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# Panic features strongly predict the subjective but not the objective benefit of pulmonary vein isolation

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## Abstract

**Purpose** Clinically observed discrepancies between electrocardiogram findings and subjective report of symptoms related to atrial fibrillation (AF) often remain unexplained. One could hypothesize that after a technically successful ablation, preoperative panic behavior might affect the report of AF-related symptoms. However, research on comorbid panic behavior in patients with AF is limited.

**Methods** In this observational prospective cohort study, we investigated psychological characteristics, in particular the prevalence of panic features, among 112 patients with AF and its possible influence on experienced outcome of subsequent ablation treatment.

**Results** Twelve percent of the AF patients ($n = 12$) were pre-operatively characterized by panic features. This group experienced higher levels of distress and more limitations in daily life compared to AF patients without panic features, but was not characterized by higher levels of neuroticism. However, AF-ablation resulted in a similar reduction of experienced limitations in daily functioning and levels of distress in both groups.

**Conclusion** Patients with panic features experience more distress and more limitations in daily life from AF, but these complaints are reduced by AF ablation in a similar rate as in patients without panic features. Additional psychological therapy is suggested as a method to further reduce subjective AF disease burden in these patients.

**Keywords** Panic · Atrial fibrillation · Ablation · Outcome

## 1 Introduction

How symptoms of atrial fibrillation are experienced varies widely between patients. Elevated levels of anxiety are quite common for patients with AF [1]. Catheter ablation of AF has evolved as a potential curative option for drug-refractory AF [2]. Compared to those treated with antiarrhythmic drug therapy, patients with AF treated with radiofrequency ablation showed a greater improvement in physical functioning [3]. Medical treatment did not result in significantly lower levels of depression or anxiety in patients with AF [4].

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Cardiac patients have a high prevalence of panic disorder (27%) and generalized anxiety disorder (5–30%) [5]. In patients with AF, the nature of paroxysmal AF (i.e., unexpected, persistent symptoms) is quite different from other chronic cardiac conditions, and anxiety scores of patients with AF are in general higher [6]. Panic attacks and AF frequently present with similar clinical symptoms [7]. Psychological distress, rather than the actual experience of recurrent AF, can clearly affect the patient's report of AF symptoms [8]. Furthermore, panic disorder is independently associated with higher incidence of an AF diagnosis to be diagnosed in the future [9]. These findings may also explain why several studies have reported that preoperative anxiety and depression had a negative effect on treatment outcome in patients with AF [10, 11].

Although scientific research on the consequences of comorbid panic behavior in patients with AF is limited, one could hypothesize that after a technically successful ablation, preoperative panic behavior might persist and even affect the report of AF-related symptoms. This could also explain the sometimes clinically observed discrepancies between electrocardiogram (ECG) findings and subjective report of AF-related symptoms.

The aims of this study were to investigate the prevalence of panic behavior among patients with AF who were scheduled for a first-time ablation. In addition, we wanted to describe the demographic, personality and AF characteristics of patients with and without panic features. Furthermore, we wanted to assess the impact of panic characteristics on the outcome of ablation and test which baseline panic characteristics might be associated with persistent subjective AF complaints despite successful ablation.

## 2 Methods

### 2.1 Patient population and procedure

This study was a single-center prospective cohort study. The local medical ethics committee had approved this study. Patients referred for catheter ablation were asked to participate in this study during pre-procedural patient education meetings. Before participation, written informed consent was obtained from all participants. Patients with a previous ablation were excluded. The Dutch version of the Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia (ASTA) [12] was used to investigate the patient's AF-related symptoms, the frequency, duration, and degree of symptom severity during ongoing tachycardia. Neuroticism was measured by the use of a subscale of the Dutch translation [13] of the Big Five Personality Inventory (BFI). The Dutch translation [14] of the Cardiac Anxiety Questionnaire (CAQ) was used to map the patient's coping with AF. Extra healthcare consumption was measured by asking the patient how often he/she consulted the general practitioner or the emergency room outside of the planned consultations with the cardiologist last year.

### 2.2 Predictor variables

Panic features were defined as a combination of high anxiety for bodily symptoms, measured by the Dutch translation [15] of the Body Sensations Questionnaire (BSQ) and catastrophizing cognitions during periods with more symptoms, measured by the Dutch translation [15] of the Agoraphobic Cognitions Questionnaire (ACQ). The reliability of both questionnaires is satisfactory (Crohnbach's alfa BSQ:0.91 and AFQ: 0.89; test-retest reliability respectively 0.81 and 0.78). The BSQ is a 17-item scale comprising items concerning sensations associated with autonomic arousal. Patients indicate the level of anxiety on a 5-point Likert scale. The ACQ is a 14-item scale comprising thoughts concerning negative consequences of experiencing anxiety. On a 5-point Likert scale, patients can indicate how often a thought has occurred. Based on standardization research, the cut-off scores were set at respectively 1.92 and 1.54. If a patient had elevated levels on both scales at baseline, the patient was identified as having panic features.

### 2.3 Outcome variables

The post-ablation arrhythmia monitoring protocol was care as usual. A 24-h Holter was requested 3 months after ablation and an ECG was recorded at baseline and at 3 month follow-up. The cardiologist rated the ablation as technically successful when no AF-symptoms were detected during a 24-h Holter recording at 3 months. Three months after ablation the patients were asked whether they still experienced AF-related symptoms. The second part of the ASTA comprises 13 items which measure the physical and mental impact of AF on health-related quality of life. Distress was quantified using the Hospital Anxiety Depression Scale (HADS) [16]. Patients who scored higher than the cut-off point of 12 were identified as having elevated distress. Patients were asked to fill in both questionnaires at baseline and 3 months after ablation.

### 2.4 Statistical analysis

For all the measurements descriptive data were provided. Demographics, baseline somatic and psychological outcome measures, and ablation outcome measures were compared with independent two-tailed *t* tests or, in case of categorical variables, with chi-squared tests or Fisher's exact tests. The effect of ablation upon levels of distress and experienced daily limitations, and the possible interaction with baseline panic features was assessed with a two-way ANOVA with repeated measures. Furthermore, we used an independent *t* test, chi-squared, or Fisher's exact test to compare the baseline characteristics of the group of patients who still experienced symptoms while the ablation seemed technically successful to the other patients. In all statistical analyses, we used an alpha of 0.05 (two-tailed). Based on literature and clinical experience of the involved cardiologists a power analysis was made on the following assumptions: 1) 70% of AF-patients is estimated to benefit from ablation; 2) Prevalence of comorbid panic features in this patient group is estimated at 30%; 3) 50% of the patient group with panic features is estimated to benefit from ablation; 4) 80% of the patients without panic features is estimated to benefit from ablation. This produces an expected tetrachoric correlation of 0.45, which is a medium impact. For a 80% certainty about this effect and a two sided alpha of 0.05, at least 93 respondents were needed.

## 3 Results

### 3.1 Baseline characteristics

In total, 112 (55%) patients participated in the baseline assessment. There were no significant differences in baseline characteristics (Table 1) between participants and non–participants. There were more patients with paroxysmal than

**Table 1** Baseline characteristics of the patient group with atrial fibrillation, divided into the group with panic features and the group without panic features

| | Total sample M (SD)/percentage | With panic features M (SD)/percentage | Without panic features M (SD)/percentage |
|---|---|---|---|
| Patient and atrial fibrillation characteristics | ($N = 112$) | ($N = 13$) | ($N = 99$) |
| Demographics | | | |
| Men | 68% | 69% | 68% |
| Women | 32% | 31% | 32% |
| Age (range: 27–79) | 61.2 (9.1) | 59.0 (7.4) | 61.5 (9.3) |
| Educational level (range 1–6) | 4.5 (1.0) | 4.6 (0.9) | 4.5 (1.0) |
| No paid work or other activities | 48% | 31% | 52% |
| Cardiac characteristics (ECG & ASTA) | | | |
| Heart rate in sinusrhythm (ECG based) | 60.8 (9.4) | 60.3 (10.1) | 60.9 (9.4) |
| Heart rate when in atrial fibrillation | 109.4 (31.7) | 122.3 (46.4) | 107.6 (29.0) |
| Paroxysmal atrial fibrillation | 89% | 85% | 89% |
| Breathlessness during activity (ASTA-based) | 89% | 100% | 87% |
| Breathlessness even at rest | 54% | 91%** | 49% |
| Dizziness | 59% | 83% $^{T}$ | 56% |
| Cold sweat | 58% | 83% $^{T}$ | 55% |
| Pronounced tiredness | 78% | 92% | 77% |
| Fatigue | 98% | 100% | 92% |
| Chest pain | 39% | 58% | 35% |
| Pressure in the chest | 62% | 83% | 59% |
| Worry/anxiety | 58% | 100%** | 58% |
| Near syncope | 37% | 54% | 35% |
| Syncope | 9% | 8% | 9% |
| Medication | 97% | 85% | 99% |
| Anti-arrhythmics | 76% | 82% | 76% |
| Rate control | 61% | 36% | 64% |
| Anticoagulation | 71% | 82% | 70% |
| Heart failure medication | 34% | 36% | 34% |
| Beta blokker | 56% | 42% | 61% |
| Psychotropic medication | 16% | 27% | 15% |
| Psychological characteristics | | | |
| Neuroticism | 2.7 (0.7) | 3.0 (0.6) | 2.7 (0.7) |
| Pre-morbid anxiety disorder | 7% | 8% | 7% |
| Cardiac anxiety | 2.7 (0.5) | 3.2 (0.4)** | 2.7 (0.5) |
| Extra health care consumption | 55% | 62% | 55% |
| Anxiety for bodily symptoms | 1.7 (0.5) | 2.4 (0.4)** | 1.6 (0.5) |
| Catastrophizing cognitions | 1.3 (0.3) | 1.8 (0.2)** | 1.2 (0.2) |
| Limitations in activities of daily life | 0.9 (0.5) | 1.4 (0.5)** | 0.8 (0.5) |
| Influence physical functioning | 1.0 (0.6) | 1.5 (0.7)** | 0.9 (0.6) |
| Influence mental functioning | 0.7 (0.5) | 1.2 (0.4)** | 0.7 (0.4) |
| Level of distress (HADS) | 10.5 (6.1) | 15.8 (5.6)** | 9.8 (5.8) |
| Elevated distress (HADS > 12) | 41% | 83%** | 37% |

$^{T}$ (Trend) < .1; *$p < .05$; **$p < 0.01$;

persistent AF in this study. The paroxysmal patients used more antiarrhythmics, compared to the persistent patients (81% vs 38%, Fisher's exact test, $p = 0.002$) and had a higher score on neuroticism ($M = 2.8 \pm 0.4$ vs. $M = 2.4 \pm 0.4$; $p =$ 0.03). Within the samples, fatigue was the most reported symptom. Only a small percentage of all the patients reported ever having been diagnosed with an anxiety disorder. More than 40% of the patients reported levels of distress above the

cut-off point, but only 12% met the criteria we established for panic features. Due to the unexpectedly small size of the panic group the power to detect large group differences ($d = 0.7–1.0$ std, alpha = 0.05) would range between 60 and 80% for the continuous variables.

As expected, the patients with AF and panic features expressed significantly more AF-related symptoms than the patients with AF without panic features. Significantly, more patients with AF and panic features used psychotropic medication; although non-significant, (Fisher's exact test, $p = 0.102$) we do mention the observed differences in the use of rate control medication between both groups. The patient group with AF and panic features reported higher levels of experienced limitations in daily life due to their AF symptoms ($p < 0.01$) and suffered from higher levels of distress ($p < 0.01$) than the patient group with AF without panic features.

No significant differences were found with respect to neuroticism. In line with our hypothesis patients with AF and panic features reported higher levels of cardiac anxiety ($p < 0.01$) compared to the group with AF without panic features.

### 3.2 Ablation outcome

Seven patients were not treated with ablation. Three of them had a spontaneous decrease in AF symptoms. The others declined ablation. Eighty one patients (78%) were available for follow-up. In this patient group, 12 patients were identified as having panic features (at baseline) and 69 patients had no panic features (also see Table 2). There was a trend towards a lower response rate to return the questionnaires in the AF patients without panic features ($p = 0.087$); 92% patients with AF and panic features completed baseline and 3 month follow-up, compared to 69% patients with AF without panic features. In additional data analysis, the result of the ablation was found to have no association with dropout. Patients with a higher symptom burden at baseline were more motivated to complete the 3 month follow-up. Non-responders report less experienced limitations in daily life at baseline ($M = 0.5$, $SD = 0.4$) compared to responders ($p = 0.009$) and less distress at baseline compared to responders $p = 0.024$ (Table 2).

Based on panic features at baseline, patients were divided into two groups. Three months after ablation we compared the patient group with AF and panic features with the group without panic features (see also Table 2). Post-ablation the patient group with AF and panic features at baseline differ significantly from the group without panic features at baseline in experiencing more limitations in daily life ($p = 0.02$), higher levels of distress ($p = 0.039$) and reduced participation in employment and other activities ($p = 0.034$).

As expected [17], average sinus rhythm rate had risen 10 bpm after ablation. Three months after ablation, in the patient group with AF and panic features more atrial fibrillation was detected at compared to the group without panic features, but the difference is not significant (Fisher's exact test $p = 0.339$).

Figure 1 shows that when the two groups were compared with respect to their levels of distress, both groups benefitted significantly ($p = 0.007$) from ablation. Panic features were related to levels of distress ($p = 0.45$) but did not interact with the ablation effect ($p = 0.916$).

The electrical result of the ablation was obtained for 94 patients. For 76 patients no atrial fibrillation was detected after a 24-h Holter measurement; in 20% of the patients AF was detected 3 months after ablation, while 33% (32 patients) still experienced AF symptoms after ablation.

## 4 Discussion

### 4.1 Main findings

This prospective cohort study is, to our knowledge, the first addressing panic and anxiety in patients with AF, scheduled for ablation. It shows that not neuroticism but baseline panic symptoms strongly influence the experienced symptoms of AF. However, we found that ablation, independent of baseline panic features, resulted in a similar reduction of experienced limitations in daily functioning and levels of distress.

Although some clinicians experience the AF population as over-anxious, our study found no evidence that the AF population was characterized by high levels of neuroticism. Moreover, no association was found between panic features and levels of neuroticism, which seems consistent with previous research [18].

Although panic features did not predict persistence of AF-related symptoms after successful ablation, we did find that these patients had higher levels of cardiac anxiety at baseline. This finding is consistent with previous research [19] that found that an anxiety or mood disorder is a predictor for overestimating the severity of AF symptoms. Although this study did not find significant baseline differences in subscribed medication between the AF group with panic features and the AF group without we do address the observed differences in rate control use. Although the guidelines for management of AF [20] only uses somatic parameters to guide prescription of certain medications, recent research [5] concludes that certain panic-reducing medication and anxiolytics might be beneficial for the perceived quality of life in patients with coronary artery disease. The panic feature group in our study used rate control medication less often compared to the group without panic features. In clinical practice all patients were first treated with rate control medication, in accordance with policy. Probably due to reported side effects, patients were switched to other kinds of medication, resulting in differences

**Table 2** Patient characteristics 3 months after ablation, comparing patients with and without panic features at baseline

| | 3 months after ablation<br>M (SD)/percentage | With panic features at baseline<br>M (SD)/percentage (95% confidence interval) | Without panic features at baseline<br>M (SD)/percentage (95% confidence interval) |
|---|---|---|---|
| Patient characteristics | (*N* = 81) | (*N* = 12) | (*N* = 69) |
| Men | 68% | 67% | 69% |
| Women | 32% | 33% | 31% |
| Age (range: 27–79) | 61.1 (9.6) | 57.8 (6.4) | 61.7 (10.0) |
| Educational level (range: 1–6) | 4.9 (0.9) | 4.8 (0.8) | 4.6 (1.0) |
| Partner | 83% | 83% | 83% |
| Somatic co-morbidity | 59% | 72% | 56% |
| No paid work or other activities | 48% | 75%* | 43% |
| Cardiac characteristics | | | |
| Heart rate in sinus rhythm (*n* = 97) | 71 (12.1) | 71 (12.2) | 71 (11.8) |
| Heart rate in atrial fibrillation (*n* = 11) | 123 (32.1) | 118 (53.0) | 125 (30.4) |
| Medication | 91% | 100% (74% to 100%) | 90% (80% to 95%) |
| Anti-arrhythmics | 45% | 67% (35% to 90%) | 41% (29% to 53%) |
| Ratecontrol | 49% | 50% (21% to 79%) | 49% (37% to 62%) |
| Anticoagulation | 76% | 100%* (74% to 100%) | 71% (59% to 81%) |
| Heart failure medication | 38% | 42% (15% to 72%) | 38% (26% to 50%) |
| Beta blocker | 51% | 50% (21% to 79%) | 52% (40% to 64%) |
| Psychotropic medication | 12% | 25% (5% to 57%) | 9% (3% to 18%) |
| Psychological characteristics | | | |
| Pre-morbid anxiety disorder | 8% | 8% (0% to 38%) | 8% (3% to 18%) |
| Limitations in activities of daily life | 0.5 (0.6) | 0.9 (0.9)* | 0.4 (0.6) |
| Influence physical functioning | 0.6 (0.8) | 1.0 (1.0)$^{T}$ | 0.5 (0.7) |
| Influence mental functioning | 0.4 (0.6) | 0.8 (0.8)** | 0.3 (0.5) |
| Level of distress | 8.9 (7.5) | 13.7 (9.0)* | 8.1 (7.0) |
| Elevated distress (HADS > 12) | 27% | 44% (15% to 72%) | 25% (15% to 36%) |
| Experiencing AF symptoms 3 months after ablation (*N* = 94) | 33% | 39% (15% to 72%) | 32% (32% to 56%) |
| Atrial fibrillation detected on Holter at 3 months (*N* = 94) | 20% | 31% (10% to 65%) | 18% (15% to 36%) |

$^{T}$ (Trend) < .1; *$p$ < .05; **$p$ < 0.01;

in heart rate when in atrial fibrillation (higher for the panic group but not significant) and heart rate (trend ($p$ = 0.102) for less rate control medication for the panic group) of rate control medications between groups at baseline. At 3 months the panic group used more medication and had a lower heart frequency in atrial fibrillation. We do not think this is due to inadequate rate control, but to patient characteristics. This finding might suggest that, in high anxiety patients, lack of rate control medication (and thus a higher heart rate during atrial fibrillation) may be part of the development of panic features.

In this study, 7% of the patients with AF reported a history of a previous anxiety disorder. This number seems to be consistent with the prevalence of anxiety reported in previous studies, namely 7.7% for men and 12.4% for women [21]. In our patient group, the prevalence of anxiety and panic features exceeded these numbers but was nevertheless somewhat lower than expected compared to some other studies [5] we discussed in the introduction. The prevalence figures in the literature [5] were in contrast to our study based on a very diverse group of coronary artery diseases, including myocardial infarction (MI), bypass surgery (CABG) or heart failure (CHF). Furthermore, in these studies diagnostic interviews were used, whereas we chose to base the selection on self-report questionnaires. Although our study has a different context, another recent study [22], in a group of AF patients who visited the emergency room, reported a similar prevalence (12%).

## 4.2 Limitations

A major limitation is the relatively small number of patients that were available for follow-up and the final small group of patients with panic/anxiety features ($n$ = 12). The aim for his study was to be of clinical relevance for the electrophysiologists treating patients with atrial fibrillation (AF) and panic features.

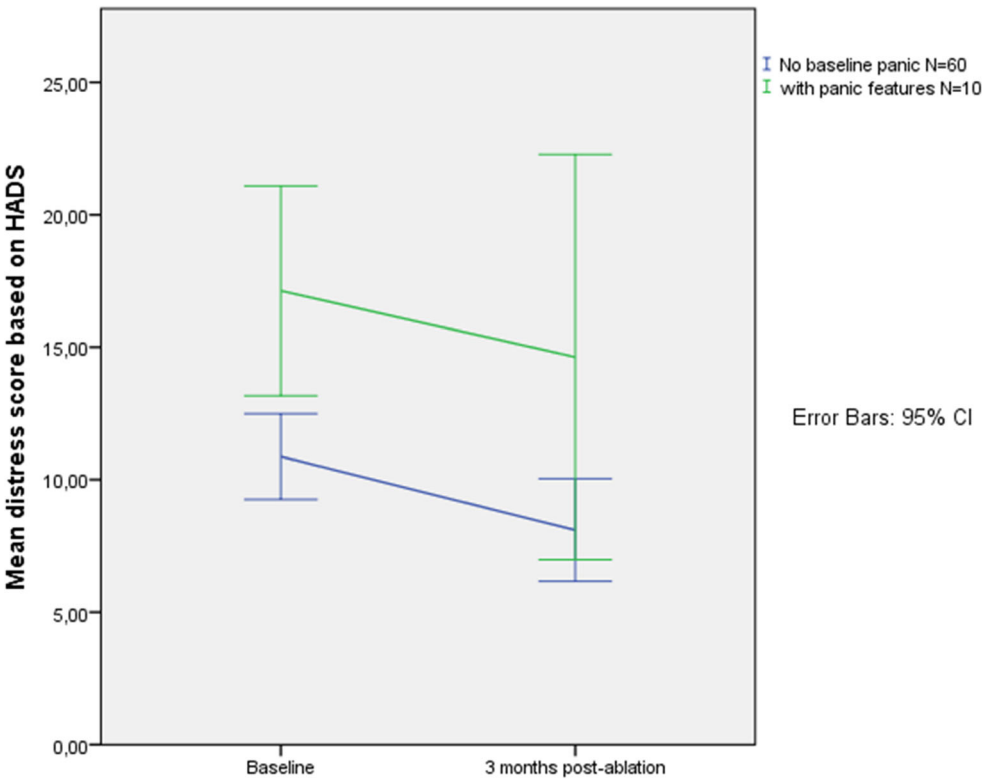


**Fig. 1** Experienced limitations in levels of distress at baseline and 3 months after ablation divided into the patient group with atrial fibrillation and panic features and the group with atrial fibrillation without panic features

We therefore hypothesized that we needed a big or moderate effect size. A small effect would not have been to any clinical significance. Based on the literature we expected more patients with AF to have panic features, than we eventually had in the sample.

In our study, we only included patients who were referred for ablation and had thus showed insufficient response from medication or were not willing to continue on medication. This might have introduced a selection bias towards patients with more profound or longer existent AF. However, the extent to which this might have affected the prevalence of panic features remains a matter of debate.

This study design lacks a group of control patients who are not planning to undergo ablation (those who choose to remain on medical therapy, for example) and/or age- and comorbid condition-matched controls without AF.

Furthermore, although our criteria to define panic features were based on DSM-5 features of panic disorder, the chosen cut-off points might have been too strict.

Follow-up of 3 months might have been too short to draw conclusions, but an extension of this period could have had invalidating effects on the psychological data, as over time more intermediating events could have occurred.

### 4.3 Clinical implications

Based on our findings, we conclude that both groups (patients with and without panic features) benefit from ablation.

Magnitude of effect of AF ablation is not diminished in patients with panic features, but post-ablation they had similar AF-related complaints as patients without panic features had before ablation. Cognitive behavioral therapy focused on treating panic in patients with high anxiety could have an extra beneficial effect on the outcome of ablation in high-anxiety patients. Screening patients with the Hospital Anxiety and Depression Scale (HADS ≥ 15) or the Cardiac Anxiety Questionnaire (CAQ ≥ 3), might be an effective way to detect patients at risk of developing comorbid panic disorder.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflicts of interest.

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