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# Changes of electrocardiography in clinical outcomes of chronic kidney disease: a retrospective study

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## Abstract

Chronic Kidney disease (CKD) is a well-established major public health problem globally. CKD has been associated with increased morbidity, mortality, and rate of hospitalization, CKD is associated with increased risk of CVDs and associated mortality. Patients with CKD have multiple comorbidities and they have well-established risks that increase the risk of CVDs that may progress to end-stage renal disease (ESRD), where the kidneys are as of now not ready to satisfy the needs of the body. Both CKD and ESRD are related to an expanded gamble of cardiovascular infections (CVDs). Electrocardiographic (ECG) changes are extremely normal in patients with renal illness, particularly in those cases who have laid out CVDs. The ECG irregularities can have a likely relationship with the different reasons for CKD and can be related to different clinical results. This study aims to compare ECG abnormalities in 310 patients with CKD compared to 111 patients without CKD. The average age of the patients was 58±13.2 years with 88 females and 199 males and 250 patients having end-stage renal failure (ESRD). The resulting data showed that ECG changes revealed that 21 patients had ischemia changes (IHD), 15 had q-wave positive changes, and 65 had left ventricular hypertrophy (LVH). In conclusion, the ECG is recommended as a routine investigation in CKD/ESRD patients with DM and HTN. Moreover, evaluations should be performed based on physical examination and plans of care even when the ECG finding is negative.

**Keywords:** End-stage renal failure (ESRD); ECG abnormalities; Ischemia heart disease

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## Introduction

The kidneys can be affected by a variety of disease processes. Diseases can be due to simple viruses and bacteria. Chronic diseases like high blood pressure and hyperglycemia due to DM are the commonest causes. During damage, the kidney is unable to work efficiently as an organ leading to various clinical consequences like high blood pressure, heart failure and in many cases death of the patients. Many patients are treated with either drug or surgery (transplant) and via dialysis. There are other causes of CKD, and they include the following:

- Genetic disorder that causes many cysts to grow in the kidneys, polycystic kidney disease (PKD).
- Inflammatory causes.
- Nephrotoxic medications.
- Systemic disorders, like lupus. Lupus nephritis is the medical name for kidney disease caused by lupus
- Focal immunological processes like,
- Autoimmune disorders like Good-pasture syndrome
- Heavy metal poisoning, such as lead poisoning
- Rare genetic conditions, such as Alport syndrome
- Hemolytic uremic syndrome in children
- Henoch-Schönlein purpura
- Renal artery stenosis

Despite the development of modern technologies, the electrocardiogram (ECG) remains an Essential diagnostic tool for the evaluation of CVDs. ECG is important in the detection of cardiac rhythm abnormalities, cardiac conduction defects, and the detection of myocardial ischemia abnormalities are common in patients with CKD and they independently predict future cardiovascular events. However, there is a wide variation in reported prevalence of various ECG abnormalities in different studies. Left ventricular hypertrophy (LVH) has been found in 27.6–83% percent of CKD population. Similarly, prolonged corrected QT interval (QTc) was found in 16.9–66%, right bundle branch block (RBBB) in 2.2–12.8%, left bundle branch block (LBBB) in 6.0–9.6% and left atrial enlargement in 21.6–30% of CKD patients in different studies. CVDs are the major cause of morbidity and mortality in patients with CKD and incidence can be as high as 40 % in large scale registries. Moreover, the following common abnormalities are usually observed in ECG diagnosis. Overall, CKD patients have one or more ECG abnormalities. In order of frequency, the most common ECG change is associated with cases of CKD due to LVH and this is followed by Q waves, normal ECG, ischemia (ST-segment elevation or depression), prolonged QRS duration, tachycardia, conduction disturbances, left axis deviation, left and right atrial enlargement, arrhythmias and P-mitrale. The commonest abnormality observed in patients with CKD is LVH (Costa et al 2009). This can be seen as high (78.4%) as in one-third of patients with CKD. There is much evidence in the literature that ECG abnormalities can be as high as 50–86% of all patients. The results from two previous studies have reported almost 60% of this percentage of abnormalities.

The commonest abnormalities are left ventricular hypertrophy (LVH) and diastolic dysfunction and they represent 56.6% and 38.33 %, respectively and diagnosed by ECHO studies. LVH is the commonest abnormality observed in CKD both on ECG and

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echocardiography. Finding LVH on ECG is significant as it is independently associated with adverse cardiovascular outcomes. Moreover, trial enlargement is one of common abnormalities as well and left atrial enlargement was found in 17.6% of the patients compared to other studies which have reported a frequency of 21.6–30%.

There is higher incidence of cardiac arrest among the patient with CKD, especially when all causes of death are taken into consideration where approximately 30% are classified as cardiac arrest, death from an unknown cause or from cardiac arrhythmia. Acquired prolonged QT interval syndrome is a highly prevalent condition in patients with CKD, especially in those patients who are undergoing haemodialysis and it is one of the known pathophysiological mechanisms of sudden cardiac death in this population. QT interval prolongation is a common finding among CKD patients. Furthermore, previous data suggest that a prolonged QT interval represents a marker of cardiac repolarization defects and it is linked to the risk of cardiac arrhythmias and SCD. Patients with chronic kidney disease (CKD) have a high risk of fatal arrhythmias. One of the common abnormality observed in these patients is prolonged QT interval. The extended severe corrected QT (QTc) interval is a hallmark of ventricular arrhythmias and sudden cardiac death. Patients with CKD have mostly an acquired Long QT interval. There are various literature reports about the prevalence of LQTS and in a large scale study, it has been reported as high as 56.97%, and the prevalence of QTc prolongation (>500 ms) was 10.07%. The various potential causes for the prolongation of QT interval in these patients with CKD are, the elderly patients, impaired kidney function, hemodialysis, low serum potassium and low left ventricular ejection fraction (LVEF). Studies have suggested that corrected QT (QTc) interval is longer in individuals with CKD than those without CKD. Prolonged QTc is associated with ventricular arrhythmias, sudden cardiac death and all-cause mortality.{Zhang, 2011 #105}There is an interest in assessing the role of screening LQTC in ECG to predicting risk of adverse outcomes
in patients with CKD.

## Patients and Methods

This retrospective study employed 383 CKD (283 males and 100 females) patients and another 146 (123 males and 23 females) non-CKD patients for comparison. The history of each patient, medical records and laboratory information were reviewed to obtain data on age, sex, history of DM, hypertension and their duration, CVDs, serum creatinine, glomerular filtration rate (eGFR) and urine protein to creatinine ratio on each patient. The study had the relevant ethical clearance from Canadian Hospital in Dubai and UCLan to undertake the retrospective work. Patients were considered to have CVDs if history or review of prior medical records revealed that the patients had known prior history of cerebrovascular disease, coronary artery disease or peripheral vascular disease. All patients (n=354) had earlier undergone 12 lead electrocardiograms (ECG) at the time of admission. ECG was interpreted by a qualified physician trained in the interpretation of ECG abnormalities. ECG abnormalities were defined

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based on accepted standard criteria (Alabd et al, 2011; Moyer et al, 2012; Green et al 2011). PR interval was considered to be prolonged if it was above 200 msec. Thresh hold criteria for prolonged QRS duration was above 100 msec. Corrected QT interval (QTc) was calculated by using the following formula: QTc=QT interval divided by the square root of RR interval (in seconds). QTc was considered prolonged if it was above 446 msec in females and 444 msec in males. Tachycardia was defined as a heart rate above 100 beats/min and bradycardia was defined as a heart rate less than 60 beats/min respectively. The right axis was defined as the presence of negative QRS deflection in lead I and positive QRS deflection in lead a-VF. The left axis was defined as the presence of positive deflection of the QRS complex in lead I and negative deflection in lead II. ST-segment depression was considered to be present if there was downward or horizontal sloping of ST-segment greater than 0.05 mV below baseline measured at 0.08 second after J point in two contiguous leads.ST-segment elevation was considered to be present if ST-segment elevation was present by equal or greater than 0.1 mV and by equal or greater than 0.2 mV in leads V2 and V3, measured at the J point. Q wave was considered to be present if there was any Q-wave in leads V2–V3 equal or more than 0.02 s or Q-wave equal or more than 0.03 s in other leads. Sokolow-Lyon indices were used to establish left ventricular hypertrophy (Sherif et al 2014). Right ventricular hypertrophy (RVH), left and right atrial enlargement, left and right bundle branch blocks and bi-fascicular blocks were identified using accepted standard criteria (Moyer et al, 2012).

## Statistical Analysis

All statistical data analysis was done using the Statistical Package for Social Sciences (SPSS) and ANOVA. The data collected were tallied according to the assigned groups; Group (1) and group (2). Each question on the questionnaire was dealt with individually and the percentage of corrected responses was illustrated for each group. Data were expressed as mean ± standard deviation (SD). A value of $p<0.05$ was taken as statistically significant.

## Results

Figure 3.1 shows a typical example of a 12 lead ECG original trace in one patient with CKD (A/B). Trace (A) reveals an element of Left Bundle Branch Block Morphology. The voltage changes in the figure indicate that the patient has left ventricular hypertrophy ( LVH) There are also appropriate repolarization changes secondary to the LVH, including 1-2mm of ST elevation in V2 and V3 (B).

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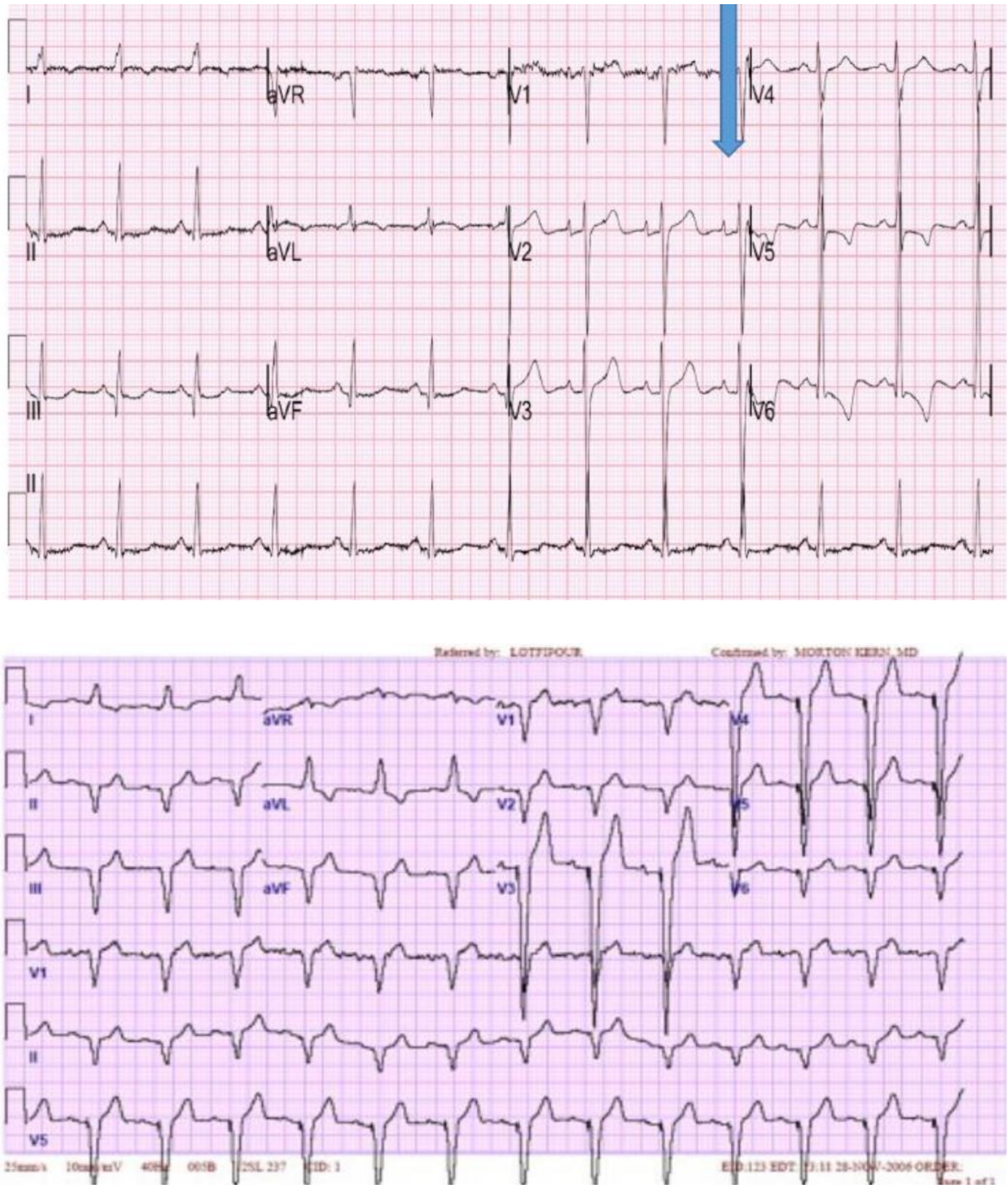


Figure 3.1:A typical example of the 12- lead original ECG recording of patients with CKD. Tracings showing a Left Bundle Branch Block Morphology (A). There is a voltage criteria that is also suggestive of LVH (B). There are appropriate repolarization changes secondary to the LVH, including 1-2 mm of ST elevation in V2 and V3. These traces are typical ECG patterns seen in patients with CKD

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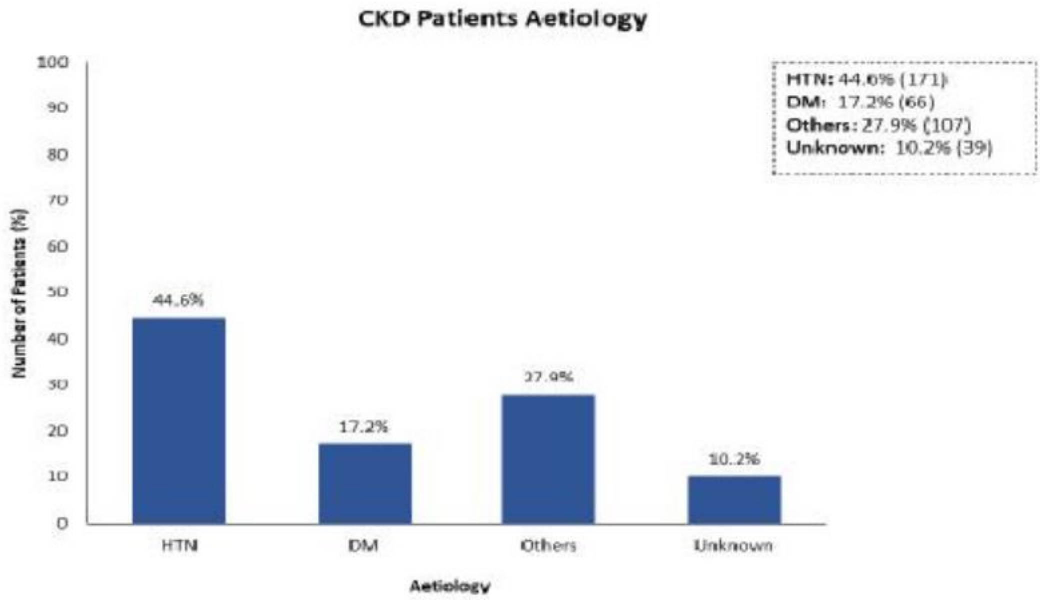


Figure 3.3: Bar charts showing the aetiologies (hypertension; HTN; Diabetes, DM, others and unknown) of the CKD patients. The data are expressed as a percentage. The inset shows both percentage and actual numbers.

Figure 3.3 shows the number of CKD patients with ECG abnormalities due to different etiologies such as hypertension (HTN; n=171), diabetes (DM; n=66), others (n=107) and unknown factors (n=39). The results show that hypertension is the commonest cause for ECG changes among CKD patients.

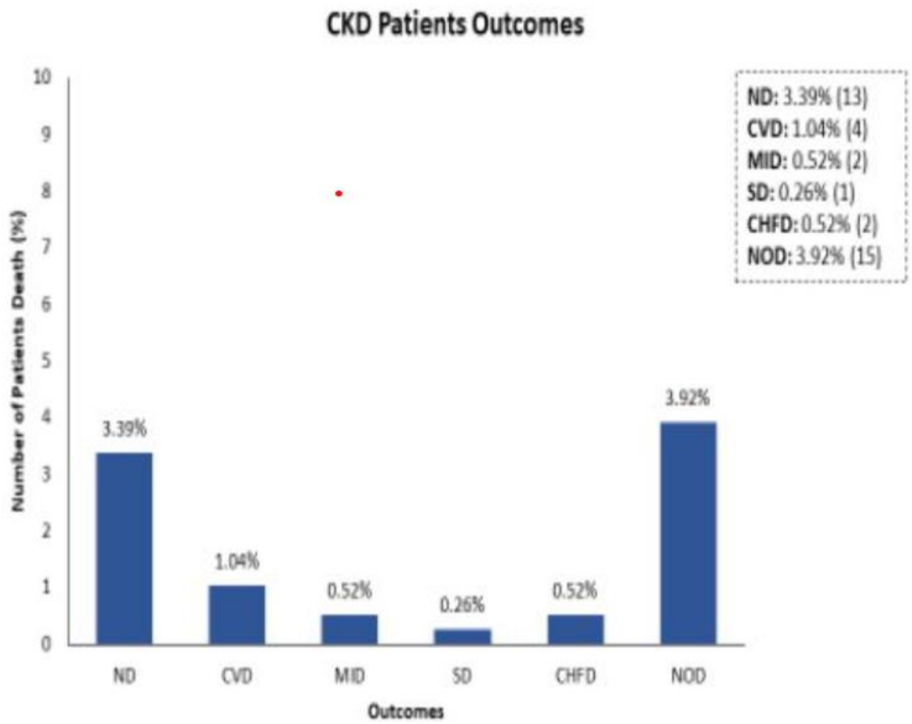

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Figure 3.4: Bar charts showing the final outcomes (who died either naturally, from CVDs, MI, strokes, CHF or new-onset dialysis) of the CKD patients. The data are expressed as a percentage. The inset shows both percentage and actual numbers.

Figure 3.4 shows the number of CKD patients who had ECG abnormalities and died because of natural deaths (ND; n=13), cardiovascular deaths (CVD; n=4), myocardial infarction deaths (MID;n=2), stroke death (SD;n=1), congestive heart failure (CHF;n= 2) and new-onset dialysis (NOD;n=15). The results show that most of the CKD patients who displayed ECG abnormalities either died from natural deaths and had new-onset dialysis. Other cardiovascular events, strokes, myocardial infarction, and heart failure were also associated with ECG abnormalities.

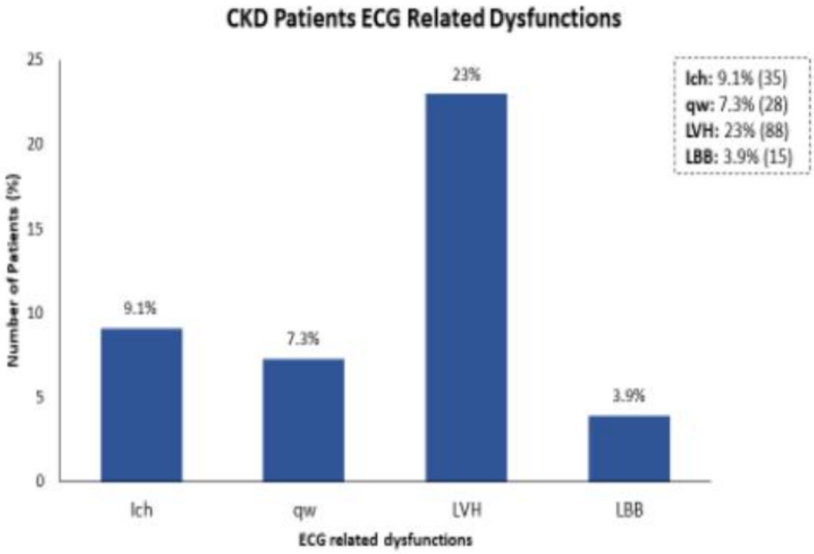


Figure 3.5: Bar charts showing typical ECG-related dysfunctions (either Ich (ischemia); qw (p-wave dysfunction); LVH, (left ventricular hypertrophy) or LBBB, (left bundle branch block) in the CKD patients. The data are expressed as a percentage. The inset shows both percentage and actual numbers.

The results presented in figure 3.5 show the number of patients who displayed ECG abnormalities due to ischemia (Ich; n=35), p-wave dysfunction (qw; n=28), left ventricular hypertrophy (LVH; n=88) and left bundle branch block (LBBB;n= 15) compared to the (n=354 )patients who had 12- lead ECG/EKG investigations. The data reveal that only (n=166 )CKD patients displayed ECG abnormalities from a total number of n=354, representing 46.89% of the patients. The results are very interesting since they suggest that almost half of all CKD patients usually have some form of cardiovascular abnormalities.

**Discussion**

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The literature confirms that patients without CKD have better survival. (80.5 ± 3.4% vs. 68.5 ± 4.0%, P = 0.017) There is some evidence that mortality benefit of CABG over PCI is not seen in dialysis patients and some other reported studies reported that even in patients with multi-vessel and/ or left main disease undergoing dialysis, PCI is not inferior to CABG in patients with CKD. It has been noted that PCI has an advantage of less stroke as compared to CABG in patients with ESRD. Chronic kidney disease (CKD) has a high prevalence in the Western world and the incidence is rising due to an increase in underlying disease processes like obesity, DM and hypertension which affect the kidney. The significant proportion of these patients progress to end-stage renal disease (ESRD) and as a result, they require either renal replacement therapy (RRT) or renal transplantation. However, the leading cause of death in these patients remains the cardiovascular disease process. It is also noteworthy that heart diseases, in particular, CAD, can lead to a heart attack which is very common in patients with kidney disease. Many comorbidities and risk factors like diabetes mellitus, dyslipidemia, obesity, and tobacco use are risks for kidney and heart diseases. In modern health care systems with good clinical care of patients and well-controlled DM and HTN, the progression of the disease to CKD can be reduced, hence improving the quality of life of patients. Non-invasive imaging to assess CAD The assessment and diagnosis of these patients with CKD/ESRD are difficult if they have no symptoms of ischemia, like chest pain or shortness of breath. One of the challenges is to demonstrate the functional capability of these patients. If the functional capacity is moderate and patients can manage (defined as ≥ 4 metabolic equivalents, then generally, it is recommended that no testing is required. However, in patients with poor functional capacity, like capacity of <4 metabolic equivalents or unknown functional status, it is a general recommended, that depending on the combined clinical and surgical risk factors, some sort of non-invasive tests should be performed for the assessment of cardiovascular risks. In the present study, CKD patients had multiple risk factors, like diabetes and hypertension, and it is generally a good practice to have a non-invasive assessment before any surgical procedure or intervention is done. A variety of investigations or tests can be done to evaluate ischemia. Simple investigations like ECG, electrocardiogram and pharmacological therapy or exercise test can be done to evaluate the CAD. Patients with CKD/ESRD are different from other patients with atherosclerotic-induced CAD as they have more intimal calcium and not much of lipid in the atheromatous plaque. However, whenever there is ischemia on non-invasive tests, then the threshold of performing the coronary angiography should be low to evaluate these patients. Patients who have atherosclerosis at other peripheral beds should also be evaluated for CAD.

1 year after device implantation. The incidence of device infection in patients with ESRD is 2 to 5 times greater than in patients without ESRD and this may be the result of frequent bloodstream access for haemodialysis. Device extraction is usually recommended as part of the treatment for device induced infection but patients with ESRD are often treated medically, Effects of renal transplantation on LV systolic function. Patients on

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dialysis with systolic heart failure are often not referred for renal transplantation because of concern about perioperative mortality and the increased risk of cardiovascular events after transplantation. Recent studies, however, have indicated that not only is the risk of perioperative death low, but improvement in LV systolic function is also frequently observed. Recommendations for Management of CHF.

All CKD patients under evaluation should have baseline echocardiography at the dry weight. For patients with an LVEF <35% not yet on RRT, right and left heart catheterization should be performed to assess for ischemic heart disease and targets for revascularization, with either PCI or CABG. Patients with CKD and who are not yet on RRT and ultra-low contrast angiography, followed by staged low- or no-contrast PCI should be considered if feasible. Treatments, such as beta-blockers and ACE inhibitors or angiotensin receptor, are recommended for these patients. This study recruited 383 patients (283 males and 100 females with a mean age of 56+-12 years) with CKD/ESRD due to diabetes, hypertension to ascertain the frequency of 12- lead ECG abnormalities and relationship to various causes of CKD. The results clearly demonstrated that ECG abnormalities are common and seen in the high proportion of patients. (166 patients). Unfortunately, 13 patients died during the study due to various cardiovascular causes. For comparison, the study recruited another 146 non-CKD patients (123 males and 23 females) who were either diabetic (66) or hypertensive (78) to investigate for any abnormal ECG and outcomes. The results show that 16 patients had ECG abnormalities (13 with t-wave and 3 with LBBB) and no patient died during the study. Most of the patients (105) were in their working years (20-60 years) compared to the older age group (31) of 61-90 years. The patients went to the UAE from 28 different countries globally, not including Emirati. Most of these non-CKD patients were Emirati and Americans. From the results, it can be concluded that early ECG changes among the patients with CKD/ESRD are common and they can help in identifying the various pathologies and it is recommended that ECG should be routinely used in a similar cohort of patients 4.20 Importance of the current study The importance of this study is that this gives us clue that ECG changes are common in these patients and every patient should have detailed medical history and examination and a baseline ECG should be performed in all patients. Further investigations and evaluations should be performed on the basis of clinical status and future plans of care. Even when the tests are negative, the interpretation of tests should be done based on pre-test probability of the tests. These patients are high risk and have multiple comorbidities and should be taken care of in specialized care centers.

## Conclusions

the ECG is recommended as a routine investigation in CKD/ESRD patients with DM and HTN. Moreover, evaluations should be performed based on physical examination and plans of care even when the ECG finding is negative.

**Conflict of Interest**

No conflicts of interest were declared by the authors.

**Financial Disclosure**

The authors declared that this study has received no financial support.

**Ethics Statement**

Not applicable.

**Authors' contributions**

All authors shared in the conception and design and interpretation of data, drafting of the manuscript and critical revision of the case study for intellectual content and final approval of the version to be published. All authors read and approved the final manuscript.

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