

EVALUATION OF VENTRICULAR REPOLARIZATION IN FAMILIAL MEDITERRANEAN FEVER PATIENTS WITH/WITHOUT AMYLOIDOSIS

Ekrem Kara, Elbis Ahbap, Tamer Sakaci, Tuncay Sahutoglu, Mustafa Sevinc, Taner Basturk, Yener Koc, Cuneyt Akgol, Zuhul Atan Ucar, Arzu Ozdemir Kayalar, Feyza Bayraktar, Abdulkadir Unsal

Sisli Etfal Training and Research Hospital, Department of Nephrology, Istanbul, Turkey

Objectives:

Familial Mediterranean Fever (FMF) is an autoinflammatory and genetically inherited disease, that is characterized by episodic attacks of chronic inflammation and resulting with systemic amyloid A amyloidosis if untreated. Cardiac arrhythmias were shown to be part of the cardiovascular involvement in some of the rheumatic diseases, but data about FMF is conflicting. It has been shown that the increase in duration of ventricular repolarization is associated with life-threatening ventricular arrhythmias. Thus, we aimed to investigate ventricular repolarization indexes in FMF patients with/without amyloidosis.

Methods:

FMF patients who were being followed up between 2010-2014 in the outpatient clinic and age/gender comparable healthy controls were included. All patients were attack free and subject with disease or drugs that are known to alter cardiac electrophysiology were excluded. Diagnosis of FMF was confirmed according Tel-Hashomer criteria and the diagnosis of amyloidosis was made by renal biopsy. Demographic, laboratory and electrocardiographic data were obtained and analyzed.

Table 1. Comparison of demographic and laboratory parameters between healthy controls and FMF patients.

	Control (n=30)	FMF (n=67)	p
Demographics			
Age (years)	37.9±15.2	36.1±11.8	NS
Sex (male/female)	13/17	30/37	NS
FMF disease duration (years)		9.1±8.2	NS
Weight (kg)	71.9±15.6	69.9±16.1	NS
Body mass index (kg/m ²)	25.3±4.7	25.6±5.3	NS
Systolic BP (mmHg)	115.5±6.9	113.7±13.0	NS
Diastolic BP (mmHg)	74.5±5.6	71.0±7.4	0.009
Laboratory			
Urea (mg/dL)	27.0±9.0	30.7±17.1	NS
Creatinine (mg/dL)	0.8±0.1	0.9±0.4	NS
Uric acid (mmol/L)	4.8±1.1	4.7±1.5	NS
Sodium (mmol/L)	140.9±2.4	139.8±2.1	NS
Potassium (meq/L)	4.5±0.4	4.4±0.4	NS
Hemoglobin (g/dL)	13.7±1.7	13.3±1.6	NS
Total cholesterol (mmol/L)	193.3±29.3	179.9±40.7	NS
Triglyceride (mmol/L)	140.1±103.6	119.0±80.8	NS
LDL (mmol/L)	114.3±22.1	106.5±37.4	NS
HDL (mg/dL)	52.4±15.9	49.5±12.7	NS
Albumin (g/dl)	4.7±0.3	4.5±0.5	NS
Ferritin (ng/mL)	68.1±51.4	61.0±72.5	NS
Proteinuria (mg/24 hr)	69.3±34.6	605.8±1834.8	<0.001
CRP (mg/L)	4.5±2.2	7.1±11.5	NS
ESR (mm/h)	12.3±6.4	15.5±16.0	NS
Fibrinogen (mg/dL)	269.8±57.6	281.6±75.2	NS

BP: blood pressure; LDL: low density cholesterol; HDL: high density cholesterol; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

Figure 1: Correlation between levels of proteinuria and Tpe interval.

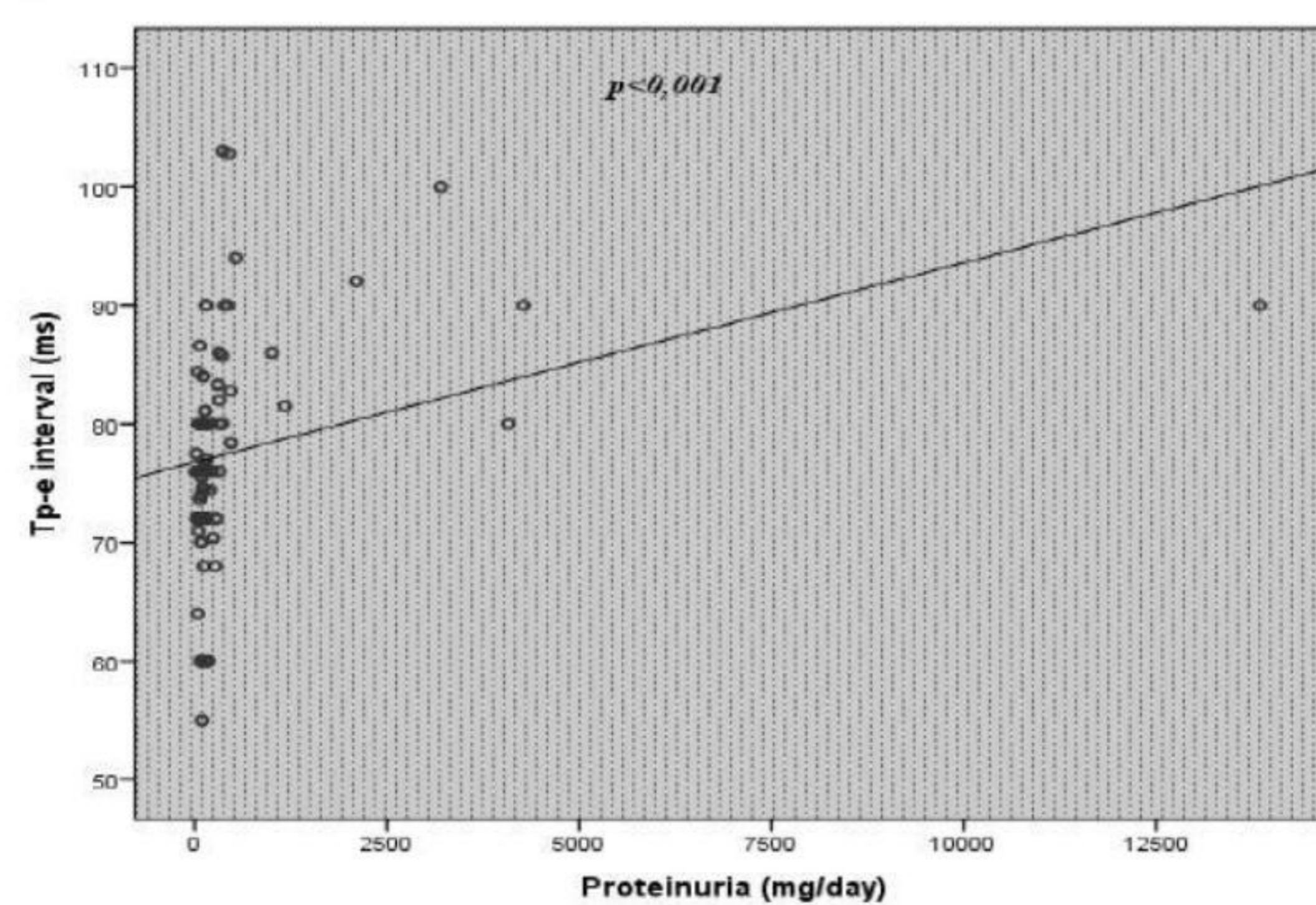


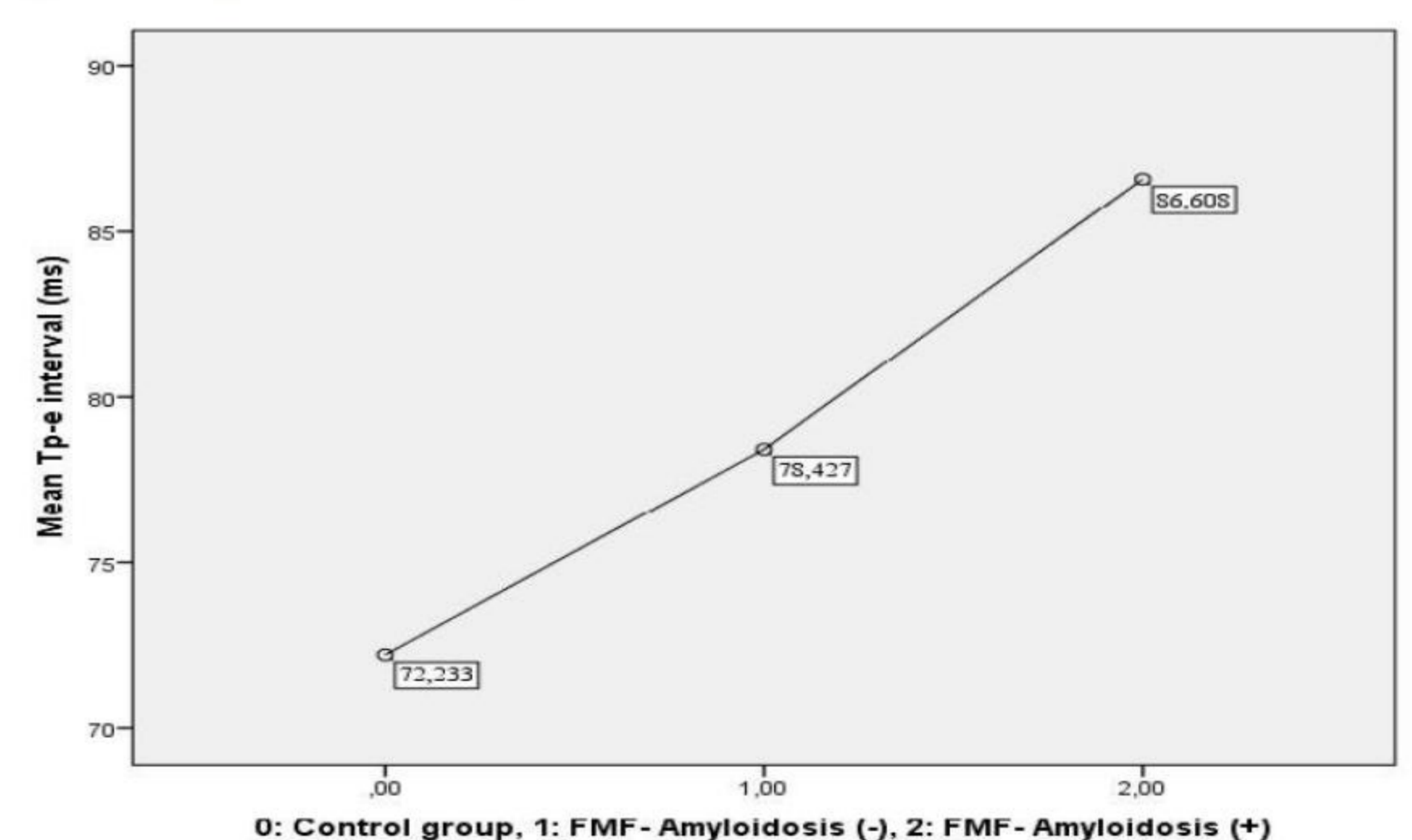
Table 2. Comparison of ventricular repolarization parameters between healthy controls and FMF patients with and without amyloidosis.

	Control (n=30)	Amyloidosis (-) (n=55)	Amyloidosis (+) (n=12)	p
Repolarization indices				
QT interval (msec)	367.1±28.9	366.2±23.1	366.9±31.3	NS
QTc interval (msec)	396.9±17.2	400.6±19.8	400.4±23.2	NS
QT dispersion (msec)	22.6±6.9	32.6±14.7	48.3±15.8	<0.001
QT dispersion variance	24.5±7.0	36.9±16.9	52.9±15.9	<0.001
Tpe interval (msec)	72.3±6.1	78.4±8.1	86.6±5.6	<0.001
Tpe/QT ratio	0.191±0.026	0.214±0.025	0.234±0.015	<0.001
Tpe/QTc ratio	0.182±0.016	0.196±0.020	0.216±0.015	<0.001

Table 3. Correlation analysis of ventricular repolarization indices with proteinuria and amyloidosis.

Repolarization indices	Proteinuria		Amyloidosis	
	r	p	r	p
QT interval (msec)	-0.142	NS	-0.037	NS
QTc interval (msec)	-0.031	NS	+0.008	NS
QT dispersion (msec)	+0.538	<0.001	+0.393	<0.001
QT dispersion variance	+0.580	<0.001	+0.384	<0.001
Tpe interval (msec)	+0.500	<0.001	+0.463	<0.001
Tpe/QT ratio	+0.537	<0.001	+0.401	<0.001
Tpe/QTc ratio	+0.475	<0.001	+0.393	<0.001

Figure 2: Comparison of mean Tpe intervals between the control group, amyloidosis negative and positive FMF patients.



Results:

There were 67 FMF patients, 12 of them with amyloidosis, and 30 healthy controls eligible to study. QT and QTc intervals were within the normal ranges and similar between FMF patients and healthy controls. QT dispersion, peak to end interval of T wave (Tpe), Tpe/QT and Tpe/QTc ratios were significantly higher in FMF patients than in healthy controls. When patients with and without amyloidosis were compared, we found that patients with amyloidosis had significantly increased QT dispersion, Tpe, Tpe/QT and Tpe/QTc. Level of proteinuria and the presence of amyloidosis were moderately correlated with QT dispersion, Tpe, Tpe/QT and Tpe/QTc.

Conclusions:

Ventricular repolarization indexes are significantly increased in FMF patients especially with secondary amyloidosis. This increase is positively correlated with high levels of proteinuria. This findings suggest that FMF patients may have an increased arrhythmogenicity and ventricular repolarization indexes could be used as early markers of life-threatening ventricular arrhythmias.