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Predictors of non-pharmacological intervention in patients with paroxysmal atrial fibrillation: Value of neuroticism

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Abstract

Background: Non-pharmacological intervention is gaining increasing popularity in the treatment of patients with paroxysmal atrial fibrillation. We sought to investigate which factors play a role in the choice for non-pharmacological intervention with a particular focus on neuroticism.

Methods: The study group comprised 73 patients with paroxysmal atrial fibrillation (mean age 55 ± 13 years, 50 males). On average, patients had a 3-year-history of one symptomatic paroxysm per week lasting 2 h. The degree of neuroticism was assessed using the short scale Eysenck Personality Questionnaire.

Results: During a mean follow-up period of 7.0 ± 0.6 years, 20 patients (27%) underwent a non-pharmacological intervention for atrial fibrillation including His bundle ablation ($n=1$), maze operation ($n=4$), DDDR-pacemaker ($n=10$), pulmonary vein ablation ($n=5$). Multivariate regression analysis showed that age < 55 years (odds ratio 5.3, 95% CI 1.1–24.5), frequency of paroxysms of atrial fibrillation > 1 per week (odds ratio 5.9, 95% CI 1.2–28.5) and total number of anti-arrhythmic drugs (class I and III) used > 2 (odds ratio 3.4, 95% CI 1.6–6.9) were predictive of non-pharmacological intervention (all $p < 0.05$). In contrast, the degree of neuroticism was similar in patients who underwent non-pharmacological intervention as opposed to patients who did not undergo non-pharmacological intervention (4.5 ± 3.3 vs. 4.0 ± 2.9 , $p = \text{NS}$).

Conclusions: On the basis of this small study, neuroticism would not appear to play an important role in the decision to perform a non-pharmacological intervention. Instead, the data indicate that younger patients with pharmacologically refractory atrial fibrillation more often undergo non-pharmacological intervention.

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Keywords: Atrial fibrillation; Non-pharmacological intervention; Predictors; Neuroticism; Eysenck personality questionnaire

1. Introduction

Recent studies have shown that “rate control” is a reasonable alternative for “rhythm control” in patients with asymptomatic or mildly symptomatic atrial fibrillation [1,2]. However, rhythm control is still desirable for highly symptomatic patients. Anti-arrhythmic drugs are the first

line of treatment to achieve rhythm control, but treatment with anti-arrhythmic drugs often fails, either due to ineffectiveness or intolerable side effects, and non-pharmacological intervention should then be considered. In recent years, several non-pharmacological treatment modalities have been developed, including His bundle ablation, Cox’s maze operation, pacemaker therapy and (modified) pulmonary vein ablation. In particular the latter option is gaining increasing popularity [3], both given its alleged effectiveness and because it leaves open the other treatment options. However, the critical issue in terms of selection of a patient for non-pharmacological treatment is how to define what

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actually constitutes “highly symptomatic”. Obviously, “objective” arrhythmia burden (duration of atrial fibrillation, duration and frequency of attacks) and perhaps demographics would appear important, but we reasoned that psychological factors might also be implicated in the choice for non-pharmacological treatment. In particular, we wondered whether neuroticism plays a role. Neuroticism is a steady personality trait, which gives an indication of the emotional stability of a person [4]. Persons with high scores on neuroticism scales tend to be anxious and to have more worries in general, and neuroticism has proved to be an important predictor of psychological distress, both in the presence and the absence of stressful circumstances. We felt it would be conceivable that neuroticism affects the complex interaction between the patient and the treating physician such that patients with atrial fibrillation and relatively high degree of neuroticism more readily receive non-pharmacological treatment. In the present study, we investigated the predictors of non-pharmacological intervention, including the potential role of neuroticism, in a well-defined group of patients with paroxysmal atrial fibrillation.

2. Materials and methods

2.1. Patient selection and study design

This study was a longitudinal, retrospective, uncontrolled study. The study group consisted of patients who participated in a previous study, which focussed on quality of life [5]. Briefly, consecutive patients from the out-patient clinic in our hospital with paroxysmal atrial fibrillation, aged >18 years, were considered eligible for the study. Paroxysmal atrial fibrillation was defined as proposed by Gallagher and Camm [6]. The presence of atrial fibrillation was based on electrocardiographic evidence, including ambulatory (Holter) monitoring. Lone atrial fibrillation was inferred when routine cardiac investigations (echocardiogram, ergometry) did not reveal structural heart disease. Patients with hypertension were considered to have structural heart disease. In the main study [5], a set of questionnaires was distributed between the patients, including a questionnaire on personality, that is, neuroticism. Of note, neither the patient nor the treating physician (MPVDB, ICVG) were informed about the neuroticism score. After the baseline measurements, patients were only followed by their treating physician. Subsequent treatment, including non-pharmacological intervention, was left at the discretion of this physician (see below). At the end of follow-up in January 2004, clinical outcome in terms of non-pharmacological intervention was extracted from the patient records by one of the investigators (MEWH). The study was performed in accordance with Declaration of Helsinki and approved by the institutional ethics committee. Informed consent was obtained from all patients.

2.2. Neuroticism

Neuroticism was assessed using the revised, short scale Eysenck Personality Questionnaire, validated for Dutch (see Appendix) [7,8]. Using this questionnaire, neuroticism is quantified using a set of 12 questions, to be answered with yes or no. Possible total score thus ranges from 0 to 12, a higher score signifying a higher degree of neuroticism.

2.3. Non-pharmacological intervention

Patients who were selected for a non-pharmacological intervention for the treatment of atrial fibrillation were required to be “highly symptomatic”, as judged by the treating physician (MPVDB, ICVG). Several techniques have been applied in recent years in our center, reflecting their rapid evolution and the reported and perceived advantages and disadvantages. Initially, His bundle ablation with VVI-pacemaker implantation and maze operation were performed relatively frequently, later DDDR pacemaker implantation (antitachy-pacing) and particularly pulmonary vein ablation became more popular. With exception of His bundle ablation, potential candidates for a non-pharmacological intervention were required to have limited or no structural heart disease.

2.4. Data analysis

Mean values \pm the standard deviation and median values with range, depending on the normality of the distribution, were calculated for continuous variables and counts with percentages for categorical variables. Differences between groups were evaluated by the Student *t*-test or Mann–Whitney *U*-test, depending on the normality of the distribution, for continuous variables and by the Fisher exact test or Chi-square test for categorical variables.

In order to determine predictors of non-pharmacological intervention univariate and multivariate logistic regression analyses were performed. All univariate variables with a *p*-value < 0.10 were added to the multivariate model. Cut-off points of the variables of interest were chosen on basis of the mean or median value. Since we were particularly interested in neuroticism, neuroticism-score was forced into the multivariate model. A value of *p* < 0.05 was considered statistically significant. Analyses were performed using the statistical package SPSS 11.0 (SPSS Inc, Chicago, IL, USA).

3. Results

3.1. Patient characteristics

Study patients were recruited between November 1996 and May 1998 and comprised 73 subjects. Mean age was 55 ± 13 years and 50 patients (68%) were male (Table 1). Lone atrial fibrillation was present in 43 patients (59%), the remaining patients suffered from ischemic heart disease

Table 1
Clinical characteristics of patients with or without non-pharmacological intervention

| | Intervention (n=20) | No intervention (n=53) | p |
|--------------------------------|------------------------|---------------------------|--------|
| Age | 52 ± 10 | 57 ± 14 | NS |
| <55 years (%) | 13 (65) | 22 (42) | NS |
| ≥55 years (%) | 7 (35) | 31 (58) | NS |
| Sex | | | |
| Male (%) | 17 (85) | 33 (62) | NS |
| Female (%) | 3 (15) | 20 (38) | NS |
| Underlying heart disease | | | |
| Ischemic (%) | 2 (10) | 10 (19) | NS |
| Valvular (%) | 4 (20) | 3 (6) | NS |
| Hypertension (%) | 3 (15) | 8 (15) | NS |
| Lone AF (%) | 11 (55) | 32 (60) | NS |
| Arrhythmia burden | | | |
| Total duration (years) | 7.0 (1.0–30.0) | 2.0 (0.2–24.0) | 0.040 |
| Frequency (per week) | 1.0 (0.04–5.0) | 0.5 (0.04–5.0) | NS |
| Duration (h) | 6.0 (0.2–48.0) | 2.0 (0.3–24.0) | NS |
| Echo parameters | | | |
| LA dimension, parasternal (mm) | 37 ± 6 | 34 ± 6 | NS |
| LA dimension, apical (mm) | 53 ± 5 | 54 ± 8 | NS |
| LVEDD (mm) | 46 ± 6 | 47 ± 5 | NS |
| LVEDS (mm) | 32 ± 4 | 32 ± 7 | NS |
| Fractional shortening | 0.31 ± 0.07 | 0.33 ± 0.10 | NS |
| Medication use | | | |
| Class I AAD (%) | 9 (45) | 18 (34) | NS |
| Class III AAD (%) | 11 (55) | 13 (25) | NS |
| β-blockers (%) | 8 (40) | 17 (32) | NS |
| Calcium-channel blockers (%) | 6 (30) | 8 (15) | NS |
| Digoxin (%) | 3 (15) | 4 (8) | NS |
| Number of AADs used | 3 (1–6) | 2 (0–5) | <0.001 |
| Neuroticism score | 4.5 ± 3.3 | 4.0 ± 2.9 | NS |

AF=atrial fibrillation, AAD=anti-arrhythmic drug, LA=left atrium, LVEDD=left ventricular enddiastolic dimension, LVEDS=left ventricular endsystolic dimension, NS=not significant.

(n=12), valvular heart disease (n=7) or hypertension (n=11). None of the patients had congestive heart failure. Mean echo-parameters (left ventricular and left atrial dimensions) were within the normal range. Self-reported arrhythmia burden in terms of the duration of the paroxysms ranged from 15 min to 2 days, whereas the frequency ranged from 2 paroxysms per year to 5 paroxysms per week. On average, patients had a 3-year-history of one paroxysm per week lasting 2 h. Fifty-one patients (70%) used an anti-arrhythmic drug to suppress their arrhythmia, whereas the remaining 22

patients (30%) used either no medication or only medication for control of ventricular rate during atrial fibrillation. The median total number of used anti-arrhythmic drugs (class I and III) was 2 (1–6). All patients fully completed and returned the Eysenck Personality Questionnaires.

3.2. Non-pharmacological intervention and its predictors

Follow-up was completed in all patients. Mean follow-up was 7.0 ± 0.6 years. During the follow-up period, 20 patients

Table 2
Predictors of non-pharmacological intervention

| | Univariate analysis* | | | Multivariate analysis | | |
|--------------------------|----------------------|------------|--------|-----------------------|------------|-------|
| | OR | 95% CI | p | OR | 95% CI | p |
| Age < 55 years | 2.6 | 0.9 – 7.6 | 0.078 | 5.3 | 1.1 – 24.5 | 0.034 |
| Male sex | 3.4 | 0.9 – 13.2 | 0.073 | | | |
| Valvular heart disease | 4.2 | 0.8 – 20.6 | 0.08 | | | |
| Total duration > 3 years | 7.1 | 2.1 – 25.0 | 0.002 | | | |
| Frequency > 1 per week | 1.6 | 1.0 – 2.5 | 0.059 | 5.9 | 1.2 – 28.5 | 0.028 |
| Duration > 2 h | 3.0 | 1.0 – 9.1 | 0.046 | | | |
| Number of AADs used > 2 | 3.0 | 1.7 – 5.6 | <0.001 | 3.4 | 1.6 – 6.9 | 0.001 |
| Neuroticism score > 4 | 1.9 | 0.7 – 5.5 | 0.21 | 1.6 | 0.4 – 6.6 | 0.50 |

AAD=anti-arrhythmic drug, OR=odds ratio, CI=confidence interval.

*Only variables with a univariate p-value < 0.1 and the variable of interest are shown.

(27%) underwent a non-pharmacological intervention; in 1 patient a His bundle ablation with implantation of a VVI-pacemaker was performed, in 4 patients maze operation was performed, 10 patients received a DDDR-pacemaker, and 5 patients underwent pulmonary vein ablation. Of note, in the present patient group maze operation and DDDR pacemaker implantation were performed for atrial fibrillation only (no associated valve or coronary surgery, no conventional pacemaker indication, i.e., antibrady-pacing). Clinical characteristics of the patients who underwent a non-pharmacological intervention as compared to those who treated pharmacologically are shown in Table 1. The total duration of the atrial fibrillation was longer and the total number of antiarrhythmic drugs used was higher in the patients who underwent an intervention, otherwise there were no significant differences. Of note, neuroticism score was comparable in the 2 groups; Eysenck Personality Questionnaire scores in the non-intervention group and intervention group were 4.0 ± 2.9 and 4.5 ± 3.3 , respectively ($p = \text{NS}$). The results of the univariate and multivariate regression analyses are shown in Table 2. In the final model, 3 variables remained as independent predictors of non-pharmacological intervention: age < 55 years, frequency of paroxysms of atrial fibrillation > 1 per week and total number of class I and III antiarrhythmic drugs used > 2. The degree of neuroticism had no predictive value.

4. Discussion

4.1. Atrial fibrillation and psychological factors

The role of psychological factors in patients with coronary artery disease is an issue of ongoing debate [9,10]. A recent study confirmed that depression and anxiety were associated with cardiac events [11]. In fact, anxiety was an independent predictor of both cardiac events and increased health care consumption and accounted for the relationship between depressive symptoms and prognosis. However, studies regarding psychological factors and atrial fibrillation are scarce. Using the Barsky Somatosensory Amplification Scale, Paquette et al. investigated the tendency of atrial fibrillation patients to somatize, i.e., to amplify benign bodily sensations, and they showed that a high tendency to somatize predicted a poor quality of life [12]. Eaker et al. recently reported an association between anger and hostility, but not type A behavior, and the development of atrial fibrillation [13]. Finally, we recently investigated the degree of neuroticism in patients with paroxysmal atrial fibrillation [14], using the same patient group as in the present study. Perhaps based on clinical experience with individual patients one might intuitively surmise that patients with paroxysmal atrial fibrillation have on average a higher degree of neuroticism than other persons. However, the results clearly indicated that this is not the case; although the Eysenck Personality Questionnaire scores on neuroticism differed among the

individual patients, mean score in the group as a whole was similar to the mean score in group of age and sex matched controls (4.1 ± 3.0 vs. 3.9 ± 3.1 , $p = \text{NS}$). In other words, patients with paroxysmal atrial fibrillation would appear to have on average a “normal” degree of neuroticism.

4.2. Prediction of non-pharmacological intervention

Notwithstanding the latter observation, we reasoned it would be conceivable that the degree of neuroticism plays a role in the choice to perform a non-pharmacological intervention, patients with a relatively high degree of neuroticism more readily asking for such treatment than patients with a relatively low degree of neuroticism. In addition, the presentation of symptoms by the patient might also be coloured by a certain measure of neuroticism such that the attending physician believes the patient is highly symptomatic. In the present study, several factors were shown to be predictive of a non-pharmacological intervention, namely a relatively young age, high frequency of paroxysms of atrial fibrillation and high total number of antiarrhythmic drugs (class I and III) used. The predictive value of latter two factors is readily conceivable, since they reflect that the patient suffers from a pharmacologically refractory arrhythmia. Also the finding that age plays a role is conceivable, since perhaps both the patient and the treating physician more readily feel that “aggressive” treatment is warranted in case of (relatively) young age. However, contrary to our supposition, a relatively high degree of neuroticism did not turn out to be a predictor of non-pharmacological intervention. Putting it differently, the decision to perform a non-pharmacological intervention appears to be governed by “objective” factors (arrhythmia burden, age), whereas neuroticism does not seem to impact the judgment by the treating physician that his/her patient with paroxysmal atrial fibrillation is highly symptomatic. As an explanation for the present finding, one might argue that patients with a relatively high degree of neuroticism are perhaps also more fearful to undergo a non-pharmacological intervention once proposed by their treating physician, but this remains sheer speculation.

4.3. Methodological considerations

An important limitation is the fact that the sample size was small. As a result, we possibly missed certain differences between the groups and were unable to differentiate between different types of non-pharmacological interventions. For instance, it is not impossible that differences exist between catheter-based interventions versus operative interventions regarding the role of neuroticism. Further, since our institute is a university referral center and we see many patients for a second opinion, the patient group may not be entirely representative of clinical practice. This possibility is supported by the relatively high number of patients with lone atrial fibrillation (59%). However, if anything, one

would expect neuroticism to play a role in these patients rather than in patients in a primary care setting. Finally, this study was not designed to determine whether the patients were “neurotic” in terms of a psychiatric disorder. Instead, the concept of neuroticism was used to describe a variant of human personality, and to investigate whether the relative degree of neuroticism is predictive of non-pharmacological intervention.

5. Conclusion

On the basis of this small study, neuroticism would not appear to play an important role in the decision to perform a non-pharmacological intervention. Instead, the data indicate that younger patients with pharmacologically refractory atrial fibrillation more often undergo non-pharmacological intervention.

Appendix

Eysenck Personality Questionnaire (revised, short scale)

Questions on neuroticism:

| | | |
|------------------------------------------------------------|-----|----|
| 1. Does your mood often go up and down? | Yes | No |
| 2. Do you ever feel ‘just miserable’ for no reason? | Yes | No |
| 3. Are you an irritable person? | Yes | No |
| 4. Are your feelings easily hurt? | Yes | No |
| 5. Do you often feel ‘fed-up’? | Yes | No |
| 6. Would you call yourself a nervous person? | Yes | No |
| 7. Are you a worrier? | Yes | No |
| 8. Would you call yourself tense or ‘highly-strung’? | Yes | No |
| 9. Do you worry too long after an embarrassing experience? | Yes | No |
| 10. Do you suffer from ‘nerves’? | Yes | No |
| 11. Do you often feel lonely? | Yes | No |
| 12. Are you often troubled about feelings of guilt? | Yes | No |

Yes= 1; No= 0. Total score is calculated by adding the scores on the individual questions.

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