Original Article

Correlation between lactate dehydrogenase and QTc interval prolongation in maintenance hemodialysis patients: a cross-sectional study

Xing-Xing Fang[#], Liang-Lan Shen[#], Wu-Bin Yao, Hong-Li Yang, Hua-Xing Huang, Dong-Mei Chen, Yan Shen^

Department of Nephrology, The Second Affiliated Hospital of Nantong University, Nantong, China

Contributions: (I) Conception and design: Y Shen; (II) Administrative support: None; (III) Provision of study materials or patients: XX Fang, Y Shen; (IV) Collection and assembly of data: XX Fang, WB Yao, HL Yang, HX Huang, DM Chen; (V) Data analysis and interpretation: XX Fang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yan Shen. Department of Nephrology, The Second Affiliated Hospital of Nantong University, No. 6 Haierxiang North Road, Nantong 226001, China. Email: ntmcsy@126.com.

Background: Corrected QT (QTc) interval prolongation is one of the common causes of sudden cardiac death in patients with maintenance hemodialysis (MHD) patients. However, there are few studies on QTc prolongation in MHD patients. The concentration of lactate dehydrogenase (LDH) in hemodialysis population increased, and LDH was associated with the mortality of MHD patients. This study aimed to investigate the relationship between QTc interval prolongation and LDH in MHD patients.

Methods: This is a cross-sectional observational study. Patients who underwent MHD for more than 3 months in the Second Affiliated Hospital of Nantong University from November 2012 to November 2019 with complete data were selected as the research subjects. The patients were divided into the normal QTc interval group and the QTc interval prolongation group. The general data of patients and clinical laboratory indicators were collected retrospectively from the electronic medical record system. Pearson correlation analysis and binary logistic regression were used to analyze the correlation between LDH and QTc interval prolongation; the cut-off value of LDH predicting QTc interval prolongation was calculated by receiver operating characteristic (ROC) curve.

Results: The LDH level in the prolonged QTc interval group was significantly higher than that in the normal group (301.96±110.91 *vs.* 215.39±67.65, t=–8.03, P<0.001). QTc interval and LDH (r=0.386) were positively correlated. Binary logistic regression analysis showed that LDH, serum potassium <4 mmol/L, serum phosphorus, and left ventricular end-diastolic diameter (LVDd) were independent related factors for QTc interval prolongation. The ROC curve results showed that LDH =220 U/L was the best cutoff point for predicting QTc interval prolongation in MHD patients, with a sensitivity of 81.45% and a specificity of 59.35%. Binary logistic regression analysis showed that the LDH >220 U/L group was 6.34 times more likely to have QTc interval prolongation than the LDH ≤220 U/L group (OR 6.34, 95% CI: 3.47–11.58, P<0.001).

Conclusions: LDH in MHD patients is closely related to QTc interval prolongation. Serum LDH, ionic calcium, serum phosphorus and potassium may predict QTc interval prolongation. Monitoring related indicators can remind clinicians to intervene as soon as possible to reduce the potential risk of arrhythmia and sudden cardiac death (SCD).

Keywords: Hemodialysis; lactate dehydrogenase (LDH); QTc interval prolongation

^ ORCID: 0000-0001-9821-9243.

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Introduction

The incidence of chronic kidney disease (CKD) is increasing, and sudden cardiac death (SCD) is the leading cause of death in hemodialysis patients. The increased risk of arrhythmia is an important cause of SCD in this disease population. According to statistics, in the dialysis population, the ratio of the number of deaths caused by arrhythmia or cardiac arrest to the total number of deaths on dialysis is close to 1/3 (1). In the hemodialysis population, cardiac arrhythmias may occur during and shortly after treatment independent of traditional cardiovascular risk factors (2,3). In patients with end-stage renal disease (ESRD), QTc interval prolongation is common, but the mechanism of its prolongation has not yet been elucidated. There are relatively few clinical studies on QTc interval prolongation in patients with CKD at home and abroad. Previous studies have shown that the causes of prolonged QTc interval include drugs, myocardial ischemia, heart failure, cardiomyopathy, bradycardia, male, advanced age, inflammation, tumor, liver and kidney insufficiency, hypothyroidism, hypokalemia, hypocalcemia, hypomagnesemia, diabetes, etc. (4-7). Lactate dehydrogenase (LDH), as a myocardial marker, is significantly increased in maintenance hemodialysis (MHD) population, and LDH is associated with the mortality of MHD patients (8). So far, there has been no research on the correlation between LDH and QTc interval prolongation. This study investigated the influencing factors of QTc interval prolongation in MHD patients and the correlation between LDH and QTc interval prolongation. We present the following article in accordance with the STARD reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-1053/rc).

Methods

Patient

A retrospective analysis was performed between November 2012 and November 2019 in the Department of Nephrology of the Second Affiliated Hospital of Nantong University. Patients who underwent MHD for more than 3 months, the dialysis vascular access was an autogenous arteriovenous fistula, those who had a 12-lead electrocardiogram (ECG), received echocardiography, and those with complete follow-up data were included in the study. The exclusion criteria were as follows: (I) arrhythmia; (II) patients with confirmed hereditary long QTc syndrome; (III) acute coronary syndrome, cardiomyopathy, or heart valve disease; (IV) other known causes of QTc interval prolongation, or diseases or conditions such as liver disease, acute stroke, malignant tumor, hypothyroidism, application of drugs that can prolong the QTc interval, etc.; (V) the information was incomplete (*Figure 1*). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Second Affiliated Hospital of Nantong University (approval number: 2022KT241) and individual consent for this retrospective analysis was waived.

Grouping

A 12-lead resting ECG was used to record the QTc of the subjects. QTc interval prolongation was defined according to QTc ≥450 ms in men and QTc ≥460 ms in women (9), and they were divided into the normal QTc interval group and QTc interval prolongation group.

Dialysis program

The frequency of dialysis was 3 times/week, 4 hours/time, and Duration on HD ≥3 months. The dialysate was bicarbonate dialysate, the dialyzer used was Nipro 15G, cellulose acetate membrane (area 1.5 m^2) was used, the dialysate flow rate was 500 mL/min, the blood flow rate was 200–300 mL/min, and the dialysate calcium was 1.5 mmol/L, dialysate potassium was 2.0 mmol/L, anticoagulation with low molecular weight heparin.

Data collection

All study subjects were enrolled at the time when they received a 12-lead ECG in our center. Fasting blood was collected before the first dialysis every week, and

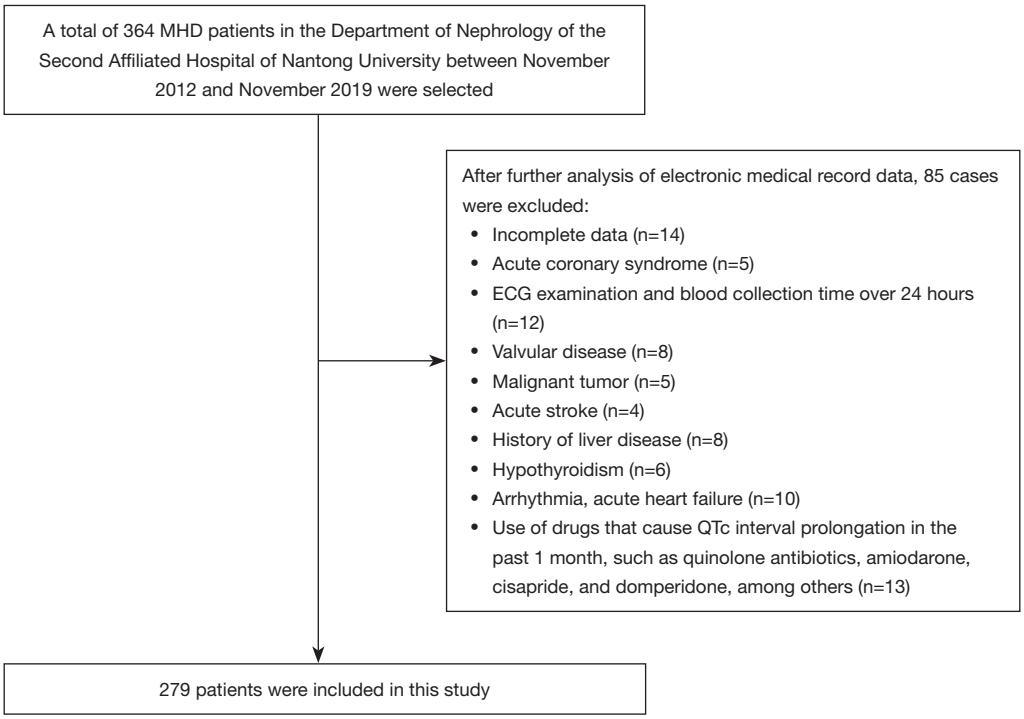

Figure 1 Flowchart of study participant selection. MHD, maintenance hemodialysis; ECG, electrocardiogram; QTc, corrected QT.

the selected blood collection time and the 12-lead ECG time interval did not exceed 24 hours. The time of echocardiography and 12-lead ECG of the enrolled patients did not exceed 1 month. The following baseline data were collected: age, gender, primary disease, body mass index (BMI), duration on HD, predialysis systolic blood pressure (SBP), predialysis diastolic blood pressure (DBP), hemoglobin (Hb), alanine aminotransferase (ALT), aspartate aminotransferase (AST), LDH, albumin (Alb), serum creatinine (Scr), uric acid (UA), blood glucose (Glu), total cholesterol (TC), triacylglycerol (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), serum potassium (K), corrected calcium (Ca), serum phosphorus (P), bicarbonate (HCO_3^-), magnesium (Mg), high-sensitivity C-reactive protein (hs-CRP), parathyroid hormone (PTH), and N-terminal precursor brain natriuretic peptide (NT-proBNP). The 12-lead ECG was performed by specialists in the ECG room of our hospital, and the ECG was recorded when the patient was in a stable condition. The ECG paper speed was 25 mm/s and the standard voltage was 10 mm/mv. The corrected QT interval was calculated using the Bazett formula [$QTc = QT/(RR^{0.5})$]. Echocardiography was performed by cardiac ultrasound specialists in our hospital using Philips EPIQ 7C, IE33 echocardiograph, with X5-1 probe/frequency 1–3 MHz, S5-1 probe/frequency 1–5 MHz, and QLAB 3DQA quantitative analysis software. The patient was instructed to lie on the left side in a calm state. Aortic diameter (AOD), left atrial diameter (LAD), ventricular septal thickness (IVS), left ventricular posterior wall thickness (LVPW), left ventricular end-diastolic diameter (LVDd), left ventricular end-systolic diameter (LVDs), Ejection fraction (EF), and left ventricular mass (LVM) were measured.

Statistical analysis

Statistical processing of data was performed with SPSS 23.0, GraphPad prism 8.0, and MedCalc 19.1 software packages. GPower3.1.9.2 was used to estimate the sample size, α=0.05 (two-sided), 95% confidence (Power =1–β), and the minimum sample size was calculated as 176 cases. Normally distributed measurement data were expressed as mean ± SD, and the *t*-test was used for comparisons between groups. Dialysis age, hs-CRP, PTH, and NT-proBNP were non-normally distributed data, and the logarithm (Lg) was converted to normal distribution data

for analysis. At the same time, non-normally distributed measurement data were represented by M ($P_{1/4}$, $P_{3/4}$), and the non-parametric test was used for comparisons between groups. Enumeration data were expressed as percentage or frequency, and the χ^2 test was used for comparisons between groups. Pearson's correlation analysis was used to analyze the correlation between relevant indicators and QTc. Relevant factors were analyzed by binary logistic regression analysis. Receiver operating characteristic (ROC) curves and the Youden index were used to evaluate the predictive effect of LDH on QTc interval prolongation in MHD patients, and the cutoff value was calculated. A difference of P<0.05 was statistically significant.

Results

Baseline information

A total of 279 patients were included in this study. Among them, there were 154 males (55.2%) and 125 females (44.8%), with an average age of 60.41±14.58 years. There were 155 cases (55.6%) in the normal QTc interval group and 124 cases (44.4%) in the QTc interval prolongation group. In the QTc interval prolongation group, the QTc was 478.31±21.64 ms. Compared with the normal QTc interval group, the proportions of males, DBP, ALT, LDH, serum potassium <4 mmol/L, P, PTH, LAD, LVDd, LVDs, and LVM in the QTc interval prolongation group were significantly higher than those in the normal QTc interval group (P<0.05). Age, Alb, corrected calcium, and EF values in the prolonged interval group were significantly lower than those in the normal group (P<0.05; *Table 1*).

Correlation between QTc interval and observational indicators

The results of Pearson correlation analysis showed that the QTc interval was closely related to ALT (r=0.150), LDH (r=0.386), Cr (r=0.123), P (r=0.205), LgPTH (r=0.123), LgBNP (r=0.141), LAD (r=0.245), LVDd (r=0.314), LVDs (r=0.325), and LVM (r=0.246) and were positively correlated, while Alb (r=−0.159), serum potassium (r=−0.133), corrected calcium (r=−0.166), and EF value (r=−0.263) were negatively correlated (*Table 2*, *Figure 2*).

Related factors and independent related factors of QTc prolongation

Univariate binary logistic regression analysis showed that gender, age, DBP, ALT, LDH, Alb, Ca, K<4 mmol/L, P, LAD, LVDd, LVDs, EF value, and LVM were the related factors for QTc prolongation. We included the results of single factor P<0.05 into the multivariate binary logistic regression analysis and the results showed that LDH, K<4 mmol/L, P, and LVDd were independent related factors for QTc interval prolongation (*Table 3*).

ROC curve of LDH in predicting QTc interval prolongation in MHD patients

To explore the predictive value of LDH for QTc interval prolongation in MHD patients, the cutoff value of LDH was determined by an ROC curve. When the cutoff level was 220 U/L, the sensitivity was 81.45%, the specificity was 59.35%, and the Youden index was 0.408 (*Figure 3*).

According to the cutoff value of LDH, we divided patients into the LDH ≤220 U/L group and LDH >220 U/L group, with QTc interval prolongation as the dependent variable. The risk of QTc interval prolongation in the high LDH group was 6.41 times that in the low LDH group. In the model adjusted for K<4 mmol/L + P + LVDd, the risk of QTc interval prolongation in the high LDH group was 6.34 times that of the low LDH group (*Table 4*).

Discussion

The QT interval on a standard 12-lead ECG represents the time from ventricular depolarization (start of Q wave) to completion of cardiac repolarization (end of T wave). The QT interval increases with the slowing of the heart rate. Therefore, when measuring, evaluating, and comparing whether there is a prolongation or shortening of the QT interval, it should be determined according to the heart rate. Most scholars use QTc to represent the heart rate-corrected QT interval. The method for calculating QTc in this study was to use the Bazett formula for correction.

MHD patients are a high-risk group for cardiovascular disease. According to the 2015 annual data report of the American Renal Data System, cardiovascular disease caused

Table 1 Comparison of clinical baseline data between the normal QTc interval group and QTc interval prolongation group

Characteristic	Normal QTc interval group (n=155)	QTc interval prolongation group (n=124)	$t/\chi^2/z$	P value
Gender, n (%)			5.36	0.021
Male	76 (49.03)	78 (62.9)		
Female	79 (50.97)	46 (37.1)		
Age (years)	61.97±13.86	58.44±15.27	2.021	0.044
Primary disease, n (%)				
CGN	51 (32.9)	50 (40.3)	1.748	0.417
DN	56 (36.1)	38 (30.6)		
Others	48 (31.0)	36 (29.0)		
BMI (kg/m^2)	23.51±3.97	24.33±4.18	−1.618	0.107
SBP (mmHg)	152.97±22.15	152.6±26.553	0.126	0.9
DBP (mmHg)	80.51±12.80	84.81±16.56	−2.443	0.015
Duration on HD (m), M [1/4, 3/4]	4 [3, 18]	4 [3, 16]	−0.374	0.708
Hb (g/L)	92.57±23.04	91.44±22.69	0.41	0.682
ALT (U/L)	10.93±7.02	14.48±12.28	−3.024	0.003
AST (U/L)	14.44±7.86	16.03±9.50	−1.533	0.126
LDH (U/L)	215.39±67.65	301.96±110.91	−8.03	<0.001
Alb (g/L)	35.37±5.68	34.02±5.75	1.976	0.049
Scr (μmol/L)	714.63±299.70	791.73±379.16	−1.897	0.059
UA (μmol/L)	397.63±154.61	404.55±150.51	−0.374	0.708
Glu (mmol/L)	5.82±2.66	5.52±2.12	1.007	0.315
TG (mmol/L)	1.88±1.16	1.71±0.89	1.355	0.177
TC (mmol/L)	4.10±1.03	3.99±1.24	0.782	0.435
LDL (mmol/L)	2.37±0.88	2.36±1.02	0.109	0.913
HDL (mmol/L)	1.07±0.28	1.01±0.32	1.816	0.07
K (mmol/L)	4.51±0.76	4.42±0.80	0.997	0.32
K<4 mmol/L, n (%)	35 (42.2)	48 (57.8)	8.575	0.003
Ca (mmol/L)	2.20±0.21	2.12±0.24	3.188	0.002
P (mmol/L)	1.68±0.51	1.88±0.60	−3.092	0.002
HCO_3^- (mmol/L)	20.77±3.23	20.43±3.19	0.885	0.377
Mg (mmol/L)	1.07±0.26	1.05±0.27	0.694	0.488
hs-CRP (mg/L), M (1/4, 3/4)	9.73 (2.28, 24.16)	9.36 (2.04, 27.38)	−0.396	0.692
PTH (pg/mL), M (1/4, 3/4)	236.55 (126.33, 405.7)	323.95 (184.2, 475.48)	−2.519	0.012
NT-proBNP (pg/mL), M (1/4, 3/4)	12,155 (4,689, 35,000)	22,920 (7,268.5, 35,000)	−1.788	0.074
AOD (mm)	31.24±3.69	31.37±4.00	−0.285	0.776
LAD (mm)	42.03±5.27	43.76±5.57	−2.645	0.009

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic	Normal QTc interval group (n=155)	QTc interval prolongation group (n=124)	$t/\chi^2/z$	P-value
IVS (mm)	12.19±1.72	12.45±2.05	–1.135	0.257
LVPW (mm)	11.38±1.62	11.6±1.77	–1.088	0.278
LVDd (mm)	52.5±5.25	55.21±5.60	–4.135	<0.001
LVDs (mm)	34.76±5.75	37.55±6.61	–3.744	<0.001
EF (%)	61.83±8.34	59.13±10.07	2.436	0.016
LVM (g)	252.4±74.12	280.57±83.89	–2.974	0.003
QTc (ms)	431.25±17.07	478.31±21.64	–20.307	<0.001

The data are shown as n (%) or mean ± SD or M (1/4, 3/4). QTc, corrected QT; QT, the beginning of the QRS wave and the ending point of the T wave; CGN, chronic glomerulonephritis; DN, diabetic nephropathy; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HD, hemodialysis; m, month; M, median; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; Alb, albumin; Scr, serum creatinine; UA, uric acid; Glu, blood glucose; TC, total cholesterol; TG, triacylglycerol; LDL, low density lipoprotein; HDL, high density lipoprotein; K, serum potassium; Ca, corrected calcium; P, serum phosphorus, HCO_3^-, bicarbonate; Mg, magnesium; hs-CRP, high-sensitivity C-reactive protein; PTH, parathyroid hormone; NT-proBNP, N-terminal precursor brain natriuretic peptide; AOD, measured aortic diameter; LAD, left atrial diameter; IVS, ventricular septal thickness; LVPW, left ventricular posterior wall thickness; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; EF, ejection fraction; LVM, left ventricular mass.

Table 2 Pearson correlation analysis results of QTc interval and observational indicators in MHD patients

Clinical indicators	r	P value
Age (y)	–0.043	0.47
BMI (kg/m^2)	0.048	0.434
SBP (mmHg)	–0.021	0.725
DBP (mmHg)	0.067	0.264
Hb (g/L)	–0.044	0.461
ALT (U/L)	0.150[a]	0.012
AST (U/L)	0.063	0.294
LDH (U/L)	0.386[b]	<0.001
Alb (g/L)	–0.159[b]	0.008
Scr (μmol/L)	0.123[a]	0.04
UA (μmol/L)	0.038	0.525
Glu (mmol/L)	–0.05	0.405
TG (mmol/L)	–0.071	0.243
TC (mmol/L)	–0.048	0.426
LDL (mmol/L)	–0.003	0.967
HDL (mmol/L)	–0.074	0.223
K (mmol/L)	–0.133[a]	0.027
Ca (mmol/L)	–0.166[b]	0.005
P (mmol/L)	0.205[b]	0.001
HCO_3^- (mmol/L)	–0.06	0.317
Mg (mmol/L)	–0.055	0.363
LgCRP	0.064	0.284
LgPTH	0.123[a]	0.042
LgBNP	0.141[a]	0.041
AOD (mm)	0.061	0.311
LAD (mm)	0.245[b]	<0.001
IVS (mm)	0.089	0.142
LVPW (mm)	0.106	0.08
LVDd (mm)	0.314[b]	<0.001
LVDs (mm)	0.325[b]	<0.001
EF (%)	–0.263[b]	<0.001
LVM	0.246[b]	<0.001

[a], P<0.05; [b], P<0.01. QTc, corrected QT; QT, the beginning of the QRS wave and the ending point of the T wave; MHD, maintenance hemodialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; Alb, albumin; Scr, serum creatinine; UA, uric acid; Glu, blood glucose; TC, total cholesterol; TG, triacylglycerol; LDL, low density lipoprotein; HDL, high density lipoprotein; K, serum potassium; Ca, corrected calcium; P, serum phosphorus; HCO_3^-, bicarbonate; Mg, magnesium; hs-CRP, high-sensitivity C-reactive protein; PTH, parathyroid hormone; NT-proBNP, N-terminal precursor brain natriuretic peptide; AOD, measured aortic diameter; LAD, left atrial diameter; IVS, ventricular septal thickness; LVPW, left ventricular posterior wall thickness; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; EF, ejection fraction; LVM, left ventricular mass.

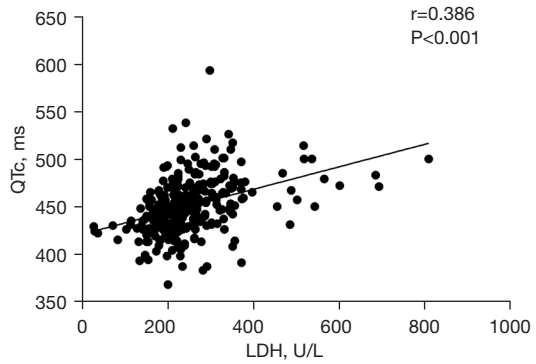

Figure 2 Correlation analysis between LDH level and QTc interval prolongation in MHD patients. QTc, corrected QT; LDH, lactate dehydrogenase; MHD, maintenance hemodialysis.

more than 40% of ESRD patient deaths, and cardiac arrhythmia and cardiac arrest accounted for about 28.0% of the deaths (10). Studies have shown that in patients with CKD or those receiving hemodialysis or peritoneal dialysis, a longer QTc interval is associated with an increased risk of death, heart failure, coronary heart disease, and sudden death (11-13). Low K low Ca, and low P are recognized risk factors for QTc interval prolongation (4,14). During hemodialysis, a rapid drop in serum calcium or potassium can lead to a prolongation of the QTc interval and an increase in QTc dispersion (15-18). In this study, there were similar results. Compared with the normal QTc interval group, the proportion of K<4 mmol/L in the QTc interval prolongation group was significantly higher than that in the normal QTc interval group. The corrected calcium in the QTc interval prolongation group was significantly lower than that in the QTc interval normal group. Serum potassium and corrected calcium were negatively correlated with QTc interval, and K<4 mmol/L was an independent related factor for QTc interval prolongation. The "Expert Consensus on Ion Management of Patients with Heart Failure in China" recommends that potassium in patients with heart failure should be controlled between 4.0–5.0 mmol/L. Even if the serum potassium is at a low normal value of 3.5–4.0 mmol/L, potassium should be supplemented appropriately. Attention should be paid to magnesium supplementation, which can reduce the risk of arrhythmia. Hypocalcemia in MHD patients is mainly caused by active vitamin D deficiency, metabolic acidosis, insufficient calcium intake, and osteodystrophy. When blood calcium is low, the influx of calcium ions into cells is slowed, and the ECG shows ST segment prolongation, normal T wave width, and total QTc interval prolongation. In addition, this study found that blood P was an independent related factor for QTc interval prolongation, which was consistent with previous literature reports (19). It shows that abnormal calcium and phosphorus metabolism in patients with CKD has a certain relationship with the prolongation of QTc interval.

In this study, LAD, LVDd, and LVM were positively correlated with QTc interval, while EF was negatively correlated with QTc interval. Furthermore, LVDd was an independent related factor for QTc interval prolongation. Cerbai *et al.* (20) found that compared with normal cardiomyocytes, there was a transient decrease in the expression of outward potassium current channels in cardiomyocytes with left ventricular hypertrophy. Therefore, it is considered that the prolonged action potential time of cardiomyocytes is related to this. The hypertrophic ventricle may set the stage for QTc prolongation and uneven recovery of excitability, which may increase the risk of arrhythmias in this condition (21,22). Liu *et al.* found that decreased left ventricular EF in CKD patients was an independent risk factor for QTc prolongation in this disease population (23). Therefore, for CKD patients with reduced cardiac function and structural heart disease, the risk of arrhythmia should be assessed carefully.

At the same time, in this study, it was found that LDH was positively correlated with QTc interval prolongation and was also an independent related factor for QTc interval prolongation, and this result was rarely found in other studies. LDH exists in the tissues and cells of the human body, with the highest content in the kidneys, and decreases in the cardiac muscle, skeletal muscle, liver, and red blood cells in turn. Conditions that lead to increased blood LDH include tissue damage, necrosis, hypoxia, hemolysis, or malignancy. Uremic patients are often accompanied by severe cardiomyopathy, and dialysis aggravates myocardial damage. The QTc interval represents the repolarization of the cardiomyocytes with the longest action potential duration, that is, M cells. Some scholars have established 2 models of lethal ventricular tachyarrhythmia (LVTA), representing LVTA caused by abnormal myocardial ion channels and myocardial ischemia (24). β-oxidation and anerobic glycolysis are enhanced, TCA is inhibited, and amino acid metabolism is disordered. As a cardiac ion channel disease, QTc interval prolongation may result in glycolysis, and LDH is one of the important enzymes in anerobic glycolysis and gluconeogenesis, and there may be

Table 3 Univariate and multivariate binary logistic regression analysis of QTc interval prolongation in MHD patients

Characteristic	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Gender	0.567	0.351–0.918	0.021			
Age (years)	0.983	0.967–1	0.045			
BMI (kg/m^2)	1.051	0.989–1.117	0.108			
SBP (mmHg)	0.999	0.99–1.009	0.899			
DBP (mmHg)	1.021	1.004–1.038	0.017			
Duration on HD (m)	1.001	0.991–1.011	0.834			
Hb (g/L)	0.998	0.988–1.008	0.681			
ALT (U/L)	1.042	1.012–1.072	0.005			
AST (U/L)	1.022	0.993–1.052	0.134			
LDH (U/L)	1.014	1.01–1.019	<0.001	1.014	1.009–1.018	<0.001
Alb (g/L)	0.959	0.92–1	0.05			
Scr (μmol/L)	1.001	1–1.001	0.064			
UA (μmol/L)	1	0.999–1.002	0.707			
Glu (mmol/L)	0.949	0.856–1.052	0.318			
TG (mmol/L)	0.851	0.673–1.076	0.178			
TC (mmol/L)	0.918	0.741–1.137	0.434			
LDL (mmol/L)	0.986	0.765–1.271	0.913			
HDL (mmol/L)	0.471	0.207–1.07	0.072			
K (mmol/L)	0.856	0.630–1.162	0.319			
K<4 mmol/L	0.462	0.274–0.778	0.004	0.317	0.163–0.615	0.004
Ca (mmol/L)	0.176	0.058–0.534	0.002			
P (mmol/L)	1.973	1.261–3.085	0.003	2.277	1.282–4.046	0.005
HCO_3^- (mmol/L)	0.967	0.898–1.041	0.376			
Mg (mmol/L)	0.724	0.290–1.805	0.488			
hs-CRP (mg/L)	1.002	0.995–1.009	0.531			
PTH (pg/mL)	1	1–1.001	0.238			
NT-proBNP (pg/mL)	1	1–1	0.091			
AOD (mm)	1.009	0.948–1.074	0.775			
LAD (mm)	1.061	1.014–1.111	0.01			
IVS (mm)	1.077	0.947–1.224	0.26			
LVPW (mm)	1.081	0.939–1.246	0.278			
LVDd (mm)	1.098	1.047–1.152	<0.001	1.084	1.029–1.143	0.003
LVDs (mm)	1.077	1.034–1.122	<0.001			
EF (%)	0.968	0.943–0.994	0.017			
LVM (g)	1.005	1.001–1.008	0.004			

QTc, corrected QT; QT, the beginning of the QRS wave and the ending point of the T wave; MHD, maintenance hemodialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HD, hemodialysis; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; Alb, albumin; Scr, serum creatinine; UA, uric acid; Glu, blood glucose; TC, total cholesterol; TG, triacylglycerol; LDL, low density lipoprotein; HDL, high density lipoprotein; K, serum potassium; Ca, corrected calcium; P, serum phosphorus; HCO_3^-, bicarbonate; Mg, magnesium; hs-CRP, high-sensitivity C-reactive protein; PTH, parathyroid hormone; NT-proBNP, N-terminal precursor brain natriuretic peptide; AOD, measured aortic diameter; LAD, left atrial diameter; IVS, ventricular septal thickness; LVPW, left ventricular posterior wall thickness, LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter, EF, ejection fraction; LVM, left ventricular mass; OR, odds ratio; CI, confidence interval.

a certain relationship between the two. Therefore, LDH level may be an effective indicator for the diagnosis of QTc interval prolongation.

The results of this study showed that the LDH level of MHD patients in the prolonged QTc interval group was significantly higher than that in the normal QTc interval group. Univariate and multivariate binary logistic regression analysis showed that LDH was an independent related factor for QTc interval prolongation in MHD patients.

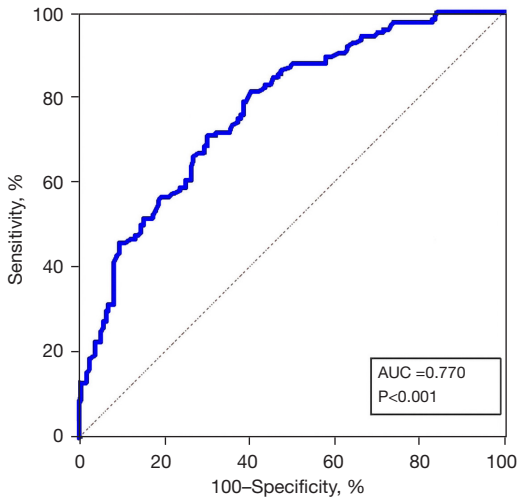

Figure 3 ROC curve of LDH in predicting QTc interval prolongation in MHD patients. AUC, area under the curve; ROC, receiver operating characteristic; LDH, lactate dehydrogenase; QTc, corrected QT; MHD, maintenance hemodialysis.

In addition, the risk ratio of QTc interval prolongation in patients with high LDH level was significantly increased. After adjusting for factors such as K<4 mmol/L, P, and LVDd, the risk of QTc interval prolongation in patients with high LDH level was still 6.34 times that of the low level group. Therefore, this study suggests that the increase of LDH level may play an important role in the pathophysiological process of QTc interval prolongation in MHD patients, and the mechanism may be related to myocardial injury and enhanced anerobic glycolysis in MHD patients.

There are some shortcomings in this study. First, this study is a single-center, retrospective analysis with a small sample size. The relationship between LDH and QTc, and whether LDH can accurately predict the occurrence of QTc interval prolongation, must be analyzed in large-scale, long-term, prospective studies for further confirmation. Second, QTc was calculated using the Bazett formula, which partially overestimates the QTc value when the patient's heart rate is high.

In conclusion, LDH in MHD patients is closely related to QTc interval prolongation, and its mechanism may be related to myocardial injury and enhanced anerobic glycolysis in MHD patients. LDH, K<4 mmol/L, serum P, and LVDd were independent related factors for QTc interval prolongation. Monitoring related indicators can remind clinicians to intervene as soon as possible to reduce the potential risk of arrhythmia and sudden cardiac death (SCD).

Table 4 Unadjusted and multivariate adjusted ORs (and 95% CI) in MHD patients with QTc interval prolongation and serum LDH >220 U/L

Project	LDH levels, U/L		P value
	≤220 (n=115)	>220 (n=164)	
Patients with QTc interval prolongation	23 (20%)	101 (61.6%)	<0.001
Unadjusted ORs	Reference	6.41 (3.68–11.17)	<0.001
Adjusted ORs, adjusted for			
K<4 mmol/L + P + LVDd	Reference	6.34 (3.47–11.58)	<0.001

OR, odds ratio; CI, confidence interval; MHD, maintenance hemodialysis; QTc, corrected QT; LDH, lactate dehydrogenase; K, serum potassium; P, serum phosphorus; LVDd, left ventricular end-diastolic diameter.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-1053/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-1053/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-1053/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Second Affiliated Hospital of Nantong University (approval number: 2022KT241) and individual consent for this retrospective analysis was waived.

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