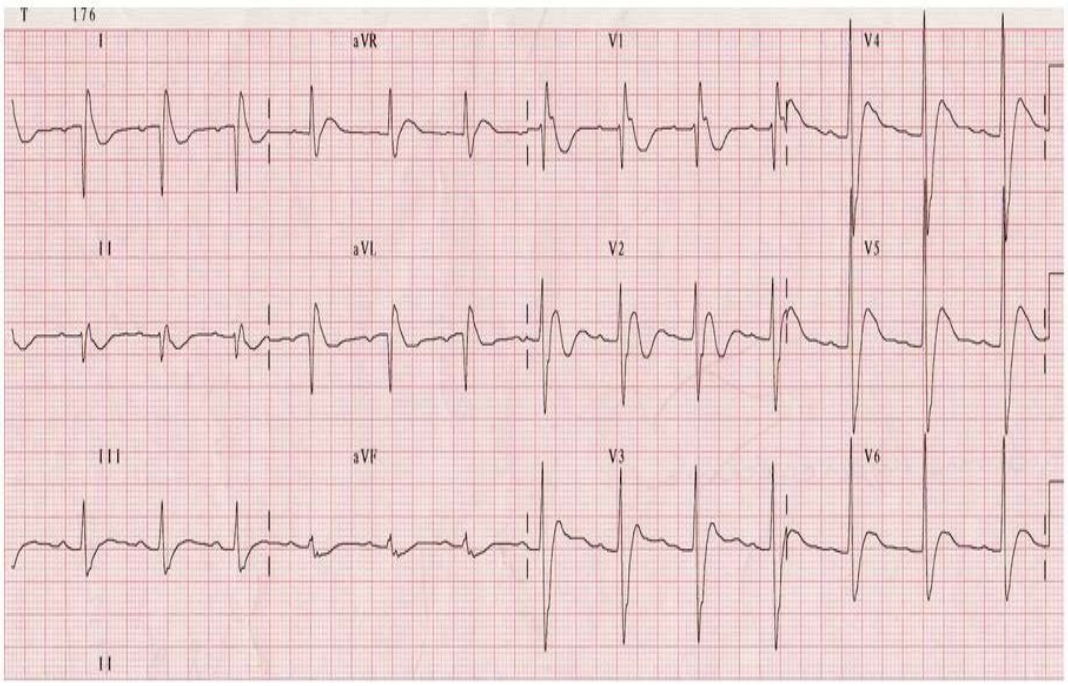


Figure 13. This is the ECG of a 41-year-old man with a parathyroid adenoma who presented to ED critically unwell with a serum calcium of 6.1 mmol/L. Bizarre looking QRS complexes, very short QT interval plus J waves-notching of the terminal QRS best seen in lead V1 (https://litfl.com/hypercalcaemia-ecg-library/).

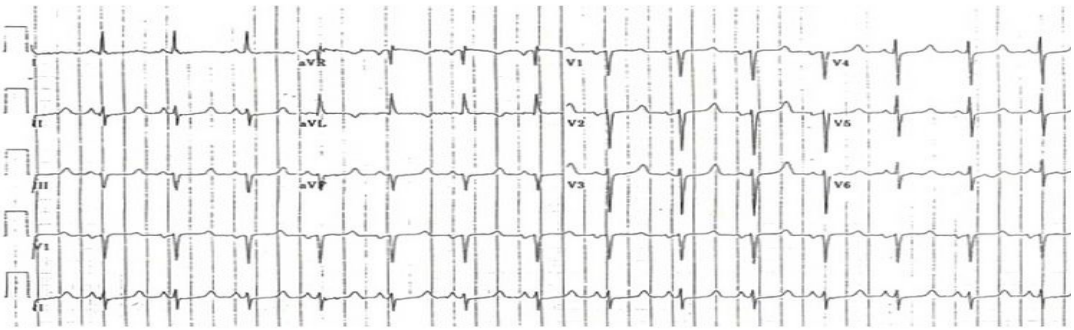


Figure 14. Hypocalcaemia causing a long QTc (510 ms) https://litfl.com/hypocalcaemia-ecg-library/.

11. Pheochromocytoma

EKG rhythms related to pheochromocytoma include right axis deviation, poor R-wave progression, inverted T waves, and QT prolongation. If there is permanent myocardial damage and development of cardiomyopathy, signs of cardiac hypertrophy and ischemia may be seen. In 20% of patients with Pheochromocytoma cardiac arrhythmias may also be seen and can include sinus tachycardia, sick sinus syndrome, supraventricular and ventricular tachycardia [55] [56] (**Figure 15**).

12. Hypothermia

In cases of mild hypothermia, the sinus rhythm predominates. The J wave, which

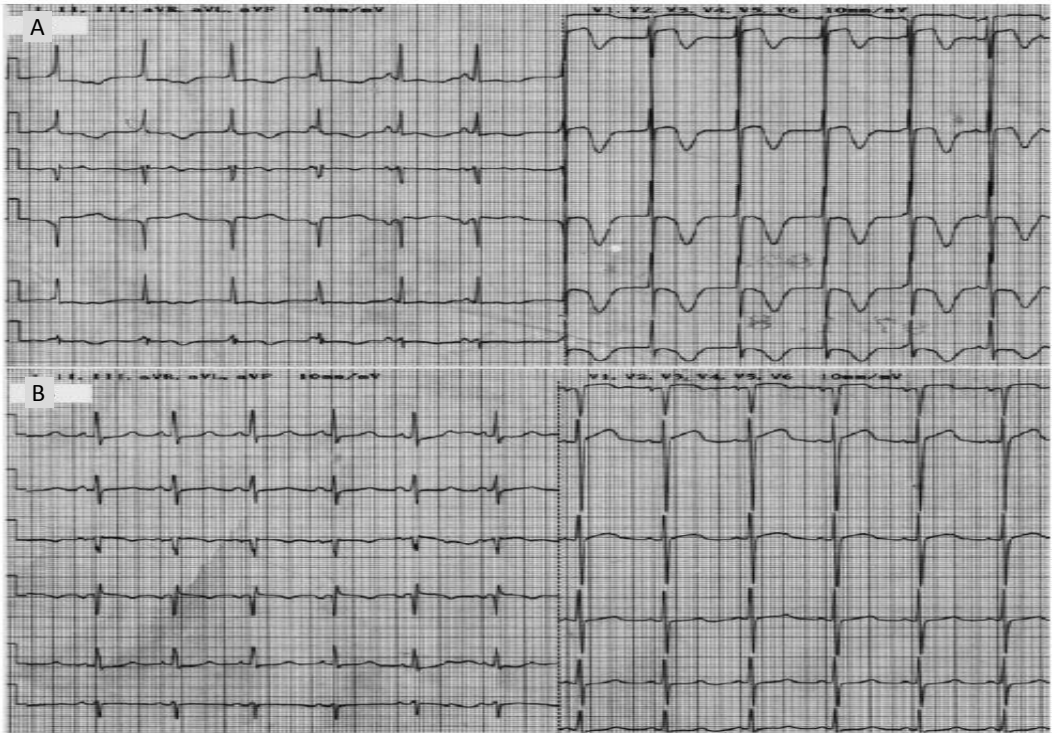


Figure 15. ECG (A) one hour after admission to the ICU showing accelerated junctional rhythm with symmetric giant T wave inversion in V2 - V6, a markedly prolonged QT interval and a ST segment elevation in V2 - V3 suggesting an acute anterior myocardial infarction. (B) After one week of treatment with phenoxybenzamine and bisoprolol, the ECG abnormalities were almost normalized (https://tpl.ncl.edu.tw/NclService/pdfdownload?filePath=lV8OirTfsslWcCxIpLbUfjpw-4y5Z-rYJXo3xSJpSiLua0Pev2U7ipxzFjBu1X1A&imgType=Bn5sH4BGpJw=&key=i8LlbJmkxhg4JkHt-u-xHu-v10UT-_WCrSYMapTPy52KgWSYS08VnQ==&xmlId=0006438412),

is also known Osborn wave or camel-hump sign, is an unique deflection observed in ECG at the point where QRS complex ends and ST segment begins [38] [39]. The J wave is usually seen when core body temperature falls below 90˚F and is consistently identified when the temperature falls below 77˚F (**Figure 16**) [57]. Sometimes it may continue to be seen in patients even after they have been rewarmed [58]. The degree of hypothermia is represented by the size of the wave. The Osborn wave (J wave) points out distorted earliest phase of membrane repolarization and are commonly identified in the precordial leads (V2 - V5), it is also rarely observed in normothermic conditions, like hypercalcemia, severe head trauma, and subarachnoid hemorrhage [58]. Another common EKG finding in patients who have hypothermia is atrial fibrillation, which occurs in 50% - 60% of cases and begins appearing at a mean body temperature of 84˚F [57]. In severe hypothermia, marked bradycardia, asystole, and ventricular fibrillation can also occur.

13. Diabetic Ketoacidosis

The ECG changes in DKA are varied, reversible, and often transient because of rapidly changing metabolic events during and after emerging from DKA. Commonly

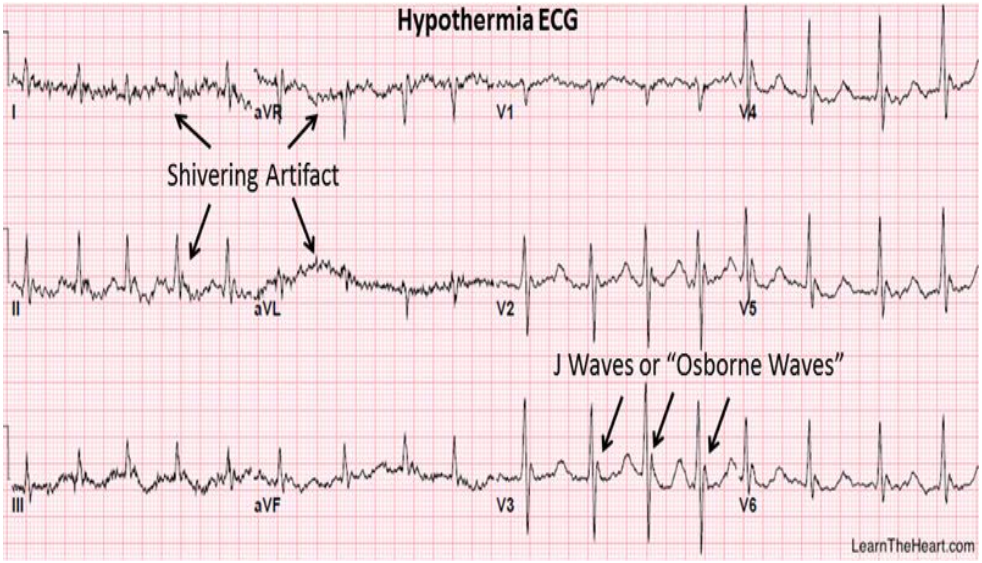


Figure 16. Image originally taken from LearnTheHeart.com.

observed ECG changes in DKA are depression of the ST segment, prolongation of the QT interval, and alterations in the amplitude and direction of T waves. Takotsubo cardiomyopathy and associated changes in ECG (eg: J wave in V4 - 5 and ST-segment elevation in V3 - 5) have been reported in a few cases of diabetic ketoacidosis [59].

14. Hypoglycemia

Electrocardiographic changes observed for hypoglycemia include ectopic activity [60] [61], flattening of the T wave, and ST depression, which have been described during both experimentally induced hypoglycemia and clinical hypoglycemic episodes [62] [63]. However, some of these changes may have been due to ischemic heart disease [64]. A brief episode of ventricular tachycardia has been reported during experimental hypoglycemia in a non-diabetic subject (**Figure 17**) [65] [66], but apart from isolated reports of transient atrial fibrillation and junctional rhythm, serious tachyarrhythmias have not been described in patients with diabetes (**Figure 18**, **Figure 19**).

15. Carcinoid Syndrome

In approximately 30% - 50% of patients with carcinoid syndrome, ECG changes are normal. The most common abnormal ECG changes seen in carcinoid syndrome are non-specific ST segment and sinus tachycardia (**Figure 20**). Occasionally P-pulmonale and right bundle branch block can also be identified. Additionally, first-degree atrioventricular block, right axis deviation or right atrial enlargement, can also be seen, though rarely [67].

16. Polycystic Ovarian Syndrome

Despite profound differences in hormonal and metabolic patterns, the ECG pattern

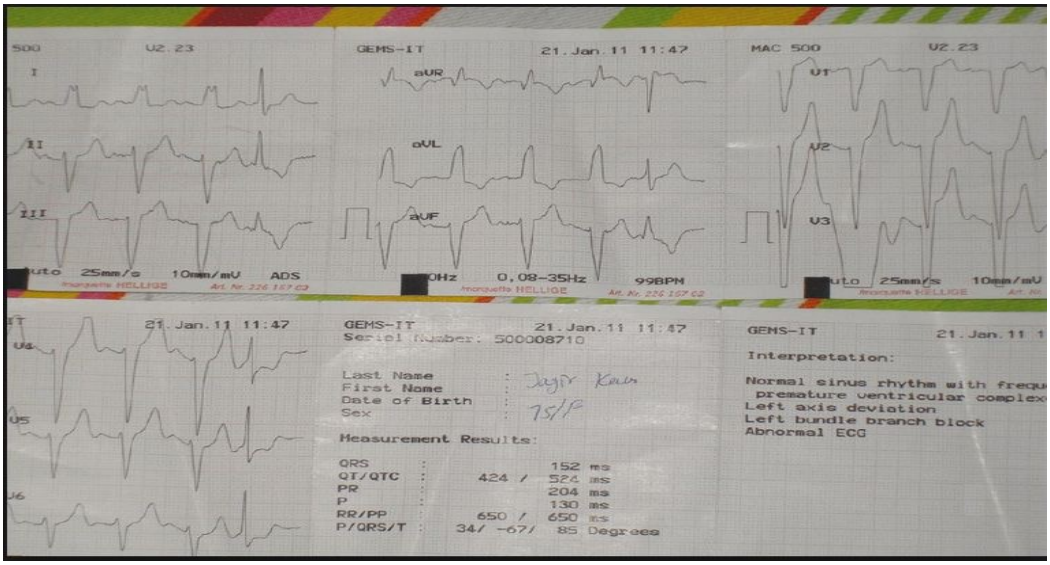


Figure 17. Normal sinus rhythm with frequent premature ventricular complexes, left axis deviation, left bundle branch block in patient with hypoglycemia (image originally taken from Indian J Endocrinol Metab. 2012 Jan-Feb; 16(1): 139-140).

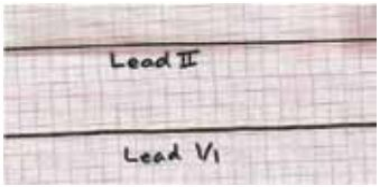


Figure 18. ECG at presentation (blood sugar 23 mgm %).

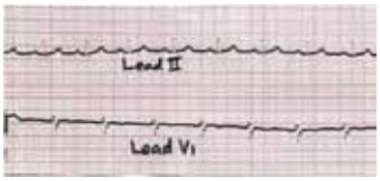


Figure 19. ECG after I/V dextrose (blood sugar 90 mgm %) (image taken from JAPI April 2011 Vol 59: ECG in Hypoglycemia: Mimic Isoelectric ECG).

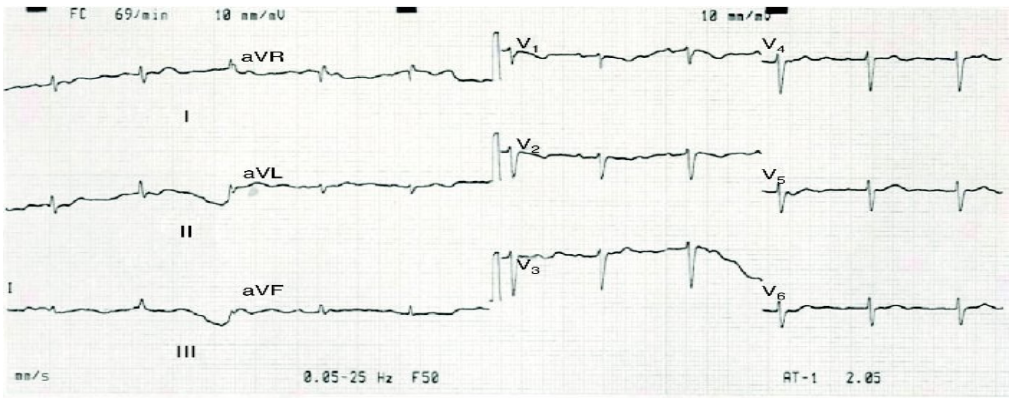


Figure 20. 12-lead electrocardiogram at admission, showing low QRS voltage in all leads in patient having carcinoid syndrome [50].

in PCOS is not significantly different from healthy individuals [68]. However, a study has suggested that PCOS is associated with widening the QRS interval [69].

17. Anorexia Nervosa

Generally, most patients with Anorexia Nervosa have normal sinus rhythm with a varying heart rate. The most striking abnormality is the frequent occurrence of T wave inversion, or flattening, and ST segment depression, which can be confused with the ECG changes in Myocardial Ischemia. Other ECG changes are lengthening of the QT interval of minor degree and escape beats in conjugation with sinus bradycardia [70].

18. Hyperkalemia

In hyperkalemia, typical ECG findings progress from tall peaked T waves and a shortened QT interval to lengthening PR interval coupled with the loss of P waves, and then a widening of the QRS complex culminating in a "sine wave" morphology [71] [72] (**Figures 21-25**).

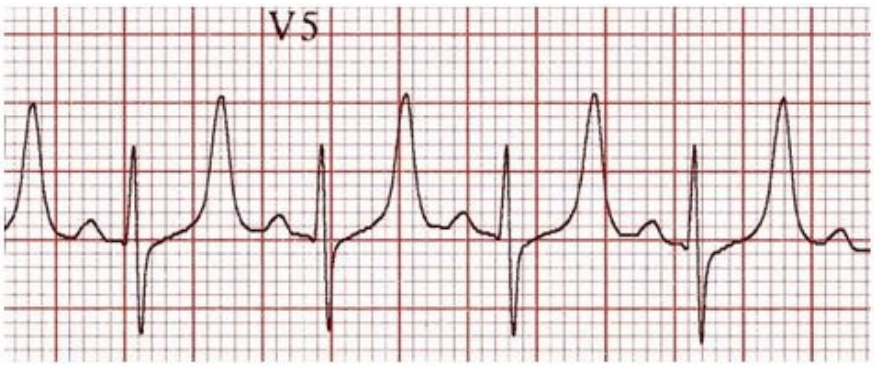


Figure 21. Amplitude of T exceeds the amplitude of R. Image originally taken from LIFTL (ECG library).

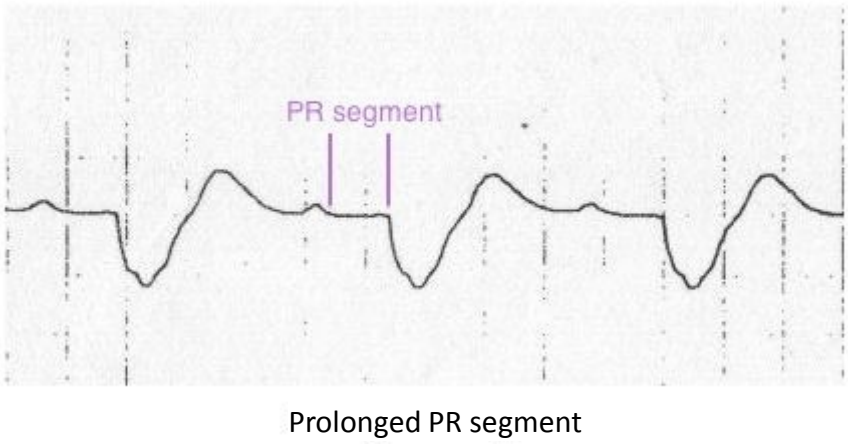
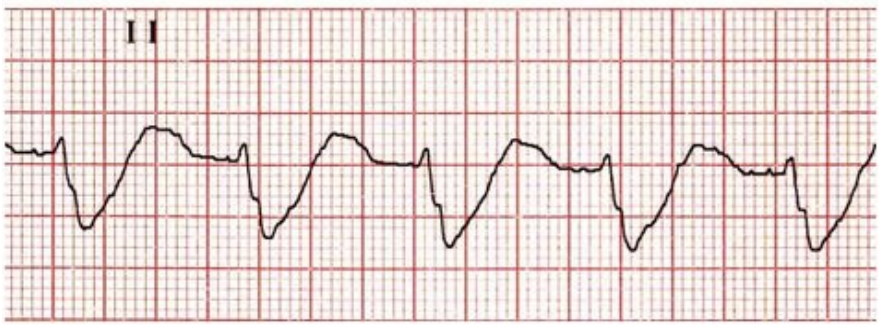
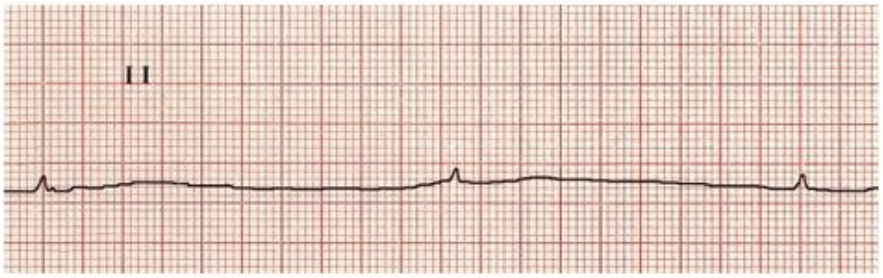


Figure 22. Image originally taken from LIFTL (ECG Library).



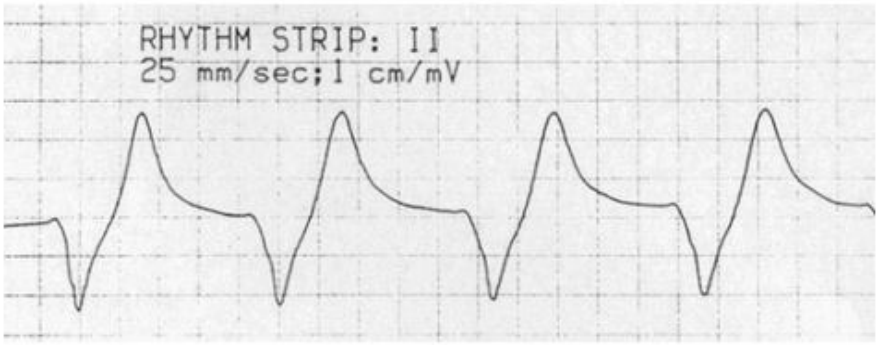
Loss of P waves

Figure 23. Image originally taken from PGHyperkalemia (milwaukee.gov).



Bradycardia

Figure 24. Image reproduced from LITFL (ECG Library).



Sine wave

Figure 25. Image reproduced from LITFL (ECG Library).

19. Hypokalemia

The common EKG manifestation associated with hypokalemia is a T wave with a smaller amplitude than usual. Reduced potassium level further, leads to depressed ST segment and T wave inversions. Prolonged PR interval along with an increase P wave amplitude is also seen. U wave is positive deflection seen after the T wave, that can be present in the mid precordial leads (V2 and V3). Serum potassium level was <3 mEq/L is identified on EKG by the increasing size of U wave amplitude than T wave amplitude. In severe hypokalemia, T and U waves fuse into big U waves leading into smaller preceding T waves. A false-prolonged QT interval, which is actually QU interval due to an absent T wave, may also be

observed. Severe hypokalemia can a use various tachyarrhythmias, that may include ventricular tachycardia/fibrillation and atrioventricular block, although rare (**Figure 26**) [73].

20. Hypermagnesemi

ECG showed prolonged PR and QT intervals with occasional ventricular arrhythmias. Hypermagnesemia may also induce ECF alterations like those induced by hyperkalemia; that is an increase in T-wave amplitude [74].

21. Hypomagnesemia

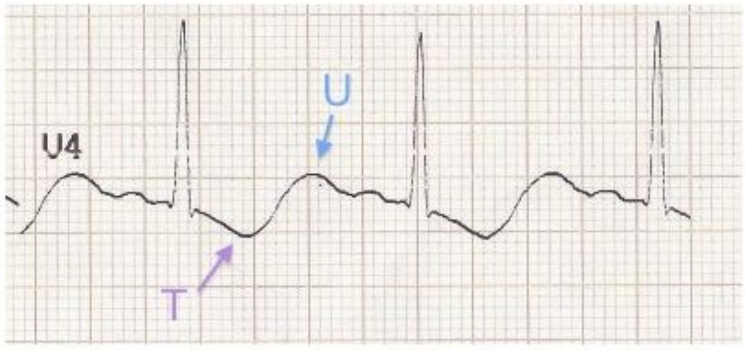
ECG showed depression of the ST segment and negative T waves.

22. Hyperphosphatemia

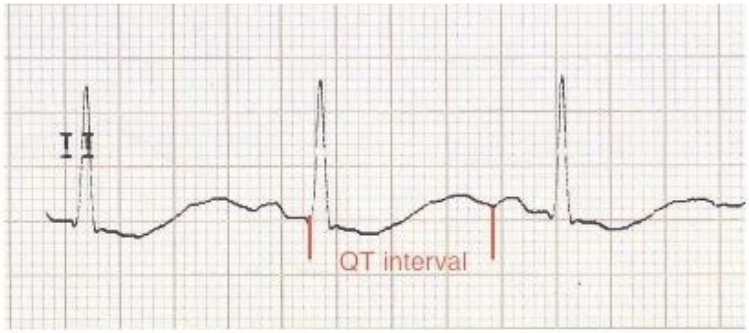
The ECG of hyperphosphatemia is prolonged QT intervals due to lengthened ST segment.

23. Diabetic Cardiac Autonomic Neuropathy

ECG of diabetic cardiac autonomic neuropathy are the higher voltage of P wave, lower voltage of T wave, shorter PQ interval, and prolonged QTc interval with tachycardia. Lower R wave voltage and the prolonged QRS complex are also seen



T wave inversion and prominent U waves in hypokalaemia



Apparent long QT interval with hypokalaemia (actually T-U fusion)

Figure 26. QU interval: the apparent pseudo prolonged QT interval is actually the QU interval with an absent T wave. Both the images originally taken from LIFTL (from ECG library).

[75]. There is significant correlation between vitamin D deficiency and heart rate variability parameters. However, there was only a borderline significant association that shows the presence of cardiac autonomic neuropathy is due to Vitamin D concentration [76].

24. Vitamin D Deficiency

Major ECG abnormalities include major Q and QS waves, ST segment depression/elevation, T wave inversion, and Ventricular conduction defects [77]. Also, there is significant correlation of Vitamin D deficiency with heart rate variability parameters [78].

25. Vitamin D Toxicity

In Vitamin D toxicity identified ECG findings are consistent with hypercalcemia. Short QT interval secondary to a shortened ST segment are the most common ECG manifestations of hypercalcemia and widened or flattened T wave may also been seen. On the other hand, significant hypercalcemia can show ECG findings that look similar to an acute myocardial infarction.

26. Menopause

Women undergoing menopause before age 40 (*i.e.*, premature menopause) have an increased risk of heart disease. Menopause declines the level of estrogen, which has a protective effect on the cardiovascular system. According to the study, more than 1.4 million womans had a higher risk of new-onset heart failure and atrial fibrillation due to premature menopause [78].

In 2020 AHA statement described a range of factors that shows a relationship between menopause and cardiovascular disease [79].

- Premature menopause increased the risk of patients of having coronary heart disease.
- Oophorectomy (*i.e.* removal of both the ovaries) causes the menopause known as surgical menopause. This process if carried out during the reproductive age can increase the risk of heart disease.
- Depression can also cause a higher risk of coronary calcification and increase cardiovascular mortality, compared to the general population with mental health disorders.
- Sleep disturbance during menopause is associated with an increased risk of metabolic syndrome, thickening of carotid intima–media, carotid plaque, aortic calcification, andarterial stiffness. Generally, these incidents are not seen in premenopausal women.

Menopausal symptoms such as hot flashes can be associated with risk factors such as hypercholesterolemia, hypertension, and insulin resistance [79].

27. Gout

Gout is a painful rheumatic disease defined as the deposition of urate crystals

between the joints and elevated serum uric acid levels, causing acute inflammatory arthritis. Several case series provided evidence of association between thyroid disorders (*i.e.*, hypothyroidism) and incident gout [80]. Thyroid hormones affect the renal functions and might cause alteration in serum uric acid levels that can lead to a major risk factor for gouty arthritis. Hypothyroidism decreases GFR that cause increased serum urate levels in patients with hypothyroidism. This alteration with kidney functions results in renal, metabolic and cardiovascular effects on the body [80]. Research correlated the relationship between gout and many cardiovascular diseases, including heart failure, heart attack, atrial fibrillation and arrhythmia. It also increases the risk of stroke and peripheral vascular disease. For example, body-wide inflammation driven by uric acid crystal buildup may damage blood vessels, according to a 2017 update on conditions linked to gout published in BMC Medicine [81]. A case report from Cumhuriyet Med J 2012 ttack and atrioventricular block. In their case, atrioventricular block appeared just after the attack of gouty arthritis and there was no other cause of AV block. Elevated levels of uric acid cause inflammation of the conduction system that may lead to transient or permanent AV block. However, this study concluded that elevated levels of uric acid should be kept in mind as one the major risk factor for Atrioventricular block and it can be treated by urate reducing therapy (**Figure 27**) [82]. Virtanen *et al.* reported a man with atrioventricular block occurring during gout attack with elevated levels of uric acid. They suggested that the cause of AV block was urate crystals deposited in the conduction system (**Figure 28**) [83]. Thus, these studies suggested that hyperuricemia may causes gouty deposits in myocardium, intima of the coronary arteries, tophus in cardiac valves, atherosclerosis leading to hypertension, AV block, and myocardial infarction [82] [83].

28. Hypogonadism

Hypogonadism is a common condition in the male population, with a higher

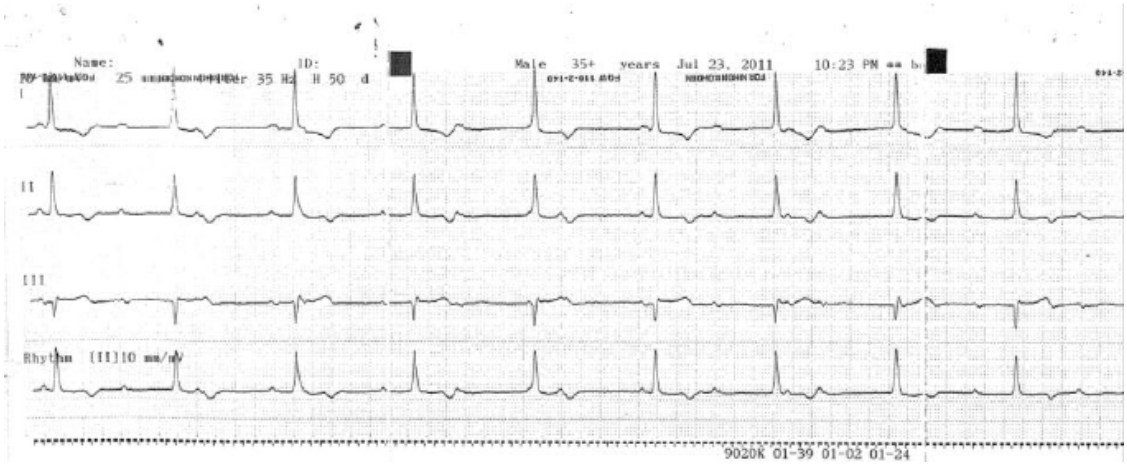


Figure 27. Initial rhythm trace consistent with initial AV blocking. (Image originally taken from Cumhuriyet Med J 2012; 34: 339-342. Case report-Olgu sunumu http://dx.doi.org/10.7197/1305-0028.1055)

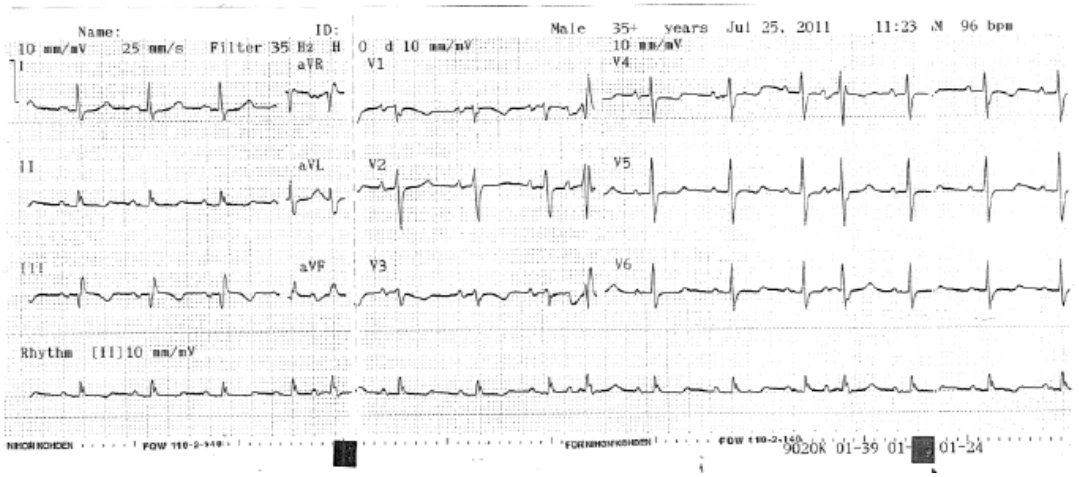


Figure 28. Electrocardiography on 5th day showing normal sinus rhythm (image originally taken from Cumhuriyet Med J 2012; 34: 339-342. Case report-Olgu sunumu https://www.researchgate.net/figure/Electrocardiography-on-the-fifth-day-showing-normal-sinus-rhythm_fig2_282644236).

prevalence in older men, obese men, and men with type 2 diabetes. Approximately 35% of men above 45 years of age, 30% - 50% with obesity and type 2 diabetes have hypogonadism [84]. Men have a higher incidence of cardiovascular disease than women, which is pointing testosterone as a risk factor cardiovascular disease. However, low testosterone has linked with obesity, metabolic syndrome, diabetes mellitus, cardiovascular disease, and erectile dysfunction. According to the experiment carried out by J Endocrinol Invest. 2019, it confirmed that corrected QTe and QTp at rest in hypogonadal patients are longer than their age-matched controls ($p < 0.05$) whereas in the recovery phase, only QTp remained significantly longer ($p < 0.050$). They also confirmed many other previous studies where it has been stated that the reduction of testosterone levels leads to QT prolongation (*i.e.*, repolarization phase). Hypogonadal patients are at an increased risk of cardiovascular disease and sudden cardiac death. Treatment of severe hypogonadism with Testosterone replacement therapy can be done by considering EKG study, independent of age and comorbidities, with preceding cardiologic counseling to avoid possible adverse events (QT) related testosterone action on the repolarization phase (**Figure 29**) [85].

29. Obesity

ECG abnormalities in obesity are due to pushed-up position of the diaphragm and the all other are results of complicated conditions. A left shift of the P, QRS and T axes, morphological deviation of the P wave, low ORS amplitude, flattening T waves (mainly in inferolateral leads) are commonly observed [86]. The prolongation of the QT and QTc intervals is caused by the increased sympathetic activity, which is a characteristic of obesity. All of this can lead to arrhythmia [86]. Patients with sleep apnea and co-existing obesity have a high risk of arrhythmia or left ventricular hypertrophy. A reduction in body weight can reverse

From: Changes in left ventricular repolarization after short-term testosterone replacement therapy in hypogonadal males

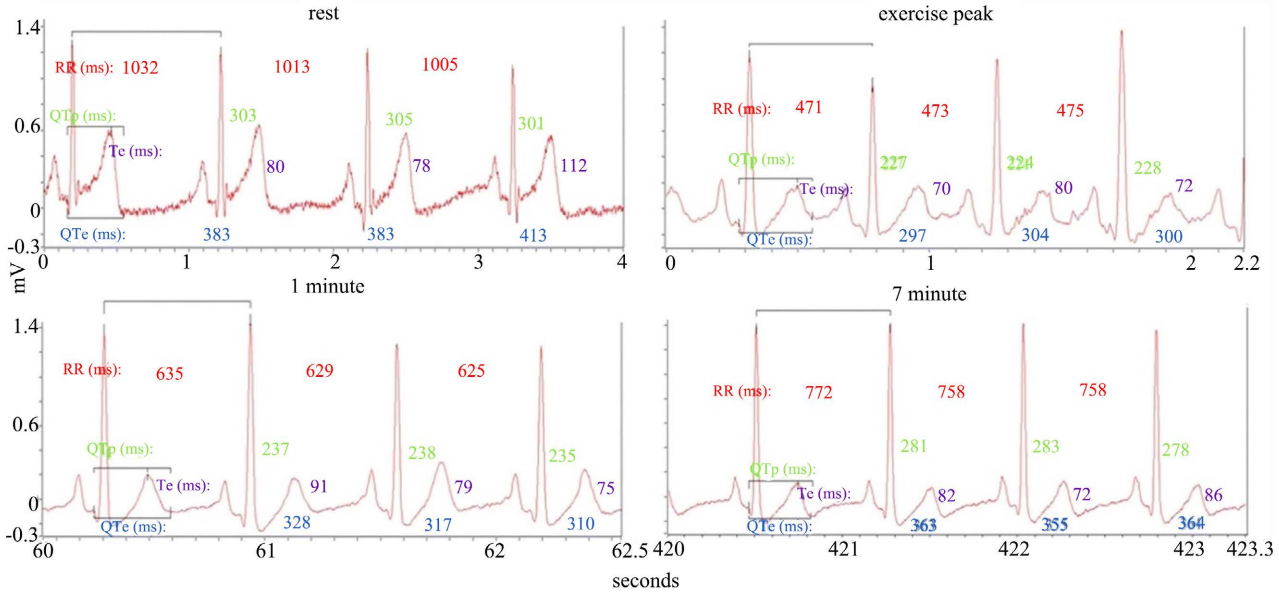


Figure 29. Representative example of RR, QTe, QTp, and Te interval measurements from a single-lead ECG at rest, during the peak, the first and the 10th min of exercise recovery (image originally taken from J Endocrinol Invest 42, 1051-1065(2019). https://doi.org/10.1007/s40618-019-01026-5).

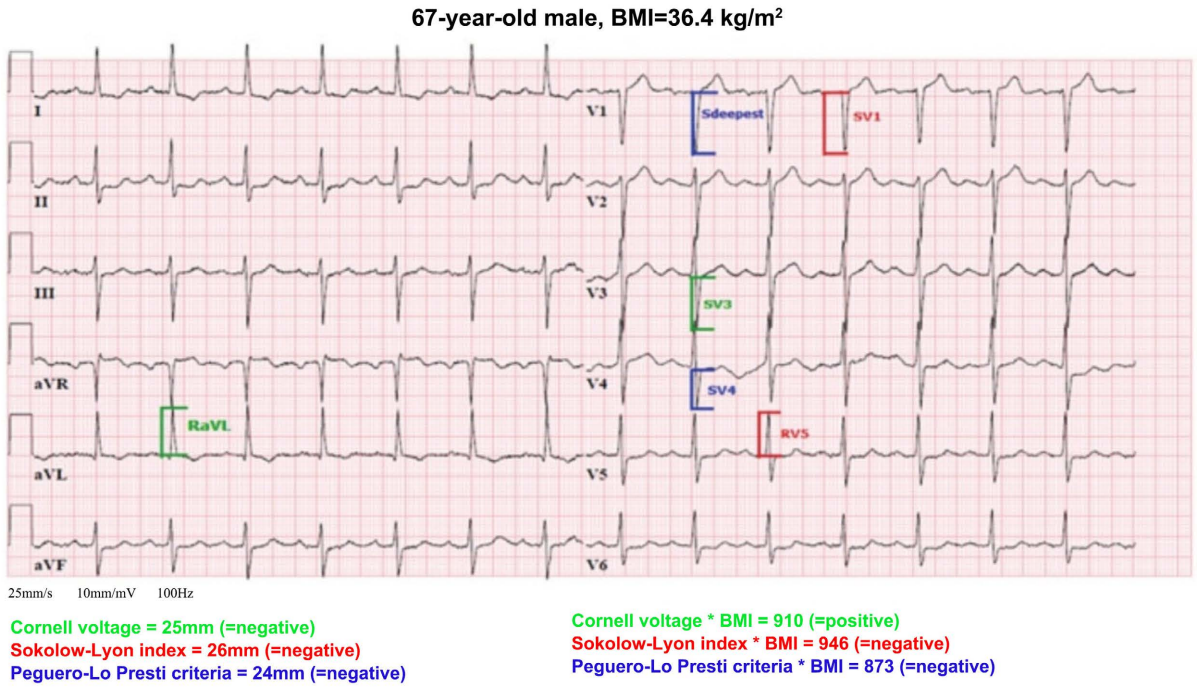


Figure 30. Electrocardiogram of a 67-year-old male obesity patient that meets the criteria for left ventricular hypertrophy based on the adjusted Cornell voltage * BMI, (RaVL + SV3) * BMI ≥ 700 mm * kg/m². The diagnosis of left ventricular hypertrophy was confirmed by an echocardiogram. Note that none of the other criteria were positive. BMI, body mass index (image originally taken from Clinical Cardiology. 2020; 43:483-490 https://doi.org/10.1002/clc.23333).

ECG abnormalities, which was confirmed in a study suggesting a reduction of mild left shift in the P and QRS axes after weight loss (**Figure 30**) [86]. The Fra-

mingham Study concluded that the mortality rate is increased 6- to 12-fold in patients with severe obesity [87]. The risk of arrhythmias and sudden death is highly increased in obese patients than in patients with cardiovascular dysfunction.

30. Osteoporosis

Osteoporosis is associated with atherosclerosis and vascular calcification. Atherosclerosis is a process of calcium deposition on the arterial wall. However, now studies have found evidence that it is not merely a process of calcium precipitation but instead an organized mechanism similar to those involved in bone mineralization [88]. Calcium plaques isolated from human atherosclerotic aorta suggested findings involved in mineral deposition, similar to that of extracellular matrix vesicles secreted from chondrocytes and osteoblasts. They have shown express proteins such as type 1 collagen, osteocalcin, BMP-2 and 4, osteopontin and many other [88]. Recent cross-sectional as well as longitudinal epidemiologic studies suggest that cardiovascular disease and bone loss are functionally interwoven. Hence, the concept that a single factor could promote mineralization in one tissue while inhibiting it in another has a biological precedent. Reduced bone mineral density has led to increased cardiovascular diseases and subclinical types of atherosclerosis in return giving rise to mortality and morbidity [87]. Third National Health and Nutrition Examination Survey (NHANES III) found a link between myocardial infarction and low BMD in multi-ethnic population of men [88] [89] Osteoporosis is widely treated with a drug called Zoledronic Acid (ZA), which is bisphosphonate. ZA increases the bone mineral density and decreases the bone fracture in patients with osteoporosis [90]. New studies pointed out that the incidence of arrhythmia and atrial fibrillation was high in patients who received intravenous infusion of ZA [90]. However, ECG results after ZA administration showed higher heart rate and significantly shorter QT intervals compared to before administration and increased in body temperature [90].

31. Conclusion

Many endocrine disorders are associated with EKG changes. The physician's awareness of EKG changes associated with endocrine disorder can help their early detection and management. Most EKG changes are reversible if detected early, and the underlying endocrinopathy is corrected.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Kahaly, G., Olshausen, K.V., Mohr-Kahaly, S., Erbel, R., Boor, S., Beyer, J., *et al.* (1992) Arrhythmia Profile in Acromegaly. *European Heart Journal*, **13**, 51-56. https://doi.org/10.1093/oxfordjournals.eurheartj.a060047

[2] Batchvarov, V. and Malik, M. (2000) Measurement and Interpretation of QT Dispersion. *Progress in Cardiovascular Diseases*, **42**, 325-344. https://doi.org/10.1053/pcad.2000.0420325

[3] Dekker, J.M., Schouten, E.G., Klootwijk, P., Pool, J. and Kromhout, D. (1994) Association between QT Interval and Coronary Heart Disease in Middle-Aged and Elderly Men. The Zutphen Study. *Circulation*, **90**, 779-785. https://doi.org/10.1161/01.CIR.90.2.779

[4] Day, C.P., McComb, J.M. and Campbell, R.W. (1994) QT Dispersion: An Indication of Arrhythmia Risk in Patients with Long QT Intervals. *Heart*, **63**, 342-344. https://doi.org/10.1136/hrt.63.6.342

[5] Mohamed, A.L., Yusoff, K., Muttalif, A.R. and Khalid, B.A. (1999) Markers of Ventricular Tachyarrythmias in Patients with Acromegaly. *Medical Journal of Malaysia*, **54**, 338-345.

[6] Haverkamp, W., Breithardt, G., Camm, A.J., Janse, M.J., Rosen, M.R., Antzelevitch, C., *et al.* (2000) The Potential for QT Prolongation and Proarrhythmia by Non-Antiarrhythmic Drugs: Clinical and Regulatory Implications. Report on a Policy Conference of the European Society of Cardiology. *European Heart Journal*, **21**, 1216-1231. https://doi.org/10.1053/euhj.2000.2249

[7] Malik, M. (2000) QT Dispersion: Time for an Obituary? *European Heart Journal*, **21**, 955-957. https://doi.org/10.1053/euhj.2000.2070

[8] Baser, H., Akar Bayram, N., Polat, B., Evranos, B., Ersoy, R., Bozkurt, E. and Cakir, B. (2014) The Evaluation of QT Intervals during Diagnosis and after Follow-up in Acromegaly Patients. *Acta Médica Portuguesa*, 27, 428-432. https://doi.org/10.20344/amp.4966

[9] Arias, M.A., Pachón, M. and Rodríguez-Padial, L. (2011) Ventricular Tachycardia in Acromegaly. *Revista Portuguesa de Cardiologia*, **30**, 223-226.

[10] Dural, M., Kabakcı, G., Çınar, N., Erbaş, T., Canpolat, U., Gürses, K.M., *et al.* (2014) Assessment of Cardiac Autonomic Functions by Heart Rate Recovery, Heart Rate Variability and QT Dynamicity Parameters in Patients with Acromegaly. *Pituitary*, **17**, 163-170. https://doi.org/10.1007/s11102-013-0482-4

[11] Ramos-Leví, A.M. and Marazuela, M. (2019) Bringing Cardiovascular Comorbidities in Acromegaly to an Update. How Should We Diagnose and Manage Them? *Frontiers in Endocrinology*, **10**, Article No. 120. https://doi.org/10.3389/fendo.2019.00120

[12] Maffei, P., Martini, C., Milanesi, A., Corfini, A., Mioni, R., de Carlo, E., *et al.* (2005) Late Potentials and Ventricular Arrhythmias in Acromegaly. *International Journal of Cardiology*, **104**, 197-203. https://doi.org/10.1016/j.ijcard.2004.12.010

[13] Fatti, L.M., Scacchi, M., Lavezzi, E., Giraldi, F.P., De Martin, M., Toja, P., Michailidis, G., Stramba-Badiale, M. and Cavagnini, F. (2006) Effects of Treatment with Somatostatin Analogues on QT Interval Duration in Acromegalic Patients. *Clinical Endocrinology*, **65**, 626-630. https://doi.org/10.1111/j.1365-2265.2006.02639.x

[14] Duron, E., Vidal, J.-S., Funalot, B., *et al.* (2014) Insulin-Like Growth Factor I, Insulin-Like Growth Factor Binding Protein 3, and Atrial Fibrillation in the Elderly. *The Journals of Gerontology*: *Series A*, **69**, 1025-1032. https://doi.org/10.1093/gerona/glt206

[15] Mancini, T., Kola, B., Mantero, F., Boscaro, M. and Arnaldi, G. (2004) High Cardiovascular Risk in Patients with Cushing's Syndrome According to 1999 WHO/ISH Guidelines. *Clinical Endocrinology*, **61**, 768-777. https://doi.org/10.1111/j.1365-2265.2004.02168.x

[16] Muiesan, M.L., Lupia, M., Salvetti, M., *et al.* (2003) Left Ventricular Structural and Functional Characteristics in Cushing's Syndrome. *Journal of the American College of Cardiology*, **41**, 2275-2279. https://doi.org/10.1016/S0735-1097(03)00493-5

[17] Alexandraki, K.I., Kaltsas, G.A., Vouliotis, A.-I., Papaioannou, T.G., Trisk, L., Zilos, A., Korbonits, M., Besser, G.M., Anastasakis, A. and Grossman, A.B. (2011) Specific Electrocardiographic Features Associated with Cushing's Disease. *Clinical Endocrinology*, **74**, 558-564. https://doi.org/10.1111/j.1365-2265.2011.03975.x

[18] Avenatti, E., Rebellato, A., Iannaccone, A., Battocchio, M., Dassie, F., Veglio, F., Milan, A. and Fallo, F. (2017) Left Ventricular Geometry and 24-H Blood Pressure Profile in Cushing's Syndrome. *Endocrine*, **55**, 547-554. https://doi.org/10.1007/s12020-016-0986-6

[19] Klein, I. and Danzi, S. (2007) Thyroid Disease and the Heart. *Circulation*, **116**, 1725-1735. https://doi.org/10.1161/CIRCULATIONAHA.106.678326

[20] Kaneko, Y., Nakajima, T., Irie, T. and Kurabayashi, M. (2011) Polymorphic Ventricular Tachycardia Complicated with Cushing Syndrome. *Internal Medicine*, **50**, 2861-2862. https://doi.org/10.2169/internalmedicine.50.6317

[21] Van Buchen, F.S.P. (1957) The Electrocardiogram and Potassium Metabolism: Electrocardiographic Abnormalities in Primary Aldosteronism and Familial Periodic Paralysis Author Links Open Overlay Panel. *The American Journal of Medicine*, **23**, 376-384. https://doi.org/10.1016/0002-9343(57)90317-0

[22] Tanabe, A., Naruse, M., Naruse, K., *et al.* (1997) Left Ventricular Hypertrophy Is More Prominent in Patients with Primary Aldosteronism than in Patients with Other Types of Secondary Hypertension. *Hypertension Research*, **20**, 85-90. https://doi.org/10.1291/hypres.20.85

[23] Milliez, P., Girerd, X., Plouin, P.F., *et al.* (2005) Evidence for an Increased Rate of Cardiovascular Events in Patients with Primary Aldosteronism. *Journal of the American College of Cardiology*, **45**, 1243-1248. https://doi.org/10.1016/j.jacc.2005.01.015

[24] Maule, S., Mulatero, P., Milan, A., *et al.* (2006) QT Interval in Patients with Primary Aldosteronism and Low-Renin Essential Hypertension. *Journal of Hypertension*, **24**, 2459-2464. https://doi.org/10.1097/01.hjh.0000251908.93298.a0

[25] Kurisu, S., Kato, Y., Mitsuba, N., *et al.* (2012) Gender Difference in QT Interval in Patients with Primary Aldosteronism. *Journal of the Renin-Angiotensin-Aldosterone System*, **13**, 435-439. https://doi.org/10.1177/1470320312447651

[26] Yang, T.-Y., Cheng, N.-J., Ko, Y.-S. and Kuo, C.-T. (2007) QT Interval Is Prolonged but QT Dispersion Is Maintained in Patients with Primary Aldosteronism. *International Journal of Clinical Practice*, **61**, 392-396. https://doi.org/10.1111/j.1742-1241.2006.00982.x

[27] Munakata, M., Imai, Y., Hashimoto, J., Omata, K., Nakao, M., Yamamoto, M. and Abe, K. (1995) Normal Sympathetic Vasomotor and Cardiac Parasympathetic Activities in Patients with Primary Aldosteronism: Assessment by Spectral Analysis. *Journal of the Autonomic Nervous System*, **52**, 213-223. https://doi.org/10.1016/0165-1838(94)00159-H

[28] Lin, Y.-H., Lin, C., Ho, Y.-H., Wu, V.-C., Lo, M.-T., Hung, K.-Y., Liu, L.-Y., Lin, L.-Y., Huang, J.-W. and Peng, C.-K. (2016) Heart Rhythm Complexity Impairment in Patients Undergoing Peritoneal Dialysis. *Scientific Reports*, **6**, Article No. 28202. https://doi.org/10.1038/srep28202

[29] Kurisu, S., Iwasaki, T., Mitsuba, N., Ishibashi, K., Dohi, Y. and Kihara, Y. (2015) Impact of Electrocardiographic Findings for Diagnosis of Left Ventricular Hyper-

trophy in Patients with Primary Aldosteronism. *Journal of the Renin-Angiotensin-Aldosterone System*, **16**, 131-136. https://doi.org/10.1177/1470320313482604

[30] Aloul, B.A., Li, J.-M., Benditt, D. and Tholakanahalli, V. (2006) Atrial Fibrillation Associated with Hypokalemia Due to Primary Hyperaldosteronism (Conn's Syndrome). *Pacing and Clinical Electrophysiology*, **29**, 1303-1305. https://doi.org/10.1111/j.1540-8159.2006.00536.x

[31] Lee, H.W., Kim, Y.J., Jin, H.Y. and Lee, K.A. (2022) Primary Aldosteronism Presenting as Embolic Myocardial Infarction. *Neuroendocrinology Letters*, **43**, 140-144.

[32] Abdo, A., Bebb, R.A. and Wilkins, G.E. (1999) Ventricular Fibrillation: An Extreme Presentation of Primary Hyperaldosteronism. *The Canadian Journal of Cardiology*, **15**, 347-348.

[33] Furukawa, A., Komatsu, R., Itoh, A., Nakamura, T., Yagishita, D., Yunoki, K., Ohashi, J., Shirai, N., Abe, Y., Nakagawa, E., Naruko, T. and Haze, K. (2007) Primary Aldosteronism with Ventricular Fibrillation: A Case Report. *Journal of Cardiology*, **50**, 77-82.

[34] Somerville, W., Levine, H.D. and Thorn, G.W. (1951) The Electrocardiogram in Addison's Disease. *Medicine*, **30**, 43-45. https://doi.org/10.1097/00005792-195102000-00003

[35] Somerville, W. (1950) The Effect of Cortisone on Cardiogram in Chronic Adrenal Insufficiency. *The BMJ*, **2**, 860-862. https://doi.org/10.1136/bmj.2.4684.860

[36] Ozcan, F., Ustun, I., Berker, D., Aydin, Y., *et al.* (2005) Inverted T Waves in Patient with Addisonian Crisis. *Journal of the National Medical Association*, **97**, 1539-1540.

[37] Dogan, M., Ertem, A.G., Cimen, T. and Yeter, E. (2015) Type-1 Brugada-Like ECG Pattern Induced by Adrenal Crisis. *Herz*, **40**, 304-306. https://doi.org/10.1007/s00059-013-3983-z

[38] Iorgoveanu, C., Zaghloul, A., Desai, A., Balakumaran, K. and Adeel, M.Y. (2018) A Case of Brugada Pattern Associated with Adrenal Insufficiency. *Cureus*, **10**, e2752. https://doi.org/10.7759/cureus.2752

[39] Singh, G., Manickam, A., Sethuraman, M. and Rathod, R.C. (2015) Takotsubo Cardiomyopathy in a Patient with Pituitary Adenoma and Secondary Adrenal Insufficiency. *Indian Journal of Critical Care Medicine*, **19**, 731-734. https://doi.org/10.4103/0972-5229.171410

[40] Manthri, S., Bandaru, S., Ibrahim, A. and Mamillapalli, C.K. (2018) Acute Pericarditis as a Presentation of Adrenal Insufficiency. *Cureus*, **10**, e2474. https://doi.org/10.7759/cureus.2474

[41] Northcote, R.J., MacFarlane, P., Kesson, C.M. and Ballantyne, D. (1986) Continuous 24-Hour Electrocardiography in Thyrotoxicosis before and after Treatment. *American Heart Journal*, **112**, 339-344. https://doi.org/10.1016/0002-8703(86)90272-3

[42] Biondi, B. and Cooper, D.S. (2008) The Clinical Significance of Subclinical Thyroid Dysfunction. *Endocrine Reviews*, **29**, 76-131. https://doi.org/10.1210/er.2006-0043

[43] Osman, F., Gammage, M.D., Sheppard, M.C. and Franklyn, J.A. (2002) Cardiac Dysrhythmias and Thyroid Dysfunction—The Hidden Menace? *The Journal of Clinical Endocrinology & Metabolism*, **87**, 963-967. https://doi.org/10.1210/jcem.87.3.8217

[44] Sawin, C.T., Geller, A., Wolf, P.A., Belanger, A.J., Baker, E., Bacharach, P., *et al.* (1994) Low Serum Thyrotropin Concentrations as a Risk Factor for Atrial Fibrillation in Older Persons. *New England Journal of Medicine*, **331**, 1249-1252.

https://doi.org/10.1056/NEJM199411103311901

[45] Osman, F., Gammage, M.D. and Franklyn, J.A. (2002) Hyperthyroidism and Cardiovascular Morbidity and Mortality. *Thyroid*, **12**, 483-487. https://doi.org/10.1089/105072502760143854

[46] Lee, Y.S., Choi, J.W., Bae, E.J., Park, W.I., Lee, H.J. and Oh, P.S. (2015) The Corrected QT (QTc) Prolongation in Hyperthyroidism and the Association of Thyroid Hormone with the QTc Interval. *Korean Journal of Pediatrics*, **58**, 263-266. https://doi.org/10.3345/kjp.2015.58.7.263

[47] Inami, T., Seino, Y., Goda, H., Okazaki, H., Shirakabe, A., Yamamoto ,M., Okajima, F., Emoto, N., Hata, N. and Shimizu, W. (2014) Acute Pericarditis: Unique Comorbidity of Thyrotoxic Crisis with Graves' Disease. *International Journal of Cardiology*, **171**, e129-e130. https://doi.org/10.1016/j.ijcard.2013.12.042

[48] Zhou, D., Qu, Z., Wang, H., Wang, Z. and Xu, Q. (2015) Severe Hyperthyroidism Presenting with Acute ST Segment Elevation Myocardial Infarction. *Case Reports in Cardiology*, **2015**, Article ID: 901214. https://doi.org/10.1155/2015/901214

[49] Tayal, B., Graff, C., Selmer, C., Kragholm, K.H., Kihlstrom, M., Nielsen, J.B., Olsen, A.S., Pietersen, A.H., Holst, A.G., Søgaard, P., Christiansen, C.B., Faber, J., Gislason, G.H., Torp-Pedersen, C. and Hansen, S.M. (2019) Thyroid Dysfunction and Electrocardiographic Changes in Subjects without Arrhythmias: A Cross-Sectional Study of Primary Healthcare Subjects from Copenhagen. *BMJ Open*, **9**, e023854. https://doi.org/10.1136/bmjopen-2018-023854

[50] Kandan, S.R. and Saha, M. (2012) Severe Primary Hypothyroidism Presenting with Torsades de Pointes. *BMJ Case Reports*, **2012**, Article ID: Bcr1220115306. https://doi.org/10.1136/bcr.12.2011.5306

[51] Schoenmakers, N., de Graaff, W.E. and Peters, R.H.J. (2008) Hypothyroidism as the Cause of Atrioventricular Block in an Elderly Patient. *Netherlands Heart Journal*, **16**, 57-59. https://doi.org/10.1007/BF03086119

[52] Wald, D.A. (2006) ECG Manifestations of Selected Metabolic and Endocrine Disorders. *Emergency Medicine Clinics of North America*, **24**, 145-157. https://doi.org/10.1016/j.emc.2005.08.010

[53] Rosenqvist, M., Nordenström, J., Andersson, M. and Edhag, O.K. (1992) Cardiac Conduction in Patients with Hypercalcaemia Due to Primary Hyperparathyroidism. *Clinical Endocrinology*, **37**, 29-33. https://doi.org/10.1111/j.1365-2265.1992.tb02279.x

[54] Lehmann, G., Deisenhofer, I., Ndrepepa, G. and Schmitt, C. (2000) ECG Changes in a 25-Year-Old Woman with Hypocalcemia Due to Hypoparathyroidism. *Chest*, **118**, 260-262. https://doi.org/10.1378/chest.118.1.260

[55] Galetta, F., Franzoni, F., Bernini, G., Poupak, F., Carpi, A., Cini, G., *et al.* (2010) Cardiovascular Complications in Patients with Pheochromocytoma: A Mini-Review. *Biomedicine & Pharmacotherapy*, **64**, 505-509. https://doi.org/10.1016/j.biopha.2009.09.014

[56] Kassim, T.A., Clarke, D.D., Mai, V.Q., Clyde, P.W. and Mohamed Shakir, K.M. (2008) Catecholamine-Induced Cardiomyopathy. *Endocrine Practice*, **14**, 1137-1149. https://doi.org/10.4158/EP.14.9.1137

[57] Mattu, A., Brady, W.J. and Perron, A.D. (2002) Electrocardiographic Manifestations of Hypothermia. *The American Journal of Emergency Medicine*, **20**, 314-326. https://doi.org/10.1053/ajem.2002.32633

[58] Vassallo, S.U., Delaney, K.A., Hoffman, R.S., Slater, W. and Goldfrank, L.R. (1999)

A Prospective Evaluation of Electrocardiographic Manifestations of Hypothermia. *Academic Emergency Medicine*, **6**, 1121-1126. https://doi.org/10.1111/j.1553-2712.1999.tb00114.x

[59] Katayama, Y., Hifumi, T., Inoue, J. and Koido, Y. (2013) A Case of Takotsubo Cardiomyopathy Induced by Accidental Hypothermia and Diabetic Ketoacidosis. *BMJ Case Reports*, **2013**, Article ID: Bcr2012008143. https://doi.org/10.1136/bcr-2012-008143

[60] Judson, W.E. and Hollander, W. (1956) The Effects of Insulin-Induced Hypoglycemia in Patients with Angina Pectoris: Before and after Intravenous Hexamethonium. *American Heart Journal*, **52**, 198-209. https://doi.org/10.1016/0002-8703(56)90259-9

[61] Shimada, R., Nakashima, T., Nunoi, K., Kohno, Y., Takeshita, A. and Omae, T. (1984) Arrhythmia during Insulin-Induced Hypoglycemia in a Diabetic Patient. *Archives of Internal Medicine*, **144**, 1068-1069. https://doi.org/10.1001/archinte.1984.00350170236036

[62] Parrish, A.E., Sugar, S.J.N. and Fazekas, J.F. (1952) A Relationship between Electrocardiographic Changes and Hypokalemia in Insulin-Induced Hypoglycemia. *American Heart Journal*, **43**, 815-820. https://doi.org/10.1016/0002-8703(52)90236-6

[63] Lloyd-Mostyn, R.H. and Oram, S. (1975) Modification by Propranolol of Cardiovascular Effects of Induced Hypoglycemia. *Lancet*, **305**, 1213-1215. https://doi.org/10.1016/S0140-6736(75)92195-9

[64] Fisher, B.M. and Frier, B.M. (1993) Effect on Vascular Disease. In: Frier, B.M. and Fisher, B.M., Eds., *Hypoglycaemia and Diabetes Clinical and Physiological Aspects*, Edward Arnold, London, 355-361.

[65] Collier, A., Matthews, D.M., Young, R.J. and Clarke, B.F. (1987) Transient Atrial Fibrillation Precipitated by Hypoglycaemia: Two Case Reports. *Postgraduate Medical Journal*, **63**, 895-897. https://doi.org/10.1136/pgmj.63.744.895

[66] Baxter, M.A., Garewal, C., Jordan, R., Wright, A.D. and Nattrass, M. (1995) Hypoglycaemia and Atrial Fibrillation. *Postgraduate Medical Journal*, **66**, 981. https://doi.org/10.1136/pgmj.66.781.981

[67] Pellikka, P.A., Tajik, A.J., Khandheria, B.K., *et al.* (1993) Carcinoid Heart Disease. Clinical and Echocardiographic Spectrum in 74 Patients. *Circulation*, **87**, 1188-1196. https://doi.org/10.1161/01.CIR.87.4.1188

[68] Orio, F., Palomba, S., Cascella, T., *et al.* (2007) Lack of Electrocardiographic Changes in Women with Polycystic Ovary Syndrome. *Clinical Endocrinology*, **67**, 46-50. https://doi.org/10.1111/j.1365-2265.2007.02833.x

[69] Huang, J.H., Tsai, J.C., Hsu, M.-I. and Chen, Y.-J. (2010) Cardiac Conductive Disturbance in Patients with Polycystic Ovary Syndrome. *Gynecological Endocrinology*, **26**, 883-888. https://doi.org/10.3109/09513590.2010.487593

[70] Thurston, J. and Marks, P. (1974) Electrocardiographic Abnormalities in Patients with Anorexia Nervosa. *Heart*, **36**, 719-723. https://doi.org/10.1136/hrt.36.7.719

[71] Mitchell, S.H. and Brady, W.J. (2023) The Electrocardiogram in Hyperkalemia. In Hudson, K.B., Sudhir, A., Glass, G. and Brady, W.J., eds., *The Electrocardiogram in Emergency and Acute Care*, John Wiley & Sons Ltd., Hoboken. https://doi.org/10.1002/9781119266938.ch16

[72] Levis, T.J. (2013) ECG Diagnosis: Hyperkalemia. *The Permanente Journal*, **17**, 69. https://doi.org/10.7812/TPP/12-088

[73] Levis, T.J. (2012) ECG Diagnosis: Hypokalemia. *The Permanente Journal*, **16**, 57.

https://doi.org/10.7812/tpp/12-015

[74] Zaman, F., Krake, P.R., Pervez, A. and Abreo, K. (2003) Severe Hypermagnesemia Resulting from Laxative Use in a Patient with Renal Insufficiency. *Southern Medical Journal*, **96**, 102-103. https://doi.org/10.1097/01.SMJ.0000049844.49028.1D

[75] Krahulec, B. and Balazovjech, I. (2002) The Effect of Cardiovascular Autonomic Neuropathy on Resting ECG in Type 1 Diabetic Patients. *Bratislavske Lekarske Listy*, **103**, 54-58.

[76] Jung, C.-H., Jung, S.-H., Kim, K.-J., Kim, B.-Y., Kim, C.-H., Kang, S.-K. and Mok, J.-O. (2015) The Relationship between Vitamin D Status and Cardiac Autonomic Neuropathy in Patients with Type 2 Diabetes Mellitus. *Diabetes & Vascular Disease Research*, **12**, 342-351. https://doi.org/10.1177/1479164115588546

[77] Tuliani, T.A., Shenoy, M., Deshmukh, A., *et al.* (2014) Major Electrocardiographic Abnormalities and 25-Hydroxy Vitamin D Deficiency: Insights from National Health and Nutrition Examination Survey-III. *Clinical Cardiology*, **37**, 11660-666. https://doi.org/10.1002/clc.22329

[78] Shin, J., Han, K., Jung, J.-H., *et al.* (2022) Age at Menopause and Risk of Heart Failure and Atrial Fibrillation: A Nationwide Cohort Study. *European Heart Journal*, **43**, 4148-4157. https://doi.org/10.1093/eurheartj/ehac364

[79] El Khoudary, S.R., Aggarwal, B., Beckie, T.M., *et al.* (2020) Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement from the American Heart Association. *Circulation*, **142**, e506-e532. https://doi.org/10.1161/CIR.0000000000000912

[80] Bruderer, S.G., Meier, C.R., Jick, S.S. and Bodmer, M. (2017) The Association between Thyroid Disorders and Incident Gout: A Populationbased Case-Control Study. *Clinical Epidemiology*, **9**, 205-215. https://doi.org/10.2147/CLEP.S128627

[81] Bardin, T. and Richette, P. (2017) Impact of Comorbidities on Gout and Hyperuricaemia: An Update on Prevalence and Treatment Options. *BMC Medicine*, **15**, Article No. 123. https://doi.org/10.1186/s12916-017-0890-9

[82] Lüneburg, O.V.G. (2012) Veränderungssperre zur Freihaltung eines ganzen Landschaftsteils. *Natur und Recht*, **34**, 339-342. https://doi.org/10.1007/s10357-012-2269-1

[83] Virtanen, K.S.I. and Halonen, P.I. (1969) Total Heart Block as a Complication of Gout. *Cardiologia*, **54**, 359-363. https://doi.org/10.1159/000166272

[84] Endocrine Society (2022) Hypogonadism in Men. Endocrine Society. https://www.endocrine.org/patient-engagement/endocrine-library/hypogonadism

[85] Piccirillo, G., Moscucci, F., Pofi, R., D'Alessandro, G., Minnetti, M., Isidori, A.M., Francomano, D., Lenzi, A., Puddu, P.E., Alexandre, J., Magrì, D. and Aversa, A. (2019) Changes in Left Ventricular Repolarization after Short-Term Testosterone Replacement Therapy in Hypogonadal Males. *Journal of Endocrinological Investigation*, **42**, 1051-1065. https://doi.org/10.1007/s40618-019-01026-5

[86] Simonyi, G. (2014) Electrocardiological Features in Obesity: The Benefits of Body Surface Potential Mapping. *Cardiorenal Medicine*, **4**, 123-129. https://doi.org/10.1159/000365012

[87] Kannel, W.B., Plehn, J.F. and Cupples, L.A. (1988) Cardiac Failure and Sudden Death in the Framingham Study. *American Heart Journal*, **115**, 869-875. https://doi.org/10.1016/0002-8703(88)90891-5

[88] Farhat, G.N. and Cauley, J.A. (2008) The Link between Osteoporosis and Cardiovascular Disease. *Clinical Cases in Mineral and Bone Metabolism*, **5**, 19-34.

[89] Magnus, J.H. and Broussard, D.L. (2005) Relationship between Bone Mineral Density and Myocardial Infarction in US Adults. *Osteoporosis International*, **16**, 2053-2062. https://doi.org/10.1007/s00198-005-1999-9

[90] Zhuang, H.F., *et al.* (2021) A Single-Center Prospective Study of 116 Women with Osteoporosis Treated with Zoledronic Acid Monitored by Echocardiography for the Development of Cardiac Arrhythmia During the Acute Phase in China. *Medical Science Monitor*, **27**, e928637. https://doi.org/10.12659/MSM.928637