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Study of Cognitive Disorders in Stroke-free Patients with a History of Atrial Fibrillation

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Abstract: Atrial fibrillation is associated with cerebral stroke, congestive heart insufficiency and mortality. The present study aimed at evaluating of cognitive disorders in patients with history of atrial fibrillation without cerebral stroke. In a case-control study, 100 patients with first-ever atrial fibrillation seizure without history of cerebral stroke were evaluated. One hundred healthy subjects with normal sinus rhythm matched with the patients in terms of age and gender were regarded as the control group. The case and control groups were followed up for at least one year after occurring of atrial fibrillation. Cognitive disorders were evaluated at the last visit. The case group was consisted of 51 men and 42 women with mean age of 71.08 ± 5.35 years and there were 53 men and 43 women with mean age of 71.34 ± 5.04 years in the control group. Previous history of hypertension, diabetes mellitus, hyperlipidemia, hypercholesterolemia, smoking, consuming of alcohol and warfarin in the case group were 49.5, 23.7, 18.3, 31.2, 14, 7.5 and 9.7% and in the control group 6.4, 35.4, 24, 36.5, 21.9, 13.5 and 12.5%, respectively. In this regard, there was not statistically meaningful difference between these two groups. Dementia was detected in 3 (3.2%) of the case and 1 (1%) of the control group subjects ($p = 0.29$). Comparing two groups with and without dementia demonstrated that there was not any meaningful risk factor. According to the results, dementia in patients with positive history of atrial fibrillation was more than normal population.

Key words: Atrial fibrillation, cognitive disorders, prevalence

INTRODUCTION

Atrial Fibrillation (AF) is the most common type of arrhythmia. It is the most prevalent sustained supraventricular tachycardia (Kermode-Scott, 2012). Episodes of atrial fibrillation can come and go, or you may have chronic atrial fibrillation (Duron and Hanon, 2008, 2010). Although, atrial fibrillation itself usually isn't life-threatening, it is a serious medical condition that sometimes requires emergency treatment. It can lead to complications (Mark Estes III, 2010). Incidence rate of cerebral stroke in patients with AF is almost five times more than subjects with sinus rhythm (Haft, 2011). Developing of cerebral emboli with left atrium origin is the most important mechanism of cerebral strokes. Additionally, cardiac output decreases in AF which can decrease cerebral blood flow and increase incidence rate of cerebral stroke (Tendolkar *et al.*, 2012). A prothrombotic condition may be developed in AF facilitating incidence of cerebral stroke. Considering that AF increases risk of cerebral stroke, it is generally thought

that it can play a role in developing cognitive disorders through developing silent cerebral emboli and infarction (Schwarz *et al.*, 2010). Silent infarctions which are often cortical are two times common in cerebral images of the patients with (Aliyev *et al.*, 2009). Although, it is assumed that the infarctions are developed by cardiac emboli, its incidence by other risk factors of cerebral vessel disease including hypertension, diabetes mellitus, smoking, etc., is also possible (Rauramaa *et al.*, 2011). Interestingly, this risk factor in AF patients is more common than persons with sinus rhythm. Considering that dementia is regarded a main problem and AF is the most prevalent sustained arrhythmia, it is of high importance to evaluate the relationship found between them (Rockwood *et al.*, 2009). The subject becomes more important when ambiguous results are observed in this regard (Sachdev *et al.*, 2007). A definite relationship has not already been defined between AF and dementia. There are several factors such as difference in the studied sample volume, methods used to select the patients from the society, definition and dementia, status of the evaluator, dementia in terms of

existence or non-existence of AF in the patients, AF definition and evaluation methods, several inventor factors and how they are controlled and so many other factors which can affect this indefiniteness (Patel *et al.*, 2010). Therefore, it was decided to evaluate prevalence of dementia in patients with AF and without cerebral stroke and the relationship found between AF and incidence of cognitive disorders through a controlled study.

MATERIALS AND METHODS

In a case-control study, 100 patients with first-ever AF and without history of cerebral stroke (case group) and 100 healthy subjects with normal sinus rhythm matched with the patients in terms of age and gender (control group) were evaluated at Tabriz, Madani hospital for one year. Passing at least one year of AF diagnosis and being older than 60 years were considered as the inclusion criteria. While, the exclusion criteria included history of dementia and cognitive disorders, dementia and cognitive disorders in first class relatives, thyroid disease, renal disease, pulmonary obstructive diseases, malignancy, peripheral arteries diseases, stroke, cardiomyopathy and open heart surgery and existence of other directive disorders other than A. After one year, 93 and 96 subjects were followed up in the case and control groups, respectively. Frequency of cognitive disorders (dementia) was determined and compared in both groups at the end of one year. The study duration was 15 months and the required data was collected and analyzed from Nov. 2010–April, 2012. In this study, there were 93 patients with definite acute AF (case group) and 96 subjects without AF and with sinus rhythm (control group). They were evaluated in terms of existence or non-existence of dementia one year after the first AF registration. It should be mentioned that these two groups were matched considering age, gender, educational level, history of hypertension, diabetes mellitus, hyperlipidemia, hypercholesterolemia, BMI, smoking, consuming of alcohol and warfarin, history of heart disease (insufficiency, valvula, myocardial infarction). To detect incidence of atrial fibrillation rhythm, 3 criteria are used in 12-lead superficial electrocardiogram: (1) Lack of wave P, (2) Coarse or fine defibrillator waves and (3) Completely irregular RR-int. All patients and members of the control group were evaluated by a psychologist who were not aware of their grouping one year after incidence of the first AF and in terms of cognitive disorders. Diagnostic criteria of cognitive disorders were based on DSM-IV. Considering lack of nay intervention, there was not any special case regarding moral considerations and no extra charges have been imposed on the patients. The study

was approved by ethic committee of Tabriz university of Medical Sciences. The studied parameters included age, gender, BMI, educational level, history of hypertension, diabetes mellitus, high cholesterol, smoking, consumption of alcohol and warfarin, heart disease and cognitive disorders (dementia). The obtained data was stated as Mean±SD, frequency and percentage. To compare qualitative and quantitative data, independent samples t-test and Chi-square or Fischer's exact test were used and SPSS-15 was applied as the statistical software. Logistic regression analysis test was used to evaluate the independent parameters. In all cases, $p \leq 0.05$ was regarded meaningful.

RESULTS

In this study, there were 93 and 96 subjects in the case and control groups, respectively. The case group was consisted of 51 men (54.8%) and 42 women (45.2%) and the control group was consisted of 53 men (55.2%) and 43 women (44.8%). There was not any statistically meaningful difference between these two groups in this regard ($p = 0.95$). Mean age was 71.08 ± 5.35 years (61-82 years old) and 71.34 ± 5.04 years (63-82 years old) for the case and control groups, respectively. In this regard, there was not any statistically significant difference between two groups ($p = 0.72$). Features of members of both groups have been summarized and compared in Table 1. Accordingly, there was not any statistically meaningful difference in these two groups. At the end of one year of follow-up, dementia was observed in 3 (3.2%) and 1 (1%) of the case and control group subjects, respectively. In this regard, there was not statistically significant difference between the groups (95% CI: 0.03-3.09, OR = 0.32, $p = 0.29$). Evaluating

Table 1: Features of case and control group members and their comparison

Variable	Case (n = 93)	Control (n = 96)	p-value
Gender			
Male	51 (54.8)	53 (55.2)	0.96
Female	42 (45.2)	43 (44.8)	
Age (year)	71.08 ± 5.35	71.34 ± 5.04	0.72
Body mass index (kg m^{-2})	25.74 ± 2.79	26.11 ± 2.84	0.36
Education			
Illiterate	18 (19.4)	16 (16.7)	0.39
Under high school diploma	45 (48.4)	43 (4.8)	
High school diploma	25 (26.9)	25 (26)	
University	5 (5.4)	12 (12.5)	
Medical history			
History of hypertension	46 (49.5)	58 (60.4)	0.13
History of diabetes mellitus	22 (23.7)	34 (35.4)	0.34
History of hyperlipidemia	17 (18.3)	23 (24)	0.44
History of smoking	13 (14)	21 (21.9)	0.16
History of consumption of alcohol	7 (7.5)	13 (13.5)	0.18
History of consumption of Warfarin	4 (4.3)	0 (0)	0.54

Values in brackets are percentage

different parameters studied in two groups with and without dementia, no meaningful and independent multi variable parameter was found ($p > 0.05$).

DISCUSSION

The present study considered frequency of cognitive disorders within one year after AF in patients without history of cerebral stroke as well as healthy subjects. Accordingly, cognitive disorders (dementia) were observed in 3.2% of cases in the group with history of AF. It was about 1% in the control group. In this regard, there was not any statistically meaningful difference between two groups with and without history of AF ($p = 0.29$). Few studies have been already conducted in this regard but the reported results vary. In a similar study, Miyasaka *et al.* (2007) evaluated frequency of cognitive disorders in patients with history of first-ever AF. During follow-up period, dementia was reported in 299 cases (10.5%). Dementia frequency within the first year of follow-up was estimated about 2.7% in this study. Finally, they concluded that dementia and cognitive disorders are commonly seen after first AF (Miyasaka *et al.*, 2007). As observed, results of our study obtained during one year of follow-up period are almost similar to the results reported within one year follow-up of the above-mentioned study. Ott *et al.* (1997) concluded that cognitive disorders in patients with AF are about two times more prevalent than the control group subjects. It was about three times in our study. The difference can be attributed to the patient's features such as AF condition (chronic/acute) and age. Within a 9-year period, Puccio *et al.* (2009) indicated to association between AF history and cerebral stroke while denied any relationship between dementia and AF. It results from the fact that dementia has multi variable background causes at high ages (Puccio *et al.*, 2009). The above-mentioned study differs from ours because of existence of history of cerebral stroke as well as high age of the patients. Although, there was not any meaningful relationship between AF and dementia in our study, frequency percentage of the disorder was high in the case group. In another study, Wozakowska-Kaplon *et al.* (2009) evaluated older than 65 years patients with AF. The cases have not experienced cerebral vessel events. Finally, it was demonstrated that cognitive conditions of the patients were at lower levels in comparison with the control group (Wozakowska-Kaplon *et al.*, 2009) in their study on 122 patients with AF and without cerebral stroke, Knecht *et al.* (2008) suggested that paramnesia and frequency of cerebral atrophy in the case group was significantly more than the control one. Although,

mechanism of cognitive disorders is not well known in AF, previous studies have demonstrated that vascular problems are independently involved in 20% of the cases (Duron and Hanon, 2008). Forti *et al.* (2007) suggested that dementia following cerebral stroke is associated with AF. Tilvis *et al.* (2004) concluded that AF with/without history of cerebral stroke significantly increases incidence rate of dementia and cognitive disorders. On the other hand, Pohjasvaara *et al.* (1997) demonstrated that there is not a definite relationship between AF and cognitive disorders. As observed and emphasized, results of different studies conducted in this regard are not homogenous. Some factors of the difference were previously mentioned but volume of the studied sample, diagnostic method, paying attention to cognitive disorders and dementia and duration of the follow-up period are of other important cases. Multi-variability of cognitive disorders is another important factor in this regard. We evaluated effects of different parameters in two groups with/without cognitive disorders but there was not any meaningful case.

CONCLUSION

During one year of follow-up period, it was made clear that 3.2% of patients with AF and without cerebral stroke and 1% of healthy subjects who were matched with the case group in terms of age and gender suffered from cognitive disorders (dementia). In this regard, there was not any statistically meaningful difference between two groups with and without history of AF.

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