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THE RELATIONSHIP BETWEEN PATIENT SURVIVAL AND ECG aVR T WAVE POSITIVITY IN HEMODIALYSIS PATIENTS

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Abstract

Aim: Evidence suggests a relationship between electrocardiography (ECG) aVR (augmented voltage right) T wave and cardiovascular mortality in hemodialysis patients. The aim of our study was to investigate the relationship between ECG T aVR positivity and overall mortality together with other known risk factors in hemodialysis patients.

Methods: One hundred and one hemodialysis patients were retrospectively screened for ECG T aVR wave positivity. In parallel, the relationship between T aVR positivity and age, gender, calcium phosphorus index, heart rate, ECG and echocardiographic parameters, mortality, smoking, presence of diabetes mellitus, hypertension, myocardial infarction were investigated.

Results: Univariate analyzes revealed that patients with positive T aVR (16%) had a statistically lower dialysis time and ejection fraction compared to patient with negative T aVR (p=0.041 and p=0.046, respectively). Survival analysis revealed statistically significantly better prognosis for T aVR-negative patients compared to T aVR-positive patients (5-year survival 70.9%, and 45.5%, respectively; p=0.027). Among tested parameters, independent risk factors affecting survival in hemodialysis patients were found to be age (hazard ratio, HR: 1.03), high heart rate (HR: 1.03), smoking (HR: 3.37) and presence of diabetes mellitus (HR: 2.91).

Conclusions: Our results indicate that routine monitorization of T wave in aVR derivation together with evaluation of other risk factors may provide information about the cardiovascular risk profile, mortality and life habits of hemodialysis patients.

Keywords: *Electrocardiography, hemodialysis, mortality*

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Introduction

Cardiovascular diseases are the most important cause of mortality in patients with end-stage renal disease (ESRD), corresponding to approximately half of deaths in this patient group[1]. Compared to general population, mortality due to cardiovascular causes has been reported to be approximately ten times higher among hemodialysis patients[2].

Electrocardiography (ECG) is a method used in diagnosis and prognosis in cardiac diseases. T wave anomalies are among the common pathological ECG findings in the healthy population. The relationship between T wave anomalies in augmented voltage right (aVR) derivation and cardiovascular mortality has been shown in several studies[3,4]. One of the groups in which cardiovascular problems and ECG abnormalities frequently detected has been shown to be the hemodialysis patients.

Lead aVR provides information on the upper right side of the heart which is not easily detected in other leads[4]. The direction of the T wave vector has been shown to change towards the injured myocardial region when the repolarization of injured myocardial cells was delayed[5]. Therefore, positive T waves in the aVR derivation may represent the presence of ischemic injured myocardium in the apical, lower and lower lateral regions of the heart which are known to be supplied with blood from the left anterior descending (LAD), right coronary or left circle coronary artery. Therefore, lesions or diseases in these arteries located more proximally in the left main coronary artery (LMCA) are expected to switch the negative T aVR to positive[6].

T wave anomalies are considered important when detected in many leads, but these anomalies and their cardiovascular effects in lead aVR have been neglected. Some recent studies have emphasized that T wave variability in aVR lead may be an independent prognostic indicator[7].However, data on this relationship is scarce in hemodialysis patient groups. In this study, the objective was to evaluate the frequency of T wave positivity in aVR lead and to explore its possible relationship with poor prognosis and mortality rates in hemodialysis patients.

Materials and Methods

Patients

Between 2007-2019, 196 patients who underwent dialysis were retrospectively screened. Ethics committee approval was obtained in October 2016 (Protocol number: 13). Fifty-five of these patients who lost their lives in this hospital and their records were reached. Of the remaining 141 patients, 72 patients have continued to be dialyzed or transplanted at our center or have continued to follow up at our center while continuing dialysis at another dialysis center. Since the current information of the rest of the patients could not be retrieved, they were not included in the final analyses. Eight of 72 alive patients and 18 of 55 patients who had lost their lives were excluded from the study due to branch block or AF (atrial fibrillation) on ECG. Thus, to the final analyses 101 patients were included (64 alive and 37 with exitus). Dialysis was performed to the patients as 3×4 hours/week. Patients' age, gender, smoking (> 1 pack-year), presence of hypertension, presence of diabetes mellitus, presence of myocardial infarction history, dialysis duration, electrocardiographic and echocardiographic data, and calcium-phosphorus index were collected for further analyses.

Electrocardiography

Electrocardiographic records of the patients were obtained from medical records. The standard 12-lead surface electrocardiograms (25 mm/s and 10 mm = 1 mV) recorded every six months from the first application of dialysis were evaluated. Conventional ECG parameters including heart rate, PR interval, QRS time, QT time, branch block, QRS axis, abnormal Q waves, T wave inversion, left ventricular hypertrophy

(Sokolow and Lyon voltage amplitude criteria SV1 + RV5 or V6) were calculated. The T wave amplitude was defined as the first deviation after the QRS complex and/or the maximum deviation from the PR isoelectric line. The positive T wave deflection was defined as a wave with a positive deviation larger than 0 mV. Negative T aVR was defined as TaVR less than or equal to 0 mV. T wave amplitudes in aVR derivation were measured manually. The 12-lead electrocardiograms of each patient were evaluated by an independent cardiologist who was blind to the clinical results of the patients. Patients who were positive and negative in T aVR at baseline and follow-up were identified.

Echocardiography

Echocardiographic records of the patients were obtained from medical records. For patients for whom ECG was performed annually at the center, the average of the values was recorded leading to more than one echocardiography record during follow-up. For two patients, only one echocardiography record each without ejection fractions (EF) were available. For the rest of the patients the EF records (n = 99) were evaluated.

Biochemical measurements

The multiplication indexes of calcium and phosphorus values measured monthly during the follow-up period were calculated every three months starting from the beginning of hemodialysis treatment. Also their own average indexes were recorded during the follow-up.

Ethical aspects

The study was approved by the ethical committee in October 2016 (Protocol number: 13). Written consent was not taken due to the retrospective character of the study.

Statistical analysis

Statistical analysis of the data was analyzed with SPSS 25.0 (IBM, Chicago, USA) package program. Numbers and percentages were used to summarize categorical measurements. Continuous measurements were shown as mean and standard deviation. Comparison of categorical variables were calculated with Chi square test or Fisher test. Distributions were plotted while comparing continuous measurements between groups. On order to provide parametric distribution assumption student T test was used. For parameters that could not provide parametric distribution assumption Mann-Whitney U test was used. Long-rank test was used to calculate survival differences. Cox regression analysis was used to test the independent variables that affect survival. In all tests statistical significance level was considered as 0.05.

Results

Forty-nine of 101 patients enrolled in the study were male and mean age was 56.3 ± 17.7 in men and 57.6 ± 15.9 in women. The demographic characteristics of the patients are summarized in Table 1. When dialysis was initiated (i.e. baseline), 17 patients (16.83%) were positive for T aVR and the positivity was preserved during the follow-up period. Of the 84 patients with negative T aVR wave at baseline, no positivity was observed during the follow-up period. The distribution of T wave positivity in living and exitus patients is given in Table 1. The age, dialysis time, heart rate, calcium phosphorus product index, ECG T wave amplitude (mV), ECG Qtc (corrected QT interval) time (msn), ECG QRS time (msn), echocardiographic data and mass index of the patients are given in Table 2.

Univariate analyzes revealed that dialysis duration, EF, gender and smoking may affect T wave positivity (Table 2). Dialysis duration and EF rates were statistically lower in patients with T wave positivity (p=0.041 and p=0.046, respectively).

Table 1. Demographic distribution of data

	Female n:52	Male n:49	p
Age- years ± SE	57.6 ± 15.9	56.3 ± 17.7	0.706
Dialysis vintage - Months (range)	52.8 (2.0-180.5)	50.7 (2.0-201.0)	0.985
Smoking >1 pack/day - n (%)	7 (13.5)	23 (46.9)	0.0001
Diabetes mellitus- n (%)	17 (%32,6)	20 (%40,8)	0,435
Hypertension - n (%)	41 (%78,8)	33 (%67,3)	0,761
Prior myocardial infarction history - n (%)	10 (%19,2)	7 (%14,2)	0,634
T aVR negative (exitus/alive) - n	39(15/24)	45 (13/32)	0,247
T aVR positive (exitus/alive) - n	13 (8/5)	4 (1/3)	0,069

T aVR = T wave in augmented voltage right.

Table 2. Univariate analysis of biochemical/echocardiographic determinant of ECG aVR T wave in hemodialysis patients

	All patients (n = 101)	ECG aVR T wave Negative (n = 84)	Positive (n = 17)	p
Age (year)[a]	56.9 ± 16.8	57.5 ± 16.4	54.4 ± 18.9	0.492
Dialysis vintage (month)[b]	50.7 (2.0-201.0)	54.3 (2.9-201.0)	20.4 (2.0-90.6)	0.041
Hearth rate (beat/minutes)[a]	81.9 ± 16.3	80.5 ± 14.1	88.2 ± 22.9	0.080
ECG T wave amplitude (mV)[b]	1 (0-4)	1 (0-4)	2 (0.5-2)	0.973
ECG QTc duration (msn)[a]	0.44 ± 0.01	0.44 ± 0.03	0.45 ± 0.05	0.427
ECG QRS duration (msn)[b]	0.09 (0.07-0.98)	0.09 (0.07-0.95)	0.09 (0.08-0.98)	0.350
ECHO LV diastolic size (mm)[a]	46.0 ± 5.2	45.9 ± 4.9	46.3 ± 6.4	0.760
ECHO posterior wall diameter (mm)[a]	10.8 ± 1.7	10.7 ± 1.6	11.1 ± 2.0	0.295
ECHO Ejection fracture (%)[a]	60.3 ± 8.2	61.1 ± 7.206	56.78 ± 11.3	0.046
ECHO IV septum diameter (mm)[a]	11.5 ± 2.1	11.4 ± 1.9	11.8 ± 2.5	0.421
ECHO mass [a]	219.2 ± 77.3	215.2 ± 76.6	239.2 ± 80.0	0.245
Calcium x Phosphorus index[b]	36.4 (13.7-93.8)	36.8 (3.7-93.8)	35.2 (19.4-60.0)	0.707

ECG = electrocardiography ; aVR = augmented voltage right ; ECHO = echocardiography; IV: interventricular. [a]: Mean ± SE; [b]: Mean (Range)

It was also found that T wave positivity was statistically significantly higher in women (p=0.033). Finally, smoking rates were statistically more frequent among the T wave negative patients (p=0.019). Higher T aVR positivity (3.7 times higher) and lower smoking rates in women may explain this result (Table 3). The short dialysis duration in T aVR positive patients was related to the earlier death of these patients. However, it is important to mention that two of these patients had cadaveric kidney transplantation and the patients were still alive.

In the whole patient population, the five-year survival rate was found to be 68% (Table 4). This rate among patients with ECG T aVRT positivity was statistically lower compared to their counterparts with negative T aVRT (45.5% versus 70.9%, P = 0.027).

Independent risk factors affecting survival were evaluated by Cox regression analysis. The results of these analyses showed that elder age, higher heart rate, smoking and presence of diabetes mellitus were independent risk factors for survival (Table 5).

Table 3. Univariate analysis of comorbidity and habit determinants of ECG aVR T wave in hemodialysis patients Univariate analysis between ECG aVR T wave and gender, living / exitus status, smoking, diabetes, hypertension and history of MI

	ECG aVR T wave					
	Negative (n = 84)		Positive (n = 17)			
	n	%	n	%	p	Odds ratio (95% CI)
Male	45	53.6	4	23.5	0.033	3.7(1.1-12.4)
Female	39	46.4	13	76.5		
Alive	56	66.7	8	47.1	0.168	-
Deceased	28	33.3	9	52.9		
Smoking > 1 pack/day	29	34.5	1	5.9	0.019*	8.4(1.1-66.8)
Diabetes Mellitus	29	34.5	8	47.1	0.410*	-
Hypertension	63	75.0	11	64.7	0.382*	-
Prior MI	14	16.7	3	17.6	1.000*	-

ECG = electrocardiography; aVR = augmented voltage right; CI = confidence interval; MI: Myocardial infarction. *Compared to negative group for these conditions.

Table 4. Survival rates of patients

	Mean ± SE	95% CI	Survival %			
			1 year	2 years	3 years	5 years
MST (total)	116 ± 10.1	97.0 - 136.4	87.9	84.6	75.7	68.0
ECG aVR T wave						
Negative[a]	123.6 ± 10.8	102.5 - 114.7	90.3	88.8	81.3	70.9
Positive[b]	54.2 ± 9.2	36.2 - 72.2	70.1	63.7	54.6	45.5
p-value (a vs b)			0,046	0.031	0.03	0.027

SE = standart error; CI = confidence interval; MST =mean survival time; ECG = electrocardiography; aVR =augmented voltage right.

Table 5. Independent risk factors for survival

	B	SE	Wald	df	p-value	HR	95.0% CI for HR	
							Lower	Upper
Age	0.03	0.012	5.91	1	0.015	1.03	1.01	1.06
Heart Rate	0.03	0.011	9.37	1	0.002	1.03	1.01	1.06
Smoking	1.21	0.462	6.92	1	0.009	3.37	1.36	8.34
Diabetes	1.07	0.36	8.83	1	0.003	2.91	1.43	5.89
ECG aVR T wave	0.28	0.409	0.48	1	0.490	1.3	0.59	2.54

B = regression coefficient; SE = standart error; df = degrees of freedom; CI = confidence interval; HR = hazard ratio; aVR = augmented voltage right.

Table 6. Relationship between TaVR positivity and biochemical and electrocardiograhical parameters in hemodialysis patients.

		CaxP index	Age	Dialysis vintage (month)	Heart rate (beat/min)	QTc duration (msn)	QRS duration (msn)	ECHO LV diastolic size (mm)	ECHO posterior wall (mm)	Ef (%)	ECHO IVS (mm)
aVR T (-)	Ex	37.91 ± 16.28 19.50-93.80	62.96 ± 14.42 23-85	49.97 ± 41.85 3-180.47 41.08*	83.70 ± 16.64 51-114	0.42 ± 0.04 0.30-0.49	0.08 ± 0.00 0.07-0.10	47.00 ± 5.46 35.00-55.00	10.85 ± 1.73 9.00-15.00	60.28 ± 7.84 28-68	11.60 ± 2.36 9.00-19.00
	Alive	38.38 ± 13.38 13.70 ± 82.30	54.76 ± 16.74 18-85	68.18 ± 43.87 5.20-201.03 68.45*	78.47 ± 12.08 57-109	0.44 ± 0.02 0.38-0.50	0.09 ± 0.01 0.07-0.11	45.45 ± 4.67 37-58	10.59 ± 1.52 7-15	61.52 ± 6.95 30-70	11.27 ± 1.74 7-15
aVR T(+)	Ex	40.68 ± 13.82 19.40-60.03	59.88 ± 14.16 36-856	28.97 ± 32.52 2-75 10.66*	99.88 ± 24.19 49-124	0.45 ± 0.06 0.34-0.56	0.09-0.10 0.08-0.11	47.55 ± 7.82 38.00-61.00	11.73 ± 2.15 9-16	51.11 ± 12.98 35-65	12.50 ± 2.57 9-18
	Alive	32.78 ± 5.01 24.30-40.03	48.25 ± 22.54 23-82	54.97 ± 35.57 7.27-90.57 61.76*	75.00 ± 12.29 58-91	0.43 ± 0.02 0.40-0.46	0.08 ± 0.00 0.078-0.104	45.00 ± 4.34 41-54	10.50 ± 1.75 8-13	63.12 ± 3.48 60-68	11.12 ± 2.32 8.50-15.0
		0.734	0.492	0.083	0.08	0.384	0.344	0.788	0.293	0.047	0.402

*Median dialysis times.
Qtc: corrected QT interval; Ca: Calcium; P: phosphorus; Ef: ejection fraction; LV: left ventricle; IVS: interventricular septum; ECHO: echocardiography

Finally, comparison of cardiac parameters and T aVR status of the living and deceased patients were evaluated (Table 6). Among the cardiac parameters, only EF was found to be lower in deceased patients with T wave positivity compared to other groups.

Discussion

Compared to the general population, mortality due to cardiovascular causes has been reported to be approximately ten times higher in hemodialysis patients with ESRD[2]. The T wave positivity in aVR derivation, has been considered to be the determinant of cardiovascular risk in general population. In this study, the relationship between T aVR positivity and mortality in hemodialysis patients was evaluated.

Among our hemodialysis patients, the frequency of T aVR positivity was found to be 16.83%. The frequency of positive T aVR, which was less than 2% in the general population, was reported to be 17.5% in patients with heart failure and 16.2% in patients who had undergone myocardial infarction (MI)[8,9,10]. Patients who had T aVR positivity at the start of hemodialysis continued to preserve the positivity during follow-up visits. On the other hand, patients who were T aVR-negative at baseline, did not develop positivity during the follow-up period.

Median death times were 10 months in patients with T aVR positivity, and 41 months in patients with T aVR negativity. Dialysis duration of living patients was 54 and 68

months for T aVR positive and negative patients, respectively. The death rates were higher in T aVR-positive patients (52%) compared to T aVR-negative patients (33.3%). In accordance with these findings, in another study with 233 hemodialysis patients, the frequency of T aVR positivity was reported to be 16%, and the risk of death was shown to be increased among T aVR-positive patients[11]. Because the aVR lead is electrically opposite the lateral precordial leads, ST-segment depression in V5 to V6 is often accompanied by ST-segment elevation in aVR[12]. In general, the fact that negative T waves in the lateral precordial leads are accompanied by a positive T wave in aVR may be an explanation for the negative prognostic effect of aVRT+ demonstrated in this study[13].

Mortality rates were observed to be higher in T aVR-positive patients starting from the end of the first year of follow-up. The survival rates at the end of first, second, third and fifth years were 90.3%, 88.8%, 81.3% and 70.9% in T aVR-negative patients, respectively; and 70.1%, 63.7%, 54.6% and 45.5% in T aVR-positive patients, respectively. When the patients were evaluated with respect to their T aVR status and survivals over time, only EF was statistically significantly different among other ECG and echocardiographic parameters. These findings may also be consistent with the high rates of T aVR positivity in patients with heart failure. In the present study, the EF was statistically lower in T aVR-positive patients who lost their lives during the study, which is consistent with the report by Jaroszyński et al[11]. Jaroszyński et al. also showed that MI, DM and beta-blocker therapy were more frequent; and age, CaXP, wider QRS, left ventricle index were higher in T aVR-positive hemodialysis patients. In the present study, however, no differences were observed in terms of CaXP product, T aVR amplitude, QTc time, QRS time, posterior wall thickness, left ventricular end diastolic size, and interventricular septum mass. The only significant difference was observed in EF ratio which was lower among T aVR positive patients. Myocardial structural changes occur with the age and hypertension in HFpEF patients. Increased arterial stiffness causes chronic pressure overload. As a consequence, left ventricular remodeling and increase in diastolic filling pressure happen. In time, diastolic pressure overload and create HF symptom and findings. This physiopathological definiton may explain the more frequent positive T avr wave in patients with low EF[14].

Death was observed to be more frequent in patients with T aVR positivity, although this was not an independent risk factor according to the survival analysis which identified age, heart rate, smoking and presence of DM as independent risk factors. In the study by Jaroszyński et al[8], age, heart rate and T aVR positivity were independent risk factors, although the T aVR positivity rates were similar with the rates reported in the present study. Also, T aVR positivity was identified as an independent risk factor in patients with heart failure with reduced EF[14]. Similarly, in postpartum cardiomyopathy patients with T aVR positivity in the initial ECGs, cardiac death, left ventricular failure, and T aVR positivity for arrhythmic events were identified as independent risk factors in a study with 67-month follow-up period[15]. However, similar to the present study, in non-ST-segment elevation myocardial infarction patients, higher rates of T wave positivity were observed to be more frequent in older people, women and patients with low EF[16]. Also in the same study, although major adverse cardiac events (MACE) were reported to be more frequent in T aVR-positive patients, it was not identified as an independent risk factors, as in the present study.

The results in the present study indicate that positive T wave in aVR in ECG may be informative for mortality rates in hemodialysis patients in addition to known risk factors. The limitations of this study are: the limited number of patients, being single-centered and retrospective.

Conclusion

T aVR positivity in ECG in hemodialysis patients was found to be as frequent as in patients with heart failure with myocardial infarction and reduced EF. T aVR positivity, which is more common in female hemodialysis patients, was associated with a shortened lifetime and an increased frequency of death. The status of T aVR detected at the time of starting the hemodialysis program did not change during follow-up neither for patients positive nor negative at baseline. Therefore, it can be concluded that T aVR positivity is common in patients who start hemodialysis, and it might have an impact on the survival of hemodialysis patients. However, our results indicate that it is not an independent risk factor for mortality in these patients. To better understand the relationship between T aVR positivity and mortality in hemodialysis patients, additional studies as warranted with bigger cohort groups.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
This study was approved by the Cukurova University Institution Ethics Committee (57-2016).

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