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Relation	

Effects of Hypokalemia and Left Ventricular Hypertrophy on QT interval in Patients with Primary Aldosteronism

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Primary aldosteronism is characterized by hypertension, hypokalemia, suppressed plasma renin activity (PRA) and autonomous aldosterone production [1,2]. Compared to patients with similar levels of hypertension, patients with primary aldosteronism have greater left ventricular hypertrophy (LVH) and increased rate of cardiovascular complications [3-5]. QT interval prolongation, which may increase the risk of life-threatening arrhythmias, is also often found in primary aldosteronism [6,7]. QT interval prolongation can result from hypokalemia as well as LVH [8-10]. In this study, we assessed whether hypokalemia or LVH represented the principal factor determining QT interval prolongation in patients with primary aldosteronism.

The study population consisted of 52 patients with newly diagnosed primary aldosteronism. Primary aldosteronism was confirmed with captopril challenge test, furosemide plus upright test and / or salt loading test. These protocols have been previously described. Patients with bundle branch block, atrial fibrillation or ventricular pacing were excluded because these factors might affect QT interval. Patients receiving aldosterone antagonist, potassium supplementation or anti-arrhythmic drugs of any class including β-blockers were also excluded because these agents might affect serum potassium level or QT interval.

Plasma renin activity (PRA) and plasma aldosterone concentration (PAC) were measured by radioimmunoassay as previously described. Blood was collected from an antecubital vein and serum potassium concentrations were

measured using a standard ion electrode method.

A 12-lead electrocardiogram (ECG) was recorded at a paper speed of 25 mm/sec and an amplification of 10 mm/mV. The isoelectric line was defined as the level of the preceding TP segment. The QT interval was taken from the beginning of the QRS complex to the end of the downslope of the T wave (crossing of the isoelectric line). When T waves were inverted, the end was taken at the point where the trace returned to the isoelectric line. When U waves were present, the end of T wave was taken as the nadir between the T wave and the U wave. QT intervals were measured by one independent observer who was unaware of the clinical data of the patients. The QT interval considered for each patient was the maximum QT interval measured in any lead. To adjust QT interval for the heart rate, QTc interval was calculated according to Bazett's formula: QTc interval (msec) = QT interval (msec) / $RR^{1/2}$. Three ECG indexes for LVH were measured in each ECG: Sokolow-Lyon index (sum of S wave in V1 and R wave in V5), Cornell voltage index (sum of R wave in aVL and S wave in V3), and Gubner index (sum of R wave in I and S wave in III) [11-13].

Transthoracic echocardiographic data were obtained on admission using a commercial ultrasound machine. Two-dimensional guided M-mode measurements of left ventricular end-diastolic diameter (LVDD), interventricular septum thickness (IVS) and posterior wall thickness (PW) were measured. Left ventricular mass was calculated using the formula of Deverreux and Reichek: left ventricular mass (g) $=1.04[(LVDD+IVS+PW)^3-(LVDD)^3]-13.6$. Left ventricular mass (LVM) index

was calculated by dividing LVM by body surface area [14-16].

Statistical analysis was performed with chi-square and Student's t- tests. Relations between variables were determined by linear regression analysis. All data are expressed as mean±SD. Differences were considered significant if the p value was <0.05.

Patient characteristics are shown in Table 1. There were 26 male and 26 female patients with a mean age of 59±11 years. PRA and PAC were 0.51± 0.37 ng/ml/hr and 27.6 ± 22.6 pg/ml, respectively. Serum sodium and potassium were 140.9±3.3 mEq/l and 3.7±0.6 mEq/l, respectively. QTc interval was 424.1±24.5 msec.

In 18 patients (35%), serum potassium level was less than 4.0 mEq/l. There was a significant correlation between serum potassium level and QTc interval ($r=-0.45$, $p<0.001$, Figure 1). On the other hand, PAC did not correlate significantly with QTc interval ($r=0.006$, $p=0.97$). There was no significant correlation between LVM index and QTc interval ($r=0.18$, $p=0.21$, Figure 2). Three ECG parameters also did not correlate significantly with QTc interval (Sokolow-Lyon index, $r=0.10$, $p=0.47$; Cornell voltage index, $r=0.15$, $p=0.30$; Gubner index, $r=0.05$, $p=0.73$).

Several reports have shown that QT interval prolongation is associated with the risk of life-threatening arrhythmias in patients with primary aldosteronism [17,18]. Hypokalemia is known to cause QT interval prolongation. However, it remains to be controversial whether QT interval is

associated with serum potassium level in patients with primary aldosteronism. Matsumura et al previously reported that QTc interval significantly correlated with serum potassium level, but did not with PAC in 19 patients with primary aldosteronism [6]. They also showed that this correlation disappeared after adrenalectomy. On the other hand, Yang et al reported that QT interval correlated with PAC, but did not potassium level in patients with 26 patients with primary aldosteronism [7]. One possible reason of the discrepancy between their studies was a small sample size. In this study, we evaluated in a relatively large number of 56 patients, and demonstrated that QTc interval significantly correlated with serum potassium level, but did not with PAC. Our results suggested that aldosterone excess itself did not affect the QTc interval.

Previous studies showed that QT interval was associated with LVH in hypertensive patients [8,9] or diabetic subjects [10]. Although LVH of the concentric type is common in primary aldosteronism, there has been no report assessing this correlation in this disorder. In this study, we showed that there was no significant correlation between QT interval and echocardiographic as well as electrocardiographic LVH. As shown in this study, QT interval prolongation in primary aldosteronism seems to be associated with serum potassium level rather than LVH. Because QT interval prolongation may potentially increase the risk of life-threatening arrhythmias, clinician should pay careful attention to serum potassium level and QT interval in patients with primary aldosteronism.

In conclusion, QT interval prolongation was associated with serum

potassium level rather than LVH in patients with primary aldosteronism.

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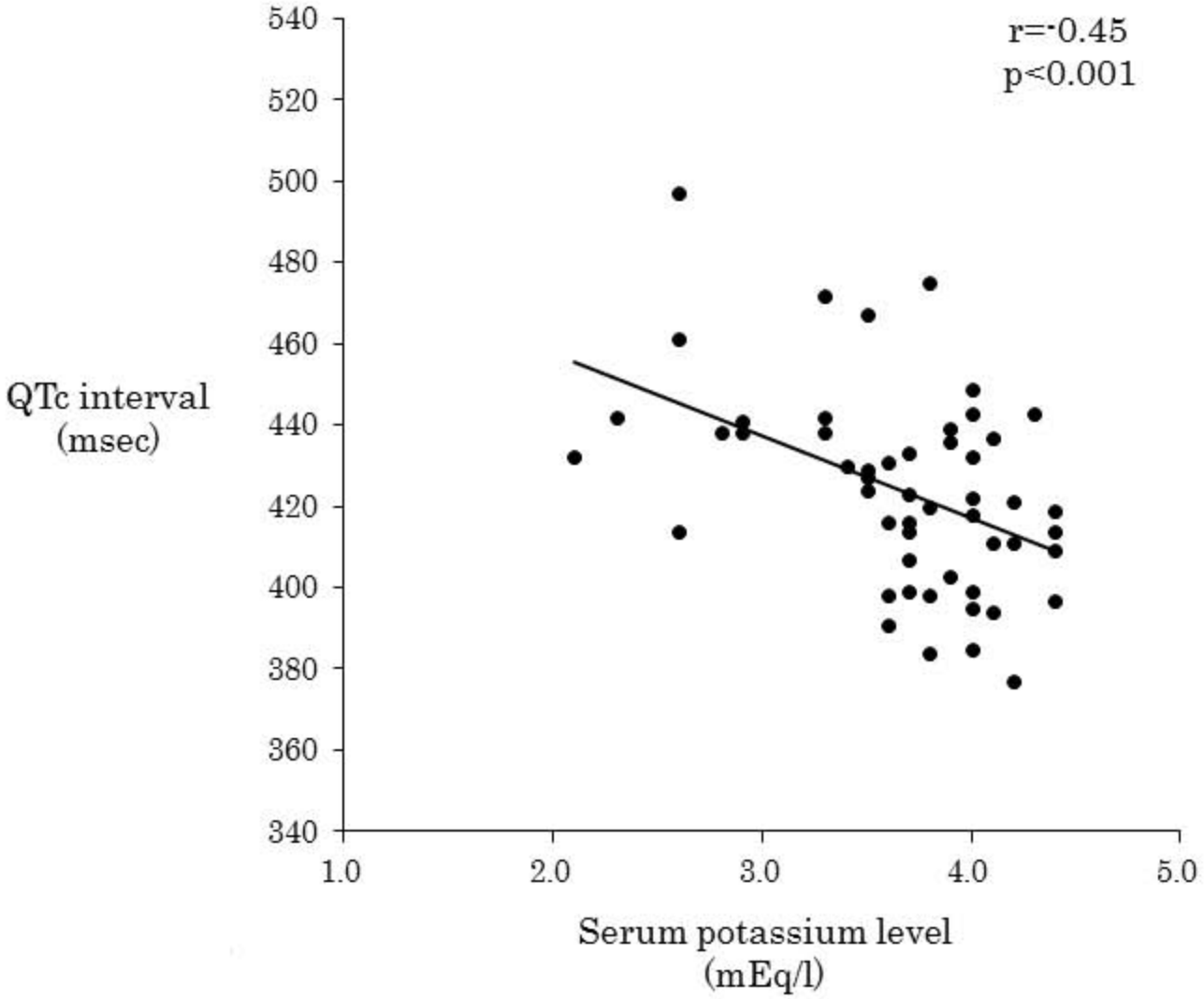
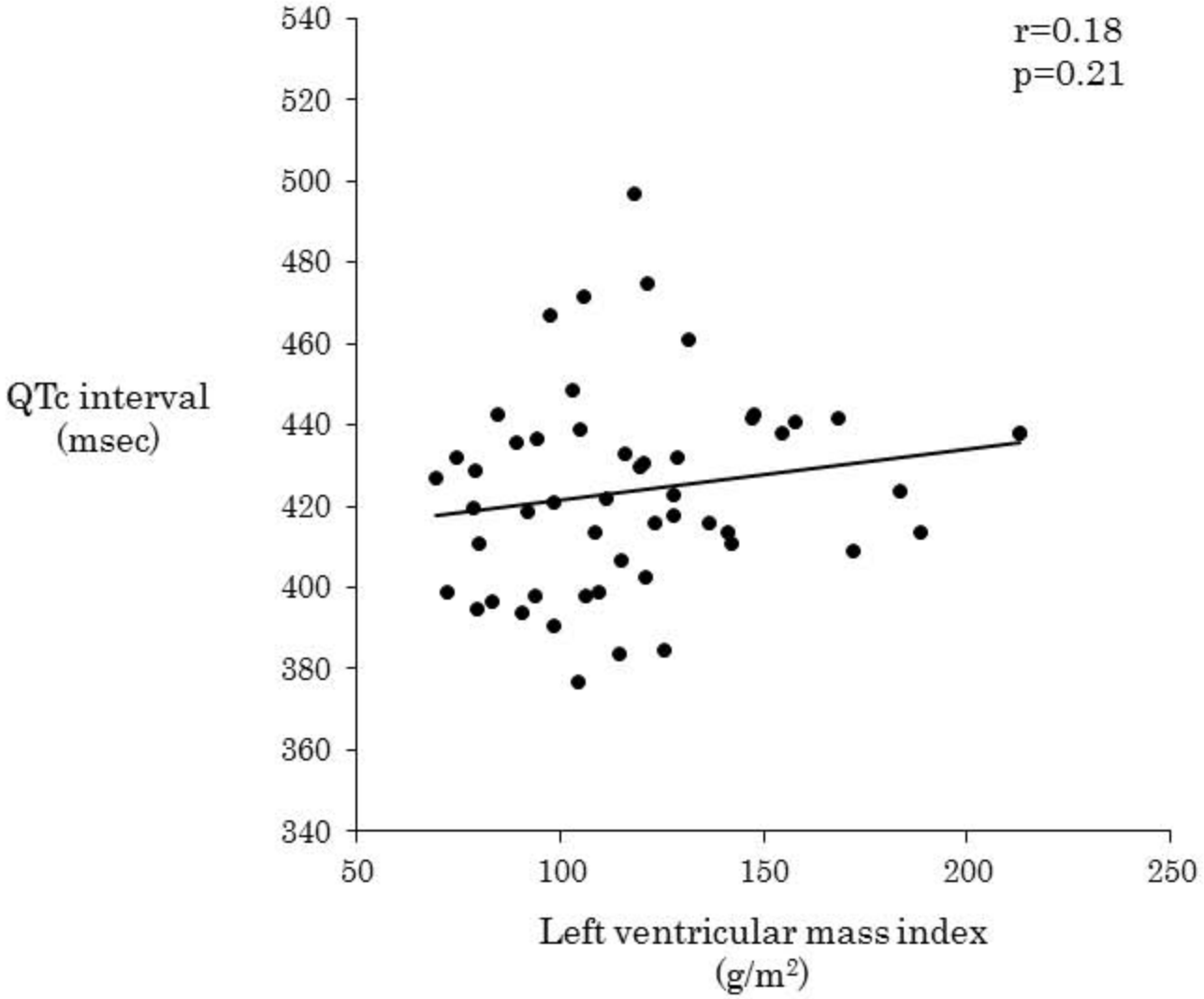
FIGURE LEGENDS

Figure 1 There was a significant correlation between serum potassium level and QTc interval ($r=-0.45$, $p<0.001$).

Figure 2 There was no significant correlation between LVM index and QTc interval ($r=0.18$, $p=0.21$).


r=-0.45
p<0.001
QTc interval
(msec)
540
520
500
480
460
440
420
400
380
360
340
1.0
2.0
3.0
4.0
5.0
Serum potassium level
(mEq/l)


r=0.18
p=0.21
QTc interval
(msec)
540
520
500
480
460
440
420
400
380
360
340
50
100
150
200
250
Left ventricular mass index
(g/m2)

Age (years)	59±11
Male gender	26 (50%)
Systolic blood presure (mmHg)	144±19
Diastolic blood pressure (mmHg)	85±12
Plasma renin activity (ng/ml/hr)	0.51±0.37
Plasma aldosterone concentration (pg/ml)	27.6±22.6
Serum sodium (mEq/l)	140.9±3.3
Serum potassium (mEq/l)	3.7±0.6
Serum creatinine (mg/dl)	0.82±0.28
Electrocardiographic findings	
QTc interval (msec)	424.1±24.5
Sokolow-Lyon index (mm)	30.8±9.0
Cornell voltage index (mm)	16.9±7.9
Gubner index (mm)	8.6±4.8
Echocardiographic findings	
Left ventricular end-diastolic diameter (mm)	47.7±7.7
Left ventricular ejection fraction (%)	65.0±5.1
Left ventricular mass index (g/m2)	118.7±34.2
Left atrial diameter (mm)	37.7±5.7

Table 1 Patient characteristics