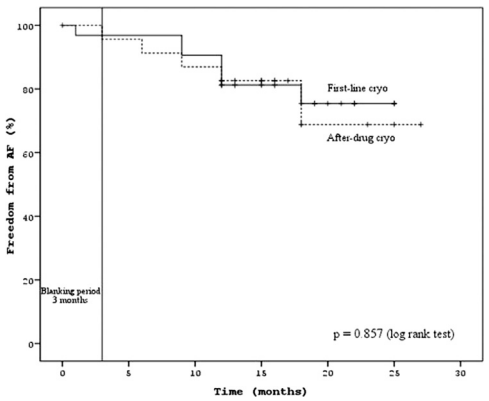

General

OP-102

Evaluation of Methyleletetrahydrofolate Reductase 677C>T Polymorphism in Patient with Atrial Fibrillation with Ischemic Stroke

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Background: Methyleletetrahydrofolate reductase (MTHFR) gene 677C>T mutation in the gene coding for MTHFR, characterized by the replacement of cytosine with thymidine, leads to reduced MTHFR activity and is associated with moderately elevated homocysteine levels. MTHFR polymorphism has been proposed by some studies to be also a thrombophilic risk factor for venous thrombosis and atherothrombosis. Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia, which confers a high risk of mortality and morbidity from stroke and thromboembolism. We aimed to investigate MTHFR gene 677C>T mutation in patients with AF who have had a stroke than in healthy controls.
Methods: MTHFR gene 677C>T mutation was analysed in 70 patients with non-valvular AF who have had a stroke and 70 healthy individuals with no documented episode of AF matched for age, race and sex. After DNA isolation, polymorphisms were analyze using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism methods. Distribution of the MTHFR 677 C>T mutation alles (allel C, allel T) and genotypes (Normal (CC) genotype, heterozygous (CT) or homozygous (TT) mutant genotype) were identified in study population. Demographic characteristics and risk factors for AF and stroke were evaluated in the study groups.
Results: There was no significant difference with respect to age and gender between groups. Genotype and allel distribution of AF patients who have had a stroke and control groups shown in the table. The frequency of CC normal genotype of the MTHFR gene 677 C>T was significantly lower in patients with AF patients who have had a stroke group compared with control group (p<0,05). The frequency of TT homozygous mutant genotype was significantly higher in AF patients who have had a stroke group than control (p<0,05). Between the two groups were compared according to the dominant genetic model (CT + TT vs. CC), The number of patients carrying at least one T mutant allele (CT + TT) were significantly higher in AF patients who have had a stroke group than control (p<0,05). With respect to allelic distribution (C vs T, additive model), the frequency of the T allele was significantly higher in AF patients who have had a stroke (p<0,05).
Conclusions: In this study, our data suggest that the MTHFR gene 677C>T mutation may be associated with AF patients who have had a stroke from other clinical risk factors, but this should be confirmed in a much larger series of patients. Screening for this mutation may help in identifying patients at risk and in deciding the antithrombotic strategy.

MTHFR 677C>T polymorphism genotype and allel frequencies

	AF patients with stroke (n:70)		Control (n:70)		P
	n:	%	n:	%	
CC genotype	19	27.1	37	52.9	0.002
CT genotype	27	386.	20	28.	0.210
TT genotype	24	34.3	13	18.6	0.035
CT + TT genotypes (Dominant genetic model)	51	72.9	33	47.1	0.002
T allel	75	53.6	46	32.9	0.006

OP-103

Presence of Fragmented QRS and Its Relationship with Cardiac Functions in Patients with Obstructive Sleep Apnea

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Presence of Fragmented QRS and Its Relationship with Cardiac Functions in Patients with Obstructive Sleep Apnea
Background: Obstructive Sleep Apnea (OSA) is associated with left ventricular dysfunction because of myocardial inflammation and fibrosis. Fragmented QRS (fQRS) has also been associated with myocardial fibrosis and heart failure. The value of fQRS as an indicator of myocardial fibrosis and heart failure in patents with OSA has unknown.
Objective: In this study, we aimed to assess the relationship between OSA and fQRS with cardiac function.
Methods: One hundred eighty eight patients underwent an overnight polysomnography were enrolled in the study. Thirty five patients were excluded from study according to exclusion criteria. Patients divided into two groups; group 1 had OSA and group 2 had not. FQRS was defined to be notching in R or S wave, the presence of additional R wave (R') or fragmented R wave (more than one R') at least two consecutive derivation of 12 lead electrocardiograms. Left and right cardiac functions were assessed by myocardial performance index (Tei index) and tricuspid annular plane systolic excursion (Tapse), respectively. Multivariable regression analysis was performed to assess the independent relationship between fQRS and cardiac function in patients with OSA.
Results: Group 1 consisted of 121 patients (mean age 50.5±10) with OSA (26 mild, 31 moderate, 64 severe) and group 2 included 32 non-OSA patients (mean age 45.34±9). Baseline demographic features were similar such as gender (p=0.71), presence of hypertension (p=0.47), presence of diabetes (p=0.51), the usage of b-blocker (p=0.91), the usage of ACE inhibitor (p=0.53) and the body mass index (p=0.11). FQRS was detected in 85 (70%) of OSA patients and 4 (12.5%) of non-OSA. Left cardiac functions were impaired in patients with OSA than non-OSA assessed by tei index (0.61±32 vs 0.43.02 p=0.001) but right cardiac function assessed by tapse was not impaired (24.13±2.6 vs 23.7±2.6, p=0.56). Also, in OSA group, patients with fQRS had impaired left cardiac functions assessed by tei index (p<0.001) than without fQRS but right cardiac function assessed by tapse was not impaired (p=0.792) than those without fQRS. In multivariable logistic analyze, left ventricular Tei index (p<0.001), lowest nocturnal oxygen saturation (p=0.018) and left ventricular mass index (p=0.003) were independently associated with fQRS in patients with OSA.
Conclusions: Patients with OSA have frequent fQRS than those without OSA. Severity of OSA is also associated with fQRS formation. FQRS is related with impaired left ventricular function in this population.

Demographic properties of OSA patients

	Group 1 FQRS (+) n=89	Group 2 FQRS (-) n=64	P-value
Age (years)	51.86±9.31	47.22±10.60	0.018
Gender (male/female)	58/ 27	22/14	0.53
Hypertension, n(%)	30 (65.2%)	16 (34.8%)	0.41
Diabetes Mellitus, n(%)	10(58.8%)	7(41.2%)	0.26
Body mass index (kg/m2)	33.89±16	31.52±5.9	0.39
Apnea-hypopnea index (events/hour)	37.79±28.14	25.51±21.14	0.004
Lowest nocturnal oxygen saturation (%)	66.91±27.56	78.86±21.14	0.025
Length of time Sp02<90% (minute)	41.67±59.6	16.2±40	0.021
ACE inhibitor n(%)	21(58.3%)	15(41.7%)	0.08
β-blocker n(%)	10(62.5%)	6(37.5%)	0.55

ACE: angiotensin converting enzyme

Echocardiographic properties of OSA patients

	FQRS (+) n=89	FQRS (-) n=64	P value
LVEDD (mm)	48.26 ±3.7	44.7±3.17	0<0.001
LVESD (mm)	29.6±2.8	26.72±2.67	0<0.001
EF (%)	67.9±3.64	69.56±4.23	0.031
IVS (mm)	10.70 ±1.06	10.31 ±1	0.066
PW (mm)	10.60 ±1.06	10 ± 1	0.003
LV MASSINDEX (kg/m^2)	92.42±18.76	77.52±13.43	0<0.001
LA (mm)	38.67 ±3.17	35.8 ±3	0<0.001
E (m/s)	66.3±13.02	76 ±15.33	0.007
A (m/s)	75.17±15.9	71±15.7	0.317
E/A ratio	0.93±0.32	1.12±0.34	0.033
Em (mm/sn)	0.1±0.2	0.7±0.3	0.109
Am (mm/sn)	0.11±0.2	0.10±0.3	0.051
Sm (mm/sn)	0.09±0.02	0.52±2.3	0.112
E/Em ratio	7±1.8	7.02±2.7	0.955
RVD (mm)	24.75±5.4	22.05±4.53	0.047
RAD (mm)	34.3±5.64	32.2±4.69	0.436
Tapse (mm)	23.66±2.7	23.84±2.56	0.792
Tei index	0.69 ±0.24	0.42 ±0.12	<0.001

A: late diastolic mitral inflow; A': late diastolic mitral annular velocity; E: early diastolic mitral inflow; E': early diastolic mitral annular velocity; EF: ejection fraction; IVS: interventricular septum; LA: left atrium; LV: left ventricle; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; EF: Ejection Fraction; PW: posterior wall; S: peak systolic mitral annular velocity; TAPSE: tricuspid annular plane systolic excursion. RAD: right atrial minör dimension,RVD: right ventricular mid cavity diameter

Univariate correlation analysis and multivariable regression analysis for FQRS

	βeta	P	OR	95% CI	P
Age	0.208	0.022	0.903	(0.823-0.991)	0.344
Apnea-hypopnea index	0.332	<0.001	0.329	(0.073-1.483)	0.070
Lowest nocturnal oxygen saturation	-0.374	<0.001	0.970	(0.946-0.995)	0.018
Length of time Sp02<90%	0.339	<0.001	1.009	(0.991-1.027)	0.344
Tei index	0.526	<0.001	1.112	(1.056-1.170)	<0.001
Lv mass ōndex	0.400	<0.001	1.087	(1.029-1.148)	0.003
EF	-0.161	0.080	0.937	(0.796-1.104)	0.437

Lv mass ōndex: Left Ventricular Mass Index, EF: Ejection Fraction

Non-invasive Arrhythmia

OP-104

Ivabradine Terminated Incessant Right and Left Atrial Tachycardia

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Introduction: Ivabradine, a nonselective blocker of HCN channel isoforms, as a heart rate decreasing agent, has been validated in the therapy of coronary artery disease, heart failure and inappropriate sinus tachycardia3. On the other hand, overexpression of HCN channels in atrial and ventricular myocytes urged investigators to consider the presumptive arrhythmogenic effects. However, this agent has not been validated as an antiarrhythmic agent so far.

Case Presentation: The first case, a 58-year old male who had coronary artery bypass surgery 3 months ago was admitted to our hospital with palpitation of whom ECG diagnosis was atrial fibrillation. Cardioversion was attempted. However, sinus rhythm was not restored and incessant atrial tachycardia ensued with a rate of 127 bpm (Fig.1a). Patient was offered Ivabradine. With his approval, ivabradine was given 7.5 mg bid and on the third day changed to 22.5 mg daily. The next day tachycardia terminated and sinusal rhythm of 60 bpm prevailed (Fig 1b). However, because of visual side effects ivabradine was withheld and the tachycardia of 117 bpm resumed on the very same day (Fig 1c). The day after, the rate increased to 133 bpm (Fig.1d). So was the patient taken to EPS and single RF application ablated right atrial tachycardia originating from coronary sinus ostium (Fig.1e).

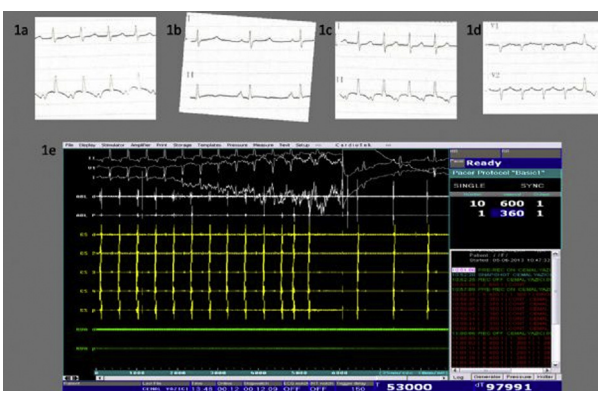
The second case was a 60-year old male to whom metoprolol, diltiazem and sotalol had been given to relieve symptom of palpitation for last two months. ECG diagnosis was repetitive incessant atrial tachycardia with varying degree atrioventricular block (Fig.2a). In the same manner ivabradine 2x7.5 mg was started. On the next day, the atrial rhythm was slower and sinus beats were intervening (Fig.2b). Two days later ivabradine was increased to 22.5 mg daily and the day after, slow atrial rhythm ensued and no sinus beats were detected (Fig. 2c).

The third case, a 67-year old female with no apparent cardiac disorder, had incessant left atrial tachycardia after failed cryoablation of pulmonary veins (PV) (Fig.3a). Flecainide was changed to ivabradine 2x 7.5 mg and two days later the rhythm was restored to sinus (Fig 3b).

The fourth case, a 59-year old female with hypertension and left ventricular hypertrophy, had paroxysmal atrial fibrillation while she was on amiodarone and metoprolol (Fig.4a). The day after amiodarone was replaced with ivabradine, the rhythm was sinusal bradycardia. Following the cessation of metoprolol the rate increased from 45 to 61 bpm (Fig.4b-4c).

Discussion: Probably our cases are the first to prove that ivabradine, at starting doses which were shown as well tolerated before, can terminate sustained atrial tachyarrhythmias resistant to potent antiarrhythmic agents.

In conclusion, ivabradine may be a choice in drug therapy of atrial tachyarrhythmias. Being effective not only on left atrial but on right atrial tachycardia as well, it may have efficacy to prevent atrial fibrillation relapses.



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