QT Prolongation Is an Independent Predictor of Mortality in End-Stage Renal Disease

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ABSTRACT

Background: Coronary artery disease (CAD) is the predominant cause of sudden cardiac death in the general population, and sudden cardiac death is the leading cause of mortality in end-stage renal disease (ESRD).

Hypothesis: QT-interval prolongation is an independent prognosticator in ESRD.

Methods: We reviewed clinical, electrocardiographic, stress test, and coronary angiography data on ESRD patients evaluated for transplantation at our institution between 2000 and 2004 who underwent coronary angiography. The QT interval was corrected for heart rate and QRS duration (QTc). All-cause mortality data were prospectively collected and verified against the Social Security Death Index database.

Results: During 40 ± 28 months of follow-up, 132 of the 280 (47%) patients died prior to renal transplantation. Patients with a prolonged QTc (39%) had 1-, 3-, and 5-year death-rates of 12%, 36%, and 47%, respectively, vs 8%, 24%, and 36% for those with normal QTc (log-rank $P = 0.03$). In a multivariate Cox regression model that adjusted for age, gender, diabetes mellitus, myocardial infarction, presence and severity of CAD on angiography, left ventricular (LV) hypertrophy, LV ejection fraction (EF), and multiple other variables, QTc remained to be an independent predictor of survival (hazard ratio [HR]: 1.008, 95% confidence interval [CI]: 1.001–1.014, $P = 0.016$). Female gender, decreasing LVEF, and decreasing severity of CAD on angiography were independent predictors of prolonged QTc.

Conclusions: QTc prolongation is an independent predictor of mortality in ESRD patients being evaluated for renal transplantation. The prognostic information gained from the QTc is additive to that provided by the LVEF and the severity of CAD.

Introduction

Chronic kidney disease is a major risk factor for the development of cardiovascular complications.[1] Lindner et al[2] in 1974 observed that patients with end-stage renal disease (ESRD) had a high cardiac mortality despite undergoing dialysis. They proposed that atherosclerosis is accelerated in patients with ESRD. In fact, although 45% of mortality in ESRD is due to cardiovascular causes, only 9% is directly related to myocardial infarction (MI), whereas more than one-fourth of the total mortality is attributed to sudden cardiac death (SCD).[3] The annual rate of SCD of an ESRD patient on dialysis is thus about 7%,[4] which is much higher than the 0.1%–0.2% estimated annual rate in the general population aged >35 years.[5] Although coronary artery disease (CAD) is the dominant cause of SCD in the general population,[5] it is not clear what role, if any, CAD has in the development of SCD in ESRD.[4] We have previously shown that in ESRD patients being evaluated for renal transplantation, the best predictor of mortality is the left ventricular (LV) ejection fraction (EF).[6,7] Furthermore, we have demonstrated that the heart rate response to an infusion of adenosine, a marker of cardiac autonomic function, is also a strong prognostic indicator in this population.[8] This, and other data, suggest that the SCD witnessed in ESRD could be arrhythmic in nature. We hypothesized that a prolonged QT interval will provide prognostic information in ESRD patients independent of the presence and severity of CAD.

Methods

Study Population

The study population consisted of ESRD patients who were evaluated for renal transplantation at the University of Alabama at Birmingham. At the time of evaluation, informed consent was obtained from the patients for the use of individual data for clinical, quality-improvement, and research purposes. In this sense, this database consists of all patients who have ESRD and were considered for transplantation, and not only those who were candidates for transplantation. The database has been fully described previously.[6–8] Briefly, information collected from the patients is entered into the database at the time of evaluation and outcome is followed prospectively and entered in real time into the database. Survival was

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verified using the US Social Security Death Master File at the end of follow-up. For this study we included all adult (age >18 years) ESRD patients who were evaluated between January 2000 and December 2004 and underwent coronary angiography within 6 months of being evaluated. Patients with previous heart, combined heart-lung, lung, or liver transplants were excluded. Variables extracted from the database included patient demographics (age, gender, socioeconomic status), comorbidities (diabetes mellitus, peripheral vascular disease, history of cerebrovascular accident, history of MI), habits (history of tobacco use), body mass index (calculated as weight in kg divided by height in m^2), duration on dialysis, and laboratory results (creatinine, blood urea nitrogen, albumin, glucose, hematocrit). The socioeconomic status was categorized by using educational level attained as a surrogate marker (ie, ≤12 years of formal schooling defined low socioeconomic status).

Cardiac Evaluation

All patients had a 12-lead electrocardiogram (ECG) done at the time of evaluation for renal transplantation. The ECGs were retrieved for all patients and parameters of interest were entered into the database (PR, QRS, QT, and RR intervals). LV hypertrophy (LVH) and left atrial enlargement were determined based on accepted guidelines.[9] The QT interval was corrected for the heart rate using the Bazett formula for patients with a QRS ≤120 milliseconds ($QTc = QT/\sqrt{RR\ [ms]}$). In patients with a QRS >120 milliseconds, the QT was corrected for heart rate and QRS duration as ($QTc = QT - 155 \times [60 / \text{heart rate} - 1] - 0.93 \times [QRS - 139] + k$, with $k = -22$ ms for men and -34 ms for women).[10] Patients were considered to have abnormal ECG parameters based on accepted cutpoints (PR ≥200 ms, QRS >110 ms, QTc ≥460 ms in women and ≥450 ms in men).[11,12]

Screening for CAD using stress (almost entirely with adenosine) single-photon emission computed tomography myocardial perfusion imaging was generally performed in patients age >50 years and in those with risk factors as previously described.[6–8] Perfusion was considered to be abnormal when either reversible or fixed defects were present and further labeled to denote ischemia (when any reversibility was present) or scar (exclusively fixed defects). The LVEF was measured using gated myocardial perfusion imaging.[13]

The coronary angiography results were obtained from clinical reports and expressed as 1-, 2, or 3-vessel disease based on >50% lumen-diameter narrowing in any of the 3 coronary arteries or their major branches. For the purpose of this analysis, >50% lumen-diameter narrowing of the left main coronary artery was considered equivalent to 2-vessel disease. In the absence of any of the above, CAD was considered to be angiographically absent.

Statistical Analysis

All statistical analyses were carried out using SPSS version 11.5 for Windows (SPSS Inc., Chicago, IL). Continuous variables are presented as mean ± SD and discrete variables as frequencies and percentages. The χ^2 test was used for the comparison of categorical variables. Continuous variables were compared using the unpaired Student *t* test or the Mann-Whitney test, as appropriate. In order to determine the independent predictors of a prolonged QTc, a multivariate binary logistic analysis was performed using all variables in Table 1 with a *P* value <0.2. Follow-up time was calculated from the time of evaluation to mortality or to end of follow-up on July 1, 2009, or at the time of renal transplantation. Event-free survival curves were constructed using the product-limit method (Kaplan-Meier method) and differences among survival curves were estimated by the log-rank test. Cox proportional hazard analysis was used to estimate adjusted (multivariate) risks for overall mortality. Estimated risks were reported as hazard ratios (HR) with correspondent 95% confidence intervals (CI). All tests were 2-tailed, and a *P* value of ≤0.05 was considered statistically significant.

Results

The study population consisted of 280 ESRD patients who were evaluated for possible renal transplantation and underwent coronary angiography. The baseline characteristics of the cohort are summarized in Table 1. Myocardial perfusion imaging was not performed in 53 patients (19%), was normal in 33 patients (12%), and was abnormal in the remaining patients, which often was the reason to undergo coronary angiography. As expected, a large proportion (60%) had diabetes mellitus and evidence of LVH by ECG (47%). One-quarter (26%) had a history of MI but more than half (63%) had CAD on coronary angiography.

The PR interval was prolonged in 43 (15%) patients and could not be measured in 4 (1.4%) patients due to the presence of atrial fibrillation or a junctional rhythm. Patients with a prolonged PR were older, had a wider QRS complex, and were more likely to have evidence of LVH on their ECG. The QRS interval was prolonged in 51 (18%) patients and those with prolonged QRS were older, had a longer PR interval, and demonstrated more severe CAD on angiography. The QTc was prolonged in 108 (39%) patients. The group with a prolonged QTc was younger and had a higher proportion of females. These patients were on dialysis for a slightly longer duration, were more obese, had a higher serum glucose level, and had more prior cerebrovascular accidents. This group had less MI and less-severe CAD on angiography. Although a similar proportion of patients on hemodialysis (n = 196) and peritoneal dialysis (n = 39) had prolonged QTc (43% and 38%, respectively, $P = 0.6$), ESRD patients who have not been started on dialysis (n = 45) had a lower prevalence

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Table 1. Baseline Characteristics

Characteristic	All Patients (n = 280)	PR <200 ms (n = 233)	PR ≥200 ms (n = 43)	*P* Value	QRS ≤110 ms (n = 229)	QRS >110 ms (n = 51)	*P* Value	QTc <450 ms in women / <460 ms in men (n = 172)	QTc ≥450 ms in women / ≥460 ms in men (n = 108)	*P* Value
Age (y)	53 ± 9	52 ± 9	56 ± 9	0.02	52 ± 9	55 ± 10	0.04	54 ± 9	51 ± 10	0.005
Female gender	107 (38)	93 (40)	14 (33)	0.4	91 (40)	16 (31)	0.3	49 (29)	58 (54)	<0.0001
DM	168 (60)	139 (60)	28 (65)	0.6	135 (59)	33 (65)	0.5	97 (56)	71 (66)	0.1
PVD	58 (21)	49 (21)	9 (21)	1.0	47 (21)	11 (22)	0.9	29 (17)	29 (27)	0.05
CVA	35 (13)	30 (13)	5 (12)	0.8	29 (13)	6 (12)	0.8	16 (9)	19 (18)	0.02
MI	73 (26)	63 (27)	10 (23)	0.6	61 (27)	12 (24)	0.6	50 (29)	23 (21)	0.04
History of tobacco use	101 (37)	85 (38)	14 (34)	0.7	87 (40)	14 (28)	0.1	65 (40)	36 (34)	0.4
Low SES[a]	172 (61)	148 (64)	21 (49)	0.09	141 (62)	31 (61)	1.0	102 (59)	70 (65)	0.4
Time on dialysis (mo)	19 ± 28	18 ± 24	30 ± 42	0.4	19 ± 27	23 ± 31	0.4	17 ± 26	23 ± 31	0.01
BUN (mg/dL)	55 ± 67	55 ± 73	55 ± 20	1.0	56 ± 74	51 ± 18	0.7	57 ± 84	51 ± 21	0.5
Creatinine (mg/dL)	8.5 ± 5.0	8.4 ± 5.3	9.0 ± 3.2	0.1	8.3 ± 3.1	9.5 ± 9.8	0.8	8.5 ± 6.1	8.5 ± 2.8	0.3
Albumin (g/dL)	3.4 ± 0.5	3.4 ± 0.5	3.4 ± 0.3	0.8	3.4 ± 0.5	3.4 ± 0.4	0.7	3.5 ± 0.5	3.4 ± 0.4	0.05
Glucose (mg/dL)	144 ± 82	144 ± 82	148 ± 87	1.0	145 ± 84	141 ± 76	0.7	138 ± 84	154 ± 79	0.04
Hct (%)	36 ± 5	36 ± 5	36 ± 5	0.7	36 ± 5	35 ± 5	0.4	36 ± 5	36 ± 5	1.0
BMI (kg/m^2)	28 ± 5	28 ± 6	29 ± 4	0.2	28 ± 5	29 ± 5	0.4	28 ± 5	30 ± 6	0.003
PR (ms)	172 ± 30	163 ± 19	222 ± 26	<0.0001	168 ± 26	189 ± 40	<0.0001	173 ± 33	169 ± 24	0.5
QRS (ms)	99 ± 17	96 ± 16	111 ± 21	<0.0001	93 ± 9	127 ± 17	<0.0001	100 ± 19	97 ± 14	0.4
QTc (ms)	447 ± 35	448 ± 34	441 ± 27	0.3	448 ± 34	442 ± 36	0.2	427 ± 22	479 ± 24	<0.0001
LVH[b]	132 (47)	104 (45)	27 (63)	0.03	102 (45)	30 (59)	0.09	81 (47)	51 (47)	1.0
LAE[b]	72 (26)	60 (26)	12 (28)	0.8	56 (25)	16 (31)	0.4	38 (22)	34 (32)	0.09
Abnormal MPI	194 (85)	158 (85)	34 (87)	1.0	155 (85)	39 (87)	1.0	125 (85)	69 (86)	0.8
Ischemia[c]	167 (74)	135 (73)	30 (77)	0.7	132 (73)	35 (78)	1.0	112 (76)	55 (69)	0.3
LVEF (%)[c]	47 ± 12	48 ± 12	45 ± 11	0.2	48 ± 12	44 ± 12	0.06	49 ± 12	45 ± 12	0.06
CAD[d]	173 (63)	142 (62)	29 (69)	0.4	137 (61)	36 (71)	0.3	120 (70)	53 (51)	0.002
No. of diseased coronary arteries[d]	1.4 ± 1.3	1.4 ± 1.3	1.7 ± 1.3	0.1	1.3 ± 1.3	1.8 ± 1.3	0.03	1.7 ± 1.3	1.0 ± 1.2	<0.0001

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; CAD, coronary artery disease; CVA, cerebrovascular accident; DM, diabetes mellitus; Hct, hematocrit; LAE, left atrial enlargement; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; MI, myocardial infarction; mo, months; MPI, myocardial perfusion imaging; n, number of patients; PVD, peripheral vascular disease; PR, PR interval; QRS, QRS interval; QTc, corrected QT interval; SES, socioeconomic status; y, years.
Continuous variables are presented as mean ± SD and discrete variables as n (%).
[a] Low SES was defined as ≤12 years of formal education.
[b] LAE and LVH were diagnosed by electrocardiography.
[c] LVEF was measured by gated MPI and ischemia was considered present when a perfusion defect on MPI exhibited partial or complete reversibility.
[d] CAD was diagnosed by coronary angiography.

of prolonged QTc (18% vs 43% for those on dialysis, $P = 0.001$). In a multivariate binary logistic model, female gender, decreasing LVEF, and decreasing severity of CAD on angiography were independent predictors of a prolonged QTc (Table 2).

The cohort was followed up for period of 40 ± 28 months, during which time 132 (47%) patients died and 84 (30%) patients underwent renal transplantation. The deaths occurred at a mean follow-up of 33 ± 23 months and the renal transplantation occurred after a mean of 25 ± 21 months from evaluation. We therefore accrued 929 person-years of follow-up. PR and QRS prolongation were not associated with worse survival on follow-up (log-rank *P* values of 0.8 and 0.4, respectively). Patients with a prolonged QTc had significantly worse survival (Figure, log-rank $P = 0.03$). The 1-, 3-, and 5-year death

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Table 2. Multivariate Predictors of Prolonged QTc in Patients With End-Stage Renal Disease Being Evaluated for Renal Transplantation

Variable	Adjusted HR	95% CI	*P* Value
Age (y)[a]	0.968	0.931–1.006	0.101
Female gender	2.272	1.102–4.683	0.026
DM	1.209	0.529–2.764	0.653
PVD	1.715	0.730–4.032	0.216
CVA	0.391	0.145–1.054	0.064
MI	1.105	0.495–2.467	0.808
Time on dialysis (mo)[a]	1.006	0.993–1.018	0.366
Albumin (g/dL)[a]	0.956	0.429–2.130	0.912
Glucose (mg/dL)[a]	1.004	1.000–1.009	0.068
BMI (kg/m²)[a]	1.060	0.991–1.135	0.091
LAE[b]	1.601	0.749–3.422	0.224
LVEF (%)[c]	0.961	0.932–0.991	0.01
CAD[d]	1.685	0.418–6.789	0.463
No. of diseased coronary arteries[d]	0.564	0.334–0.953	0.032

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CVA, cerebrovascular accident; DM, diabetes mellitus; HR, hazard ratio; LAE, left atrial enlargement; LVEF; left ventricular ejection fraction; MI, myocardial infarction; mo, months; MPI, myocardial perfusion imaging; PVD, peripheral vascular disease; y, years.
[a] Continuous variable.
[b] LAE was diagnosed by electrocardiography.
[c] LVEF was measured by gated MPI.
[d] CAD was diagnosed by coronary angiography.

rates for patients with a normal QTc were 8%, 24%, and 36%, respectively, vs 12%, 36%, and 47% for those with a prolonged QTc. In an initial Cox proportional hazard analysis model adjusted for age and gender, increasing QTc was associated with increased mortality (HR: 1.005, 95% CI: 1.000–1.010, $P = 0.03$). After further adjustments for the multiple variables listed in Table 3, QTc remained to be an independent predictor of survival. In the multivariate model, female gender, QTc, LVEF, a history of MI, and the severity of CAD were independently associated with survival. With full adjustment, each 10-millisecond increase in the QTc was associated with 8% increased mortality over the follow-up period of the study (HR: 1.008, 95% CI: 1.001–1.014, $P = 0.016$).

Discussion

The major finding of this study is that QTc prolongation on a 12-lead ECG is a common and independent predictor of mortality in ESRD patients being evaluated for renal

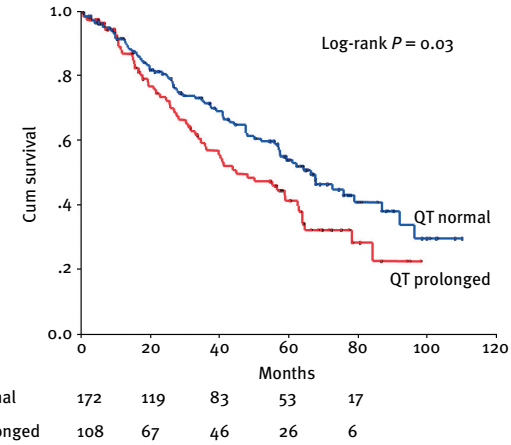

Figure 1. Kaplan-Meier analysis for survival. End-stage renal disease patients with a prolonged QTc had higher cumulative mortality than those with a normal QTc. The number of patients available at each time point is indicated below the graph. Abbreviations: CUM, cumulative.

transplantation. The survival curves for patients with prolonged and normal QTc separated within 1 year of evaluation and continued to diverge during long-term follow-up. Importantly, the prognostic information gained from the QTc duration is additive to the LVEF and to the severity of CAD, thus supplementing currently used prognostic parameters in this population.

Although SCD is the most common cause of death in patients with ESRD and is much more common than in the general population,[4,5] there is a very limited understanding of the risk factors that place these patients at high risk of SCD. In particular, there is a need for identification of novel prognostic markers that are able to predict the occurrence of SCD in patients with ESRD.[4] Since a depressed LVEF is a strong predictor of SCD in the general population, current guidelines endorse the placement of implantable cardiac defibrillators in individuals with a depressed LVEF, irrespective of a prior history of SCD or arrhythmias.[14] Our prior investigations have revealed that the strongest predictor of survival in ESRD patients is a preserved LVEF.[6,15] In a cohort of 3698 ESRD patients followed for 30 ± 15 months, a depressed LVEF was associated with higher mortality even after adjustments for LVH, myocardial ischemia, diabetes mellitus, and advanced age.[6] Nevertheless, patients with ESRD and a preserved LVEF still have a high mortality rate, suggesting that multiple other factors affect the outcome in these patients.[6]

ECG parameters, such as PR, QTc, and QRS durations, have been shown to predict mortality and cardiovascular events in the general population, especially in patients at high risk.[16–20] Although studies have suggested that ESRD patients have prolonged QTc duration and that this may be linked to the occurrence of ventricular arrhythmias,[21–23] the relationship of ECG parameters to survival has not

Table 3. Multivariate Predictors of Mortality in Patients With End-Stage Renal Disease Being Evaluated for Renal Transplantation

Variable	Adjusted HR	95% CI	*P* Value
Age (y)[a]	1.019	0.997–1.041	0.098
Female gender	1.545	1.022–2.338	0.039
DM	0.679	0.424–1.088	0.108
Low SES[b]	0.917	0.593–1.416	0.695
BMI (kg/m²)[a]	0.997	0.952–1.044	0.888
CAD[c]	0.528	0.217–1.285	0.159
No. of diseased coronary arteries[c]	1.399	1.021–1.917	0.037
MI	1.698	1.024–2.815	0.040
LVH[d]	1.035	0.670–1.599	0.878
LVEF (%)[a,e]	0.973	0.955–0.992	0.006
Hct (%)[a]	1.008	0.969–1.048	0.708
QTc (ms)[a]	1.008	1.001–1.014	0.016

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; DM, diabetes mellitus; Hct, hematocrit; HR, hazard ratio; LVEF; left ventricular ejection fraction; LVH, left ventricular hypertrophy; MI, myocardial infarction; MPI, myocardial perfusion imaging; QTc, corrected QT interval; SES, socioeconomic status; y, years.
[a] Continuous variable.
[b] Low SES was defined as ≤12 years of formal education.
[c] CAD was diagnosed by coronary angiography.
[d] LVH was diagnosed by electrocardiography.
[e] LVEF was measured by gated MPI.

been well studied. Case reports have described SCD associated with QTc prolongation in ESRD patients.[24,25] A study by Beaubien et al showed that QT dispersion was an independent predictor of adverse events, including total and cardiovascular mortality, in ESRD patients.[26] Our findings confirmed the high prevalence of QTc prolongation in ESRD, with 39% of our population having prolonged QTc. A smaller, but still significant, proportion of patients had PR and QRS prolongation. It is unclear why these patients have ECG abnormalities, but it has been demonstrated that the QTc duration (although not QRS) decreases shortly after renal transplantation.[27] Prior reports have attributed these abnormalities to the high prevalence of LVH and electrolyte imbalance,[21] while others have suggested that they could be related to dialysis, because the QTc has been shown to prolong after dialysis.[28,29] None of these reports have accounted for the presence and/or severity of CAD.

Chronic kidney disease, and especially ESRD, is an important risk factor for the development and progression of CAD, not only due to the high prevalence of conventional and nonconventional risk factors, but also due to conditions that are peculiar to these patients, such as extensive vascular calcifications and inflammation.[1] It is therefore tempting to attribute the increased cardiovascular risk in this population exclusively to CAD. In this study, independent predictors of a prolonged QTc in ESRD included female gender, LVEF, and severity of CAD. The prevalence of LVH by ECG was remarkably similar between patients with and without QTc prolongation. This finding could be related to the low sensitivity of ECG for the diagnosis of LVH, and unfortunately we do not have data on the prevalence of LVH by echocardiography in this cohort. Certainly, LVH and dysfunction have been linked to QTc prolongation and SCD.[30] In our study, decreasing LVEF, a more precise measurement of LV dysfunction, was strongly associated with QTc prolongation in accordance with prior reports.[21] More significantly, patients with a prolonged QTc were less likely to have a history of MI or have CAD by angiography, and increasing severity of CAD by angiography was inversely related to QTc prolongation even after adjustment for multiple factors (Table 2), which further stresses the dissociation of SCD risk from CAD. Although QTc prolongation is a known predictor of cardiovascular events, and QTc prolongation is known to be associated with preexisting CAD,[31] myocardial ischemia is known to shorten QTc.[32] The prevalence of QTc prolongation in patients with and without CAD and the association of CAD severity with the prevalence of QTc prolongation have not been previously studied in the ESRD population. The etiology of QTc prolongation in this specific population may be different from that in the general population and is possibly related to autonomic function.

Study Limitations

There are several limitations to this study. Our sample population is derived from a single tertiary care academic institution, and therefore we need to be wary of extrapolating the findings to all ESRD patients undergoing renal transplant evaluation, let alone ESRD patients not evaluated for transplantation. Also, all patients in this cohort underwent coronary angiography, which introduces a selection bias by design in this population. However, this allowed us to examine for the presence of CAD using a definitive approach that does not depend exclusively on history or noninvasive imaging. Another important limitation is that our study does not define the cause of death but uses all-cause mortality as the outcome. Although we are interested in the occurrence of SCD, we believe that using all-cause mortality avoids any bias in defining and diagnosing SCD even if these data were available.[33] We also did not have data on electrolyte status in these patients, which could have contributed further to our understanding of the reasons for QTc prolongation in this population. Despite these limitations, our data were obtained from a prospectively collected database and this

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is the first study that has evaluated the prognostic utility of ECG parameters in ESRD patients who have defined coronary anatomy.

References

1. Hage FG, Venkataraman R, Zoghbi GJ, Perry GJ, de Mattos AM, Iskandrian AE. The scope of coronary heart disease in patients with chronic kidney disease. *J Am Coll Cardiol*. 2009;53:2129–2140.
2. Lindner A, Charra B, Sherrard DJ, et al. Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med*. 1974;290:697–701.
3. US Renal Data System. *USRDS 2007 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; 2007.
4. Herzog CA, Mangrum JM, Passman R. Sudden cardiac death and dialysis patients. *Semin Dial*. 2008;21:300–307.
5. Myerburg RJ, Castellanos A. Emerging paradigms of the epidemiology and demographics of sudden cardiac arrest. *Heart Rhythm*. 2006;3:235–239.
6. Hage FG, Smalheiser S, Zoghbi GJ, et al. Predictors of survival in patients with end-stage renal disease evaluated for kidney transplantation. *Am J Cardiol*. 2007;100:1020–1025.
7. Venkataraman R, Hage FG, Dorfman T, et al. Role of myocardial perfusion imaging in patients with end-stage renal disease undergoing coronary angiography. *Am J Cardiol*. 2008;102: 1451–1456.
8. Venkataraman R, Hage FG, Dorfman TA, et al. Relation between heart rate response to adenosine and mortality in patients with end-stage renal disease. *Am J Cardiol*. 2009;103:1159–1164.
9. Hancock EW, Deal BJ, Mirvis DM, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part V: electrocardiogram changes associated with cardiac chamber hypertrophy: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol*. 2009;53:992–1002.
10. Rautaharju PM, Zhang ZM, Prineas R, Heiss G. Assessment of prolonged QT and JT intervals in ventricular conduction defects. *Am J Cardiol*. 2004;93:1017–1021.
11. Surawicz B, Childers R, Deal BJ, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol*. 2009;53:976–981.
12. Rautaharju PM, Surawicz B, Gettes LS, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part IV: the ST segment, T and U waves, and the QT interval: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol*. 2009;53:982–991.
13. Germano G, Kavanagh PB, Berman DS. An automatic approach to the analysis, quantitation and review of perfusion and function from myocardial perfusion SPECT images. *Int J Card Imaging*. 1997;13:337–346.
14. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2008;51:e1–e62.
15. De Mattos AM, Siedlecki A, Gaston RS, et al. Systolic dysfunction portends increased mortality among those waiting for renal transplant. *J Am Soc Nephrol*. 2008;19:1191–1196.
16. Cheng S, Keyes MJ, Larson MG, et al. Long-term outcomes in individuals with prolonged PR interval or first-degree atrioventricular block. *JAMA*. 2009;301:2571–2577.
17. Oikarinen L, Nieminen MS, Viitasalo M, et al; for LIFE Study Investigators. QRS duration and QT interval predict mortality in hypertensive patients with left ventricular hypertrophy: the Losartan Intervention for Endpoint Reduction in Hypertension Study. *Hypertension*. 2004;43:1029–1034.
18. Vrtovec B, Delgado R, Zewail A, Thomas CD, Richartz BM, Radovancevic B. Prolonged QTc interval and high B-type natriuretic peptide levels together predict mortality in patients with advanced heart failure. *Circulation*. 2003;107:1764–1769.
19. Iuliano S, Fisher SG, Karasik PE, et al. QRS duration and mortality in patients with congestive heart failure. *Am Heart J*. 2002;143:1085–1091.
20. Elhendy A, Hammill SC, Mahoney DW, et al. Relation of QRS duration on the surface 12-lead electrocardiogram with mortality in patients with known or suspected coronary artery disease. *Am J Cardiol*. 2005;96: 1082–1088.
21. Stewart GA, Gansevoort RT, Mark PB, et al. Electrocardiographic abnormalities and uremic cardiomyopathy. *Kidney Int*. 2005;67: 217–226.
22. Suzuki R, Tsumura K, Inoue T, et al. QT interval prolongation in the patients receiving maintenance hemodialysis. *Clin Nephrol*. 1998;49:240–244.
23. Voiculescu M, Ionescu C, Ismail G. Frequency and prognostic significance of QT prolongation in chronic renal failure patients. *Rom J Intern Med*. 2006;44:407–417.
24. Singh JP, Sleight P, Kardos A, et al. QT interval dynamics and heart rate variability preceding a case of cardiac arrest. *Heart*. 1997;77:375–377.
25. Patanè S, Marte F, Di Bella G, et al. QT interval prolongation, torsade de pointes and renal disease. *Int J Cardiol*. 2008;130:e71–e73.
26. Beaubien ER, Pylypchuk GB, Akhtar J, et al. Value of corrected QT interval dispersion in identifying patients initiating dialysis at increased risk of total and cardiovascular mortality. *Am J Kidney Dis*. 2002;39:834–842.
27. Yildiz A, Akkaya V, Tükek T, et al. Increased QT dispersion in hemodialysis patients improve after renal transplantation: a prospective-controlled study. *Transplantation*. 2001;72:1523–1526.
28. Covic A, Diaconita M, Gusbeth-Tatomir P, et al. Haemodialysis increases QT(c) interval but not QT(c) dispersion in ESRD patients without manifest cardiac disease. *Nephrol Dial Transplant*. 2002;17:2170–2177.
29. Lörincz I, Zilahi Z, Kun C, et al. ECG abnormalities in hemodialysis. *Am Heart J*. 1997;134:1138–1140.
30. Kang YJ. Cardiac hypertrophy: a risk factor for QT-prolongation and cardiac sudden death. *Toxicol Pathol*. 2006;34:58–66.
31. Sohaib SM, Papacosta O, Morris RW, Macfarlane PW, Whincup PH. Length of the QT interval: determinants and prognostic implications in a population-based prospective study of older men. *J Electrocardiol*. 2008;41:704–710.
32. Maeda T, Saikawa T, Niwa H, et al. QT interval shortening and ST elevation in intracoronary ECG during PTCA. *Clin Cardiol*. 1992;15:525–528.
33. Gottlieb SS. Dead is dead—artificial definitions are no substitute. *Lancet*. 1997;349:662–663.

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