

THE ROLE OF MYOCARDIAL PERFUSION IMAGING SPECT IN EPILEPSY

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Abstract

Introduction: Cardiovascular disease represents a significant contributor to the increased mortality and hospitalized morbidity in people with epilepsy, compared with the general population. Sudden unexpected death in epilepsy (SUDEP) is a well-known phenomenon of ongoing investigation. Patients with drug refractory epilepsy have cardiovascular abnormalities that might be related to a high frequency of sudden death. Myocardial perfusion imaging (MPI) represents a reliable non-invasive test for myocardial evaluation in various medical conditions.

Purpose: The aim of the present study is the comparison of MPI results in patients with epilepsy and assess whether MPI could be utilized for diagnosis of early myocardial ischemia in patients with epilepsy exhibiting non-specific cardiac symptoms and having normal ECG and cardiologic examination.

Methodology: The study included patients with active epilepsy for more than 5 years. Demographic features, biochemical parameters and established cardiovascular risk factors were recorded. All study individuals were subjected prior and after stress to ^{99m}Tc -TF-SPECT using a 1-d imaging protocol. The control group consisted age and gender matched individuals. MPI summed scores over the 17 myocardium segments were evaluated separately for stress (SSS) and rest (SRS) images. Abnormal MPI was considered when SSS was ≥ 4 . Their difference (SDS=SSS-SRS), a measure of reversibility in response to stress, was additionally calculated.

Results: Twenty-nine patients with epilepsy and 32 control individuals were recruited in the study. Twenty (68.97%) patients with epilepsy had abnormal MPI and 14/32 (43.75%) of the controls ($P = 0.04$). Regarding the gender, 18/23 (78.2%) male patients and 11/25 (44%) male controls had abnormal MPI ($P = 0.01$), with quite a significant difference for mean SSS between male patients and controls ($P = 0.002$) Furthermore, male patients demonstrated more irreversible myocardial ischemic abnormalities than control group individuals. Difference of inadequately compensated myocardial ischemia between patients treated with enzyme inducing AEDs and patients treated with valproic acid was also detected.

Conclusions: Epileptic patients with atypical cardiac symptoms are at higher risk for cardiovascular disease compared to matched control individuals. MPI may represent a non-invasive tool to detect early myocardial ischemia in patients with epilepsy and may lead to reduction of sudden cardiac death.

Keywords: epilepsy; myocardial perfusion imaging; myocardial ischemia

Purpose

Cardiovascular disease represents a significant contributor to the increased mortality and hospitalized morbidity in people with epilepsy, compared with the general population.(1)

Myocardial infarction (MI) following seizures may occur in a variety of epileptic conditions including single or repetitive, convulsive or nonconvulsive seizures.(2)

Higher prevalence of cardiovascular risk factors such as hypertension, diabetes, and high cholesterol has been reported in patients with epilepsy compared to general population. (3)

Oxidative stress circulating markers are increased in patients with epilepsy and may be associated with subclinical atherosclerosis, (4) whereas pharmacological studies have suggested that antiepileptic drugs (AEDs) modulate atherothrombotic risk factors. (5)

The aim of the present study was the comparison of MPI SPECT results in patients with epilepsy to age and gender matched control individuals and assess whether MPI SPECT could be utilized for diagnosis of early myocardial ischemia in patients with epilepsy exhibiting non-specific cardiac symptoms and having normal ECG and cardiologic examination.

The study patients with active epilepsy (epilepsy on AEDs or with one or more seizures in the past year or both) who were diagnosed with epilepsy for more than 5 years were included.

The control group consisted of gender and age matched individuals that demonstrated similar symptoms. All study participants (patients and control individuals) had no known history of coronary artery disease (CAD).

Demographic features, biochemical parameters and established cardiovascular risk factors were recorded (smoking, arterial hypertension, diabetes mellitus, hypercholesterolemia and cardiovascular disease heredity). The history of family cardiovascular disease (angina pectoris, unstable angina, myocardial infarction) was assessed by questionnaire.

Data from the medical history of patients with epilepsy were recorded, such as the age of epilepsy onset, the duration of epilepsy in years, seizures frequency and the type of epilepsy, (generalized epilepsy, focal epilepsy and of unknown origin). The administered AEDs, the number of administered AEDs at the time of recruitment, as well as the total number of AEDs prescribed were recorded. Patients were further categorized according to epilepsy type (focal/generalized and symptomatic/no symptomatic-genetic and of unknown origin), to seizures type (focal without and with awareness loss/ primary generalized and secondary generalized-focal with bilateral spasms) and whether their therapeutic schema included enzyme-inducing AEDs and/or valproic acid (VPA).

All study individuals were subjected prior and after stress to ^{99m}Tc -TF-SPECT using a 1-d imaging protocol. Images were visually evaluated by two nuclear medicine specialists, using a 17-segment polar map and scoring each segment with a scale of 0 to 4, according to the severity of the myocardial perfusion deficit separately for stress (SSS) and rest (SRS) images. Abnormal MPI was considered when SSS was ≥ 4 . Their difference (SDS=SSS-SRS), a measure of reversibility in response to stress, was additionally calculated.

Results

Twenty-nine patients with epilepsy (23 males, 6 females) and 32 control individuals (25 males, 7 females) were recruited in the study. The mean age of the patients was 56.2 ± 10.5 years vs 55.0 ± 9.3 years for control individuals ($P = .58$). There were no differences in the cardiovascular risk factors between patients with epilepsy and control group for both genders. The mean age of epilepsy onset was $30.4 (\pm 21.0)$ years, the mean duration of epilepsy was $26.4 (\pm 18.5)$ years and the mean number of AEDs receiving was $2.2 (\pm 1.2)$.

Twenty patients (68.9%) and 14 controls (43.7%) had abnormal MPI with $SSS \geq 4$, $P = .04$. Regarding the gender, 18/23 (78.2%) male patients and 11/25 (44%) male controls had abnormal MPI, $P = .01$.

No statistical difference was found for the female individuals.

The mean SSS was $4.5 (\pm 2.3)$ for the patients and $3.1 (\pm 1.8)$ for the controls, $P = .01$.

For males, a statistically significant difference was found for SSS scores and for SDS scores between patients and controls with $P = .002$ and $P = .02$ accordingly (**Table**).

The logistic regression analysis did not show any association of age and cardiovascular risk factors with MPI results. The linear regression analysis did not disclose any association of gender, age and cardiovascular risk factors with the SSS and SDS scores for patients and controls.

No difference of the demographics, the risk factors, the characteristics of epilepsy, the AEDs number and the AEDs type (enzyme inducers and VPA) with MPI results was found between patients with $MPI \geq 4$ and patients with $MPI < 4$.

The impact of enzyme inducers and valproic acid was also assessed. No difference was found for the presence of pathologic MPI and for SSS and SDS scores.

Of interest was the finding of the statistically significant difference for SDS scores between patients receiving inducers and patients receiving VPA, that favors inducers ($P = .05$).

Table

	Total (p1)	Patients with epilepsy Males (p2)	Females (p3)
Number (%)		0.58	
Age years (\pm SD)	0.38	0.60	0.35
Hyperlipidemia (%)	0.22	0.23	0.61
Hypertension (%)	0.13	0.39	0.08
Smoking (%)	0.43	0.49	0.58
Diabetes mellitus (%)	0.53	0.56	0.43
CV Heredity (%)	0.45	0.50	0.61
Abnormal MPI (%)	0.04*	0.01*	0.58
SSS, mean (\pm SD)	0.01*	0.002*	0.86
SDS, mean (\pm SD)	0.06	0.02*	0.58

MPI: myocardial perfusion imaging; p(1): comparison between the total number of patients and controls; p(2): comparison between the male patients and controls; p(3): comparison between the female patients and controls; SD: standard deviation; CV: cardiovascular; SSS: summed stress score; SRS: summed rest score; SDS: summed difference score; AED: antiepileptic drugs *: statistically significant

In the present study, we used radionuclide myocardial scanning in order to assess early cardiovascular disease in patients with epilepsy. Our findings suggested that patients with epilepsy have higher percentage of early cardiovascular disease compared to age and sex matched controls. Male patients had also statistically significant pathologic MPI.

Several mechanisms may explain why epilepsy and cardiovascular disease tend to coexist including causal associations, shared risk factors and those resulting from epilepsy or its treatment (1)

Several studies reported that patients with epilepsy exhibited increased mortality from MI or increased risk of MI. Risk for premature death was three to four times higher in people with epilepsy than in the general Chinese population, much higher in young people with epilepsy, with MI myocardial among the leading putative causes of death. (6)

The literature reports that various AEDs may themselves affect cardiovascular risk in patients with epilepsy. (1)

SPECT may detect increased risk for coronary artery disease and further cardiovascular events in patients with epilepsy. Our findings favor the conclusion that SPECT could be used for early identification and treatment of cardiovascular comorbidity in epilepsy.

In conclusion:

SPECT MPI in patients with epilepsy may reveal early myocardial ischemia that leads to appropriate management and risk reduction of SUDEP.

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