Nonfearful Panic Disorder in Chest Pain Patients:

Status after Nine-Year Follow-Up

Christine B. Bringager, M.D [a]

Katrine Gauer, Medical Student [b]

Harald Arnesen, M.D, PhD [c,d]

Svein Friis, M.D, PhD [a,e]

Toril Dammen, M.D, PhD [a,f]

[a] Department of Psychiatry, Ullevaal University Hospital, 0407 Oslo, Norway

[b] Medical Faculty, University of Oslo, 0317 Oslo, Norway

[c] Department of Cardiology, Ullevaal University Hospital, 0407 Oslo, Norway.

[d] Faculty Division Ullevaal University Hospital, University of Oslo, 0318 Oslo, Norway

[e] Institute of Psychiatry, University of Oslo, 0317 Oslo, Norway

[f] Department of Behavioural Sciences in Medicine, University of Oslo, 0317 Oslo, Norway.

Corresponding author: Christine Bull Bringager, Department for Research and Education, Psychiatric Division, Ullevaal University Hospital, 0407 Oslo, Norway

E-mail: christine.bringager@medisin.uio.no

Telephone: +47 22 11 84 45

ABSTRACT

Chest pain patients (N = 199) consecutively referred to cardiology outpatient clinics were reassessed after nine years by cardiological and psychiatric (SCID I) examinations. Of patients with nonfearful panic disorder (NFPD) (N = 17) at baseline, none fulfilled criteria for NFPD at follow-up, but 18% had panic disorder with fear (PD). The outcome of patients with NFPD and PD (N=59) at baseline did not differ significantly with respect to psychiatric comorbidity, chest pain (SF-MPQ), health care utilization, and health-related quality of life (SF-36). NFPD should be considered a subgroup of PD, which will have a significant impact on the long-term outcome of chest pain patients.

INTRODUCTION

Nonfearful panic disorder (NFPD) is a type of panic disorder (PD) that was first described by Beitman and colleagues in 1987 among cardiology patients who had panic attacks without the experience of fear.[1] These patients met the DSM III-R criteria for PD by reporting attacks of intense discomfort and at least four of the twelve remaining symptoms on the screening checklist, but they did not report subjective free floating anxiety or fear of dying, fear of 'going crazy', or doing something uncontrolled (Table 1).

To the best of our knowledge, only four previous studies in cardiology and emergency department settings have estimated the prevalence of NFPD and found that 22–44% of PD patients fulfilled the criteria for NFPD.[1–4] However, the concept of NFPD is somewhat controversial and it remains equivocal whether NFPD is a subgroup of PD or whether it is a distinct diagnostic entity.[5] Questions have also been raised as to whether NFPD may be better classified as a somatoform disorder, or whether NFPD patients have an undetected medical disorder that is wrongly identified as NFPD.[3,4]

Previous studies have concluded that it is reasonable to regard NFPD as a variety of PD rather than a distinct diagnostic entity, because no significant differences have been found between PD and NFPD patients in terms of demographic characteristics,[1,3,4] frequency of panic attacks (except the cognitive symptoms of panic attacks),[3] health-related quality of life,[4] prevalence of PD among first-degree relatives,[6] response to treatment with anxiolytic medication (imipramine or lorazepam),[7] and response to lactate infusions in neurological patients with PD and NFPD.[7] However, some studies have reported lower prevalence of comorbid

psychiatric disorders and lower scores on self-reported anxiety and panic–agoraphobia symptomatology in NFPD patients.[3,4]

Longitudinal studies are clinically important because they provide knowledge of the long-term outcome of diseases; however, we are aware of only one previous study exploring the course of NFPD. Fleet and colleagues conducted a two-year follow-up study that supported the notion that NFPD is a subgroup of PD, as over the two-year period, both groups had either not improved or worsened in self-report measures of anxiety, panic, and agoraphobia. There were no significant differences between the groups in the number of chest pain episodes, emergency department visits, hospitalizations, and perceived health status at follow-up.[3] Nevertheless, this study suffers from methodological limitations such as lack of diagnostic psychiatric assessments at follow-up, no second cardiological evaluation, and absence of assessment of health-related quality of life, which is considered an important target for treatment. The NFPD patients may have developed fear and thus fulfilled the criteria for PD at follow-up, or they may have developed heart disease or other somatic disorders, which could explain their panic-like symptoms and poor prognosis.

To the best of our knowledge, this is the first long-term follow-up study of NFPD. It was conducted to extend the knowledge of both the concept and clinical outcome of NFPD by rediagnosing the patients nine years after initial examination and comparing the outcome of PD patients with and without fear. It is, therefore, both an important supplement to the validation of the concept of NFPD, and a source of new knowledge regarding the long-term course of NFPD. From outcome studies of PD in psychiatric settings, we know that PD often has a chronic course with serious implications regarding functional and social disability[8] and quality of life.[8,9] If the course of NFPD

is similar to that of PD, it would support the concept of NFPD as a subtype of PD and emphasize the need to recognize this group of patients in order to provide treatment.

We have previously published a study of 199 patients consecutively referred to cardiology outpatient clinics because of chest pain,[4] in which 17 of the 76 patients (22.4%) suffering from PD met the criteria for NFPD. We now present the nine-year follow-up status of this population to (i) estimate the proportion of patients who fulfill the criteria for NFPD and PD at follow-up, and (ii) compare the long-term outcome of the patients with NFPD, PD, and NoPD at baseline. We do this with regard to: a) comorbid psychiatric disorders; b) self-reported anxiety, agoraphobia, somatization, depression, and chest pain; c) presence of somatic disorders; d) health-related quality of life; and e) health care utilization and use of medication.

We hypothesize that the outcome of the NFPD patients will not differ significantly from the outcome of the PD patients and that they will both have a worse outcome than the NoPD patients.

METHODS

Ethics

The study was conducted in accordance with the revised Declaration of Helsinki. The research protocol was accepted by the Regional Ethics Committee in November 1994. At the time of the baseline and follow-up investigations, all participants signed informed consent forms.

Subjects

Baseline. The baseline participants in the study were 199 patients with no previously documented heart disease who were referred for investigation of chest pain to one of four cardiology outpatient clinics in Oslo, Norway, from December 1994 to

November 1996. At the first examination, 32 patients (16%) were diagnosed as suffering from coronary artery disease (CAD) and 167 were diagnosed as having noncardiac chest pain. Seventy-six patients (38%) suffered from PD at initial examination, 17 of which (22.4%) fulfilled the criteria for NFPD. At baseline, no statistically significant difference in gender was found among the PD (patients with NFPD excluded), NFPD, and NoPD patients. Women constituted 58%, 65%, and 43% of the groups, respectively. Patients with PD or NFPD did not differ significantly in age (mean ± SD: 48.1 ± 9.2 vs 49.4 ± 12.9 years, respectively), years of education, or income. Compared to the patients with NoPD, both groups were younger (age of NoPD patients = 52.7 ± 8.8 years), had fewer years of education and lower income. A more detailed description of the study population has been published elsewhere.[4]

Follow-up. Between eight and ten years after the baseline study (mean = 8.6 years, range 8.1–9.9 years), patients were asked to participate in a follow-up study. Fourteen patients had died during the follow-up period (four of the PD and two of the NFPD patients) and one patient had suffered a major stroke and was unable to participate. Of the 184 eligible patients, 150 participated in the follow-up study (82%). Of the 34 nonparticipants, seven had left the country, 12 could not be located, and 12 patients did not participate for the following reasons: study not relevant to their condition at the time (N = 4); did not have time (N = 4); too difficult to come to the hospital (N = 1); afraid of giving away sensitive information (N = 1); disappointed with previous treatment at the hospital (N = 1); and unknown (N = 1). Three patients who filled in questionnaires did not attend psychiatric or cardiological evaluation sessions and were considered nonparticipants.

Of the 150 participating patients, 12 attended the psychiatric, but not the cardiological evaluation session, which was scheduled to take place about a week

after the psychiatric evaluation session. The reasons for their absence are unknown. They were still considered participants because information about their previous cardiac disorders could be obtained from their medical records.

Assessment of sampling bias. There were no significant differences between the 150 participants and the 34 nonparticipants regarding sex, age, years of education, or income at baseline. The participants also did not differ significantly from nonparticipants in the prevalence of CAD (12% vs 17%, respectively), PD (29.3% vs 30.6%, respectively), NFPD (7.3% vs 12.2%, respectively), or any of the outcome measures at baseline.

Procedure

From December 2003 to September 2005, an invitation to participate in the follow-up study was mailed to all eligible patients. The invitation included details of an appointment with the first author, a psychiatric resident trained in psychiatric interviewing, and an appointment for cardiological evaluation. Both meetings were located at the outpatient clinic of the Department of Cardiology, Ulleval University Hospital, Norway.

In order to ensure that the evaluations were blinded, the person who performed the psychiatric interview did not know the result of the previous psychiatric evaluation or previous or current cardiac examinations; likewise, the cardiologists were unaware of the psychiatric evaluation results.

The number of deaths was obtained from the National Death Registry.

Study Groups

The long-term outcome of three groups was compared: patients with panic disorder (PD; N = 44), patients with nonfearful panic disorder (NFPD; N = 11), and patients

without panic disorder (NoPD; N = 95) at baseline. Patients were diagnosed with PD if they met the criteria for panic disorder when using the Structured Clinical Interview for DSM IV (SCID).[10] The patients were diagnosed with NFPD if they reported having recurrent, unexpected attacks of intense discomfort without reporting fear of dying, 'going crazy', or losing control, but at least four of the remaining symptoms of a panic attack according to the criteria described by Beitman et al.[1] and adjusted to DSM IV (Table 1). The NoPD patients met neither the criteria for PD nor NFPD.

Measures

Structured psychiatric interview. Psychiatric disorders at baseline and follow-up were assessed using the Structured Clinical Interview for DSM-IV (SCID I)[10] by the last author at baseline and by the first author at follow-up. SCID I is a semistructured clinical interview that yields current and lifetime psychiatric diagnoses (axis I disorders). For the purpose of this study, we recorded PD and NFPD as current (diagnostic criteria met one month before the interview) or historical (including PD in partial and complete remission), major depression as current or historical, and the other diagnoses as current. The diagnoses were recorded immediately after the interviews. All interviews were audiotaped and 32 randomly selected tapes were rated by an experienced psychiatrist blinded to the diagnoses. The interrater reliability scores were estimated for the diagnoses of panic disorder, major depression, generalized anxiety disorder, and somatoform pain disorder. The interrater reliability scores ranged from acceptable to excellent for all psychiatric diagnoses at both baseline and follow-up (kappa 0.69–1.0).

Self-report measures. The following questionnaires were used at both baseline and follow-up: 1) questionnaire on demographic characteristics including sex, age, and

work status; 2) a chest pain questionnaire including persistence of chest pain symptoms and use of health care facilities and medication; and 3) the Symptom Checklist-90-Revised (SCL-90-R),[11] which measured psychological distress—we limited our analyses to the subscales of anxiety, somatization, and depression; 4) Agoraphobic Cognitions Questionnaire (ACQ) and Mobility Inventory for Agoraphobia (MIA) measured panic–agoraphobia symptomatology;[12] 5) the Short-Form McGill Pain Questionnaire (SF-MPQ) was applied to assess quality and intensity of chest pain;[13] and 6) health-related quality of life was assessed using the Medical Outcome Studies Short Form 36 (SF-36),[14] which consists of eight subscales: physical functioning, role limitation due to reduced physical functioning, general health, vitality, body pain, social functioning, mental health and role limitation due to emotional problems. A psychometrically sound and validated Norwegian translation of the SF-36 was used in the present study.[15,16]

Cardiological assessments and registration of somatic disorders. Follow-up evaluations of the study patients were conducted by four cardiologists, one of whom also took part in the baseline study. A cardiological assessment form was completed by the cardiologist for each patient. The form recorded data on the patients' previous or prevailing medical diseases and current medication. In all patients, a standard bicycle ergometer test was performed at baseline and follow-up according to the procedure described by Nordenfelt et al.[17] If inconclusive, the test was classified as such, and the patient was referred for further tests, such as thallium scintigraphy or coronary angiography. A cardiologist not participating in the cardiological assessment evaluated and approved all cardiological diagnoses before the final analyses. The classification criteria and procedure for this test are reported in more detail elsewhere.[18]

Statistical Analyses

Comparisons between the PD, NFPD, and NoPD patients were performed using the chi-squared test for dichotomous variables. When an overall difference was found with $p < 0.10$, we continued with between-group analyses. The independent Student's *t* test was used for normally distributed continuous variables and the Mann–Whitney *U* test was used for continuous variables without normal distributions. Distributions were visualized using histograms. All tests were two tailed. Paired-sample *t* tests were used to estimate change in scores of continuous variables from baseline to follow-up for each of the three study groups. A significance level of 5% was applied. Agreement between interviewers on psychiatric diagnoses was assessed using the kappa coefficient. The SPSS/PC 12.0 statistical package was used for all data analyses. Due to missing data, N may differ for some of the variables.

RESULTS

Prevalence of Panic Disorder and Nonfearful Panic Disorder at Follow-up

The results are shown in Table 2. Of the patients with current PD at baseline, 27% still suffered from current PD at follow-up while 34% reported a history of PD symptoms. Of the patients with NFPD at baseline, 18% had current PD at follow-up, and 45% reported a history of PD symptoms. No patients fulfilled the criteria for current or historical NFPD at follow-up.

Comparison of Patient Groups

Comorbid axis I disorders at follow-up. The results are shown in Table 3. There was no significant difference in the prevalence of agoraphobia and anxiety disorders between the study groups. NFPD patients had a significantly higher prevalence of any somatoform disorder compared to NoPD patients. The prevalence of current major

depression was significantly higher among PD than NoPD patients and there was a nonsignificant trend (p = 0.051) towards a higher prevalence of history of major depression among the NFPD compared to NoPD patients. There was no significant difference in prevalence of any specific psychiatric disorder between the PD and NFPD patients; however, while 76.3% of the PD patients had any comorbid psychiatric disorder, prevalence in NFPD patients was 54.5% (p = 0.089).

Self-reported anxiety, depression, and somatization at follow-up. Table 4 shows the patients' self-report measures of anxiety, depression, and somatization.

On the SCL-90 anxiety subscale and Agoraphobic Cognitions Questionnaire, PD patients scored significantly higher at follow-up than both NFPD and NoPD patients, and there was no significant difference between the two latter groups. Both PD and NFPD patients had improved from baseline as they had significantly lower SCL-90 anxiety scores at follow-up.

On the SCL-90 somatization subscale, the PD patients scored significantly higher than NoPD patients; otherwise, there was no significant difference between the study groups. All three groups had lower scores at follow-up compared to baseline, but the change was statistically significant for the NFPD and NoPD patients only.

On the SCL-90 depression subscale the PD patients also scored significantly higher than the two other groups at follow-up, while there was no significant difference between the NFPD and NoPD patients. All groups had experienced a small, but nonsignificant improvement from baseline to follow-up.

Chest pain at follow-up. Chest pain in the last month was reported by 65.9% of PD patients, 54.5% of NFPD patients, and 53.7% of NoPD patients, resulting in no significant differences between groups (p = 0.392). Of the 86 patients who had

experienced chest pain in the preceding month, PD patients reported significantly more intense pain than the NoPD patients, while the level of pain in the NFPD patients was between the two other groups for all MPQ scales (Table 4). Regarding the total pain intensity, as measured by a visual analogue scale, NFPD patients had the highest score, although this was not statistically significant from the other groups.

Somatic disorders at follow-up. As seen in Table 5, PD patients reported a significantly higher prevalence of dyspepsia and peptic ulcer than the NoPD patients, while NFPD patients reported a significantly higher prevalence of peptic ulcer and hypothyreosis than NoPD patients. There was no significant difference in prevalence of somatic disorders between PD and NFPD patients, although the mean number of somatic disorders was slightly higher in the PD group.

Health-related quality of life at follow-up. The quality of life results are presented in Table 6. PD patients scored significantly lower than NoPD patients (a higher score indicates better health) on all subscales of the SF-36 at follow-up. The scores of the NFPD patients did not differ significantly from those of PD patients, and although the NFPD patients scored lower than the NoPD patients on seven of eight subscales, the differences reached statistical significance for the physical functioning, body pain, and general health subscales only. There was no significant change in SF-36 scores for any of the groups from baseline to follow-up.

Health care utilization last year. A greater proportion of PD and NFPD patients reported seeking medical help for chest pain symptoms (25% and 27% vs 15%; $p = 0.264$) and for other symptoms (84% and 91% vs 77%; $p = 0.463$) than patients without PD. These differences, however, did not reach statistical significance. Although not statistically significant, a greater proportion of the NFPD patients had

consulted the emergency department (NFPD = 27%, PD = 18% and NoPD = 12%; p = 0.290), general practitioner (NFPD = 82%, PD = 64% and NoPD = 64%; p = 0.482) and medical specialist (NFPD = 46%, PD = 39% and NoPD = 39%; p = 0.915) during the last year. The mean number of medical consultations was significantly greater in NFPD compared to NoPD patients (7.5 ± 7.8 vs 3.5 ± 5.1; p = 0.05), while there was no significant difference in the number of consultations between NFPD and PD patients (5.3 ± 6.9). In addition, there were no significant differences between the three groups regarding the number of patients who had consulted a psychiatrist during the last year (PD = 4.5%, NFPD = 9.1%, NoPD = 7.4%).

Current use of medication. No significant difference between the three study groups was found regarding the use of antidepressants or anxiolytics. The proportion of PD, NFPD, and NoPD patients using antidepressants was 10%, 9%, and 7%, respectively (p = 0.891), while for anxiolytics it was 17%, 9%, and 11%, respectively (p = 0.641). However, NFPD patients reported a significantly greater use of analgesics than both PD (45% vs 17%, p = 0.042) and NoPD patients (45% vs 18%, p = 0.029).

DISCUSSION

The main finding of this study was that while 17 of 76 PD patients met the criteria for NFPD at baseline, none were diagnosed with NFPD nine years later; also, of the 11 NFPD patients who participated in the follow-up interview, more than 60% reported either current PD or a history of PD with fear. Interestingly, 39% of the PD and 36% of the NFPD patients did not fulfill the criteria for any panic disorder at follow-up. We believe this may be explained by the instability of recall, as has previously been reported in patients with somatization disorder[19] and depression.[20]

These findings suggest that a majority of the NFPD patients have experienced both fearful and nonfearful panic episodes during the course of their illness. They support the study of Rachman and colleagues[21] that found that, for several panic trials, patients could be divided into three groups: one group reporting exclusively panic attacks with fear; one group reporting exclusively panic attacks without fear; and one group reporting both fearful and nonfearful panic attacks. The participants in our study were diagnosed as having either panic attacks with or without fear, exclusively, based on the last month of attacks; this categorization assumes that this period was representative, although it may not have been. A second evaluation of the NFPD patients may have revealed more anxiety in conjunction with panic attacks than was found in the first examination.

One must also consider whether NFPD patients really did have panic attacks without fear at baseline, or whether they denied their emotional symptoms due to shame or fear of negative stigma associated with psychiatric disorders. Perhaps they were concerned that their physical symptoms would be underestimated and not thoroughly investigated if they admitted cognitive symptoms. This is in line with the finding that only 31% of the patients with PD or NFPD wanted a report with information about panic disorder and treatment options to be sent to their general practitioner after their first psychiatric evaluation. The most commonly stated reason for not experiencing a treatment need was a primary need for clarification of cardiovascular illness.[18]

The results of the psychiatric diagnostic reevaluation confirm the notion of NFPD as a subgroup of PD rather than a distinct diagnostic entity. Furthermore, as there was no significant difference between the PD and NFPD patients regarding the prevalence of any cardiological or other somatic disease, it seems unlikely that an undetected

medical disorder was the cause of symptoms in NFPD patients at baseline. In fact, the number of medical disorders was highest among the PD patients. There was no significant difference in the prevalence of somatoform disorders between the PD and NFPD patients, as the prevalence rates were 25% and 37%, respectively. If NFPD were to be better explained by a somatoform disorder, one would expect a greater overlap of the diagnoses. However, the rates of both medical and somatoform disorders were high for both PD and NFPD patients and it is difficult to know with certainty whether the reported medical conditions were actual diseases or somatoform symptoms. Apart from the cardiological investigation, these disorders were not verified by thorough medical examination, but rather recorded by a cardiologist. Thus, the patients may have reported symptoms they perceived as somatic disorders; i.e., breathing problems explained as asthma, or chest pain explained as dyspepsia or peptic ulcer, when the symptoms may not have been of organic origin. A high prevalence of unexplained physical symptoms is common in patients with anxiety disorders,[22] but a high comorbidity between panic disorder and gastrointestinal disorders as well and asthma has also been reported.[23] The symptoms caused by these disorders may serve as internal cues that initiate panic attacks in vulnerable persons.[23]

Moreover, we hypothesized that the outcome of the PD and NFPD patients would not differ significantly and that both groups would have a worse outcome than the NoPD patients. This hypothesis was only partially confirmed, as the PD patients had significantly higher scores than the NFPD patients regarding the symptoms of panic and agoraphobia, while there was no significant difference between PD and NFPD patients regarding the development of comorbid psychiatric disorders**,** persistence of chest pain episodes, health care utilization, and self-reported health-related quality of life.

Previous studies have reported a lower prevalence of agoraphobia in NFPD compared to PD patients[3,4,24] and a lower prevalence of generalized anxiety disorder in NFPD patients.[3] After nine years, there were no significant differences in prevalence of any comorbid anxiety disorders between the two groups. The rates of generalized anxiety disorder and specific phobia had increased in both groups compared to baseline and the prevalence of agoraphobia had decreased from 46% to 14% in PD patients from baseline to follow-up, most likely because only 27% of them suffered from current panic attacks at follow-up. Although 18% of NFPD patients suffered from current PD with fear at follow-up, an additional 45% reported a history of PD with fear, and there were similar rates of anxiety disorders in PD and NFPD patients. This did not seem to affect their experience, or at least their report, of typical panic symptoms. Regarding the self-reported symptoms of panic and agoraphobia, both the PD and NFPD patients had improved at follow-up. However, the PD patients still had significantly higher scores than NFPD patients who had scores no different from the NoPD patients both at baseline and follow-up. Antipanic treatment (i.e., serotonin reuptake inhibitors and high-potency benzodiazepines) may have improved these measures, but we did not collect systematic data regarding the treatment that they may have received during the follow-up period because we believed there would be recall difficulties. However, during the last year, 21% of the PD and 9% of NFPD patients had received such medical treatment. Interestingly, this was also the case for 17% of the NoPD patients.

Regarding health-related quality of life, all groups were unchanged from baseline to follow-up and the outcome of the PD and NFPD patients did not differ significantly, while they both had a worse outcome than the NoPD patients. This is an important finding, as improvement in health-related quality of life is one of the targets

for treatment of PD.[25] The outcome of the NFPD patients was particularly poor compared to NoPD patients regarding the subscales constituting the physical component of SF-36; this could not be explained by a difference in the number of medical diseases between the groups. In fact, the scores of the NFPD patients did not differ significantly from, or were worse than what is reported in patients with chronic stable angina,[26] symptomatic angina,[27] patients with coronary artery disease before surgery,[28] patients with PD,[9] and patients with other chronic disorders.[9] These findings add to the evidence that NFPD patients are particularly distressed by physical impairment and pain and that this distress is unchanged after nine years. This was also reflected in their use of analgesics, which was significantly higher than in the two other groups, as well as a more frequent use of the health care system by NFPD compared with NoPD patients.

The results of this long-term follow-up study suggest that NFPD should be regarded as a subgroup of PD and that the course of NFPD is as severe as that of PD, as both groups have a significant impairment in health-related quality of life. However, the PD and NFPD patients have a somewhat different pattern of symptomatology. It seems that the PD patients develop more of the comorbid disorders that are well known to complicate PD, like alcohol abuse[29] and major depression[30] and that NFPD patients suffer from more comorbid somatoform disorders as well as periods with depression. Although many of the NFPD patients develop panic attacks with fear, their reported psychological distress is low. This may have clinical implications as these patients will probably not be referred to psychiatric treatment, but rather seen in somatic practice, which they consult because of a range of somatic diseases as well as pain. The results of this study emphasize the need for physicians in cardiological settings or primary care to bear in mind that it is possible

to fulfill the diagnostic criteria for PD without experiencing free floating anxiety or fear, as patients with NFPD have reduced health-related quality of life and increased health care utilization and therefore are in need of treatment.

There is little empirical evidence for the effective treatment of NFPD. To the best of our knowledge, there is only one small study that examined the treatment of NFPD patients, where PD and NFPD patients responded similarly to antidepressive therapy.[7] Cognitive therapy may also be effective as it is one of the treatments of choice in panic disorder[31] and it has also been found to be effective in patients with medically unexplained physical symptoms.[32] While cognitive therapy of panic disorder is focused on modifying the patients' catastrophic interpretations of bodily sensations,[33] we speculate that this model may be less suitable in NFPD patients who report less cognitive distortions. A model focusing on stress management, activity regulation, emotional awareness, cognitive restructuring, and interpersonal communication, as that developed by Allen et al.[32] for treatment of patients with medically unexplained symptoms, may be more effective in NFPD patients.

Study Strengths and Limitations

The strengths of this study are that we followed the patients for a long period of time and performed psychiatric and cardiological reevaluation after nine years. However, we did not collect data regularly throughout the follow-up period. Therefore, we do not know if the findings at the time of follow-up reflect the psychiatric and medical morbidity of the patients throughout the nine-year period. Another important issue is whether the differences in psychiatric diagnosis from baseline to follow-up are reliable and not caused by different judgment by the interviewers. However, the last author of this article, who performed the baseline interviews, was the one who made a second evaluation of the interviews at follow-up,

and the interrater reliability scores were high. Furthermore, no systematic evaluations of medical disorders other than coronary artery disease were conducted; however, that was not considered to be the main aim of this study.

Dealing with a small study group such as the NFPD patients, which consisted of 17 people at baseline and only 11 at follow-up, weakens the statistical power of the study and makes it susceptible to type 2 errors. Differences between the NFPD and PD patients may thus actually be significant although they are statistically not significant based on the current sample. This may be the case when comparing the two groups regarding current major depression and prevalence of any psychiatric disorder. However, most of our results showed that differences between the NFPD and PD patients were either clearly not significant or clearly significant.

CONCLUSION

This long-term follow-up study of NFPD patients supports the position that NFPD is a subgroup of PD, as the majority of NFPD patients experience panic attacks with fear during the course of their illness. The outcome of NFPD patients is as severe as that of the PD patients regarding health-related quality of life, although the symptom profiles of the two groups differ somewhat. The challenge is to make primary care physicians aware of this subgroup of PD and, further, to educate and motivate the patients to receive psychiatric treatment even if they do not feel psychiatrically ill.

REFERENCES

1.Beitman BD, Basha I, Flaker G, DeRosear L, Mukerji V, Lamberti J: Non-fearful panic disorder: panic attacks without fear. Behav Res Ther 1987; 25:487–492

2.Beitman BD, Kushner M, Lamberti JW, Mukerji V: Panic disorder without fear in patients with angiographically normal coronary arteries. J Nerv Ment Dis 1990; 178:307–312

3.Fleet RP, Martel JP, Lavoie KL, Dupuis G, Beitman BD: Non-fearful panic disorder: a variant of panic in medical patients? Psychosomatics 2000; 41:311–320

4.Bringager CB, Dammen T, Friis S: Nonfearful panic disorder in chest pain patients. Psychosomatics 2004; 45:69–79

5.Kushner MG, Beitman BD: Panic attacks without fear: an overview. Behav Res Ther 1990; 28:469–479

6.Beitman BD, Thomas AM, Kushner MG: Panic disorder in the families of patients with normal coronary arteries and non-fear panic disorder. Behav Res Ther 1992; 30:403–406

7.Russell JL, Kushner MG, Beitman BD, Bartels KM: Nonfearful panic disorder in neurology patients validated by lactate challenge. Am J Psychiatry 1991; 148:361–364

8.Carpiniello B, Baita A, Carta MG, Sitzia R, Macciardi AM, Murgia S, Altamura AC: Clinical and psychosocial outcome of patients affected by panic disorder with or without agoraphobia: results from a naturalistic follow-up study. Eur Psych: Journal Assoc Eur Psych 2002; 17:394–398

9.Candilis PJ, McLean RY, Otto MW, Manfro GG, Worthington JJ, III, Penava SJ, Marzol PC, Pollack MH: Quality of life in patients with panic disorder. J Nerv Ment Dis 1999; 187:429–434

10.American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition 1994

11.Derogatis LR: The SCL-90 R: Administration, scoring and procedures manual-II for the revised version. Baltimore: Clinical Psychometric Research 1977

12.Chambless DL, Caputo GC, Bright P, Gallagher R: Assessment of fear of fear in agoraphobics: the body sensations questionnaire and the agoraphobic cognitions questionnaire. J Consult Clin Psychol 1984; 52:1090–1097

13.Melzack R: The short-form McGill Pain Questionnaire. Pain 1987; 30:191–197

14.Ware JE, Jr., Sherbourne CD: The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30:473–483

15.Loge JH, Kaasa S: Short form 36 (SF-36) health survey: normative data from the general Norwegian population. Scand J Soc Med 1998; 26:250–258

16.Loge JH, Kaasa S, Hjermstad MJ, Kvien TK: Translation and performance of the Norwegian SF-36 Health Survey in patients with rheumatoid arthritis. I. Data quality, scaling assumptions, reliability, and construct validity. J Clin Epidemiol 1998; 51:1069–1076

17.Nordenfelt I, Adolfsson L, Nilsson JE, Olsson S: Reference values for exercise tests with continuous increase in load. Clin Physiol 1985; 5:161–172

18.Dammen T, Arnesen H, Ekeberg O, Husebye T, Friis S: Panic disorder in chest pain patients referred for cardiological outpatient investigation. J Intern Med 1999; 245:497–507

19.Simon GE, Gureje O: Stability of somatization disorder and somatization symptoms among primary care patients. Arch Gen Psychiatry 1999; 56:90–95

20.Andrews G, Anstey K, Brodaty H, Issakidis C, Luscombe G: Recall of depressive episode 25 years previously. Psychol Med 1999; 29:787–791

21.Rachman S, Levitt K, Lopatka C: Panic: the links between cognitions and bodily symptoms I. Behav Res Ther 1987; 25:411–423

22.de Waal MW, Arnold IA, Eekhof JA, van Hemert AM: Somatoform disorders in general practice: prevalence, functional impairment and comorbidity with anxiety and depressive disorders. Br J Psychiatry 2004; 184:470–476

23.Zaubler TS, Katon W: Panic disorder in the general medical setting. J Psychosom Res 1998; 44:25–42

24.Wilson KG, Sandler LS, Asmundson GJ: Fearful and non-fearful panic attacks in a student population. Behav Res Ther 1993; 31:407–411

25.Mendlowicz MV, Stein MB: Quality of life in individuals with anxiety disorders. Am J Psychiatry 2000; 157:669–682

26.Lerner DJ, Amick BC, III, Malspeis S, Rogers WH, Gomes DR, Salem DN: The Angina-related Limitations at Work Questionnaire. Qual Life Res 1998; 7:23–32

27.Marquis P, Fayol C, Joire JE, Leplege A: Psychometric properties of a specific quality of life questionnaire in angina pectoris patients. Qual Life Res 1995; 4:540–546

28.Kiebzak GM, Pierson LM, Campbell M, Cook JW: Use of the SF36 general health status survey to document health-related quality of life in patients with coronary artery disease: effect of disease and response to coronary artery bypass graft surgery. Heart Lung 2002; 31:207–213

29.Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC: Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry 1997; 54:313–321

30.Roy-Byrne PP, Stang P, Wittchen HU, Ustun B, Walters EE, Kessler RC: Lifetime panic-depression comorbidity in the National Comorbidity Survey. Association with symptoms, impairment, course and help-seeking. Br J Psychiatry 2000; 176:229–235

31.Pollack MH, Allgulander C, Bandelow B, Cassano GB, Greist JH, Hollander E, Nutt DJ, Okasha A, Swinson RP: WCA recommendations for the long-term treatment of panic disorder. CNS Spectr 2003; 8:17–30

32.Allen LA, Woolfolk RL, Escobar JI, Gara MA, Hamer RM: Cognitive-behavioral therapy for somatization disorder: a randomized controlled trial. Arch Intern Med 2006; 166:1512–1518

33.Gelder MG, Clark DM, Salkovskis P: Cognitive treatment for panic disorder. J Psychiatr Res 1993; 27 Suppl 1:171–178

TABLE 1. DSM-IV Criteria for Nonfearful Panic Disorder

A. Both (1) and (2)
    1. Recurrent unexpected attacks of intense discomfort without fear.
    2. At least one of the attacks has been followed by a significant change in behavior related to the attack lasting for one month or more.

B. The attacks consisted of at least four of the following: palpitations, sweating, trembling, shortness of breath, choking, chest pain, nausea, dizziness, derealization or depersonalization, paresthesias, chills or flushes (no fear of dying, of going crazy or losing control).

C. The panic attacks are not due to the direct physiological effect of a substance (e.g., drug abuse, medication) or a general medical condition (e.g., hyperthyroidism).

D. The panic attacks are not better accounted for by another mental disorder.

TABLE 2. Prevalence of Current and Historical Panic Disorder and Nonfearful Panic Disorder at Follow-Up in Patients who met the Criteria for Panic Disorder, Nonfearful Panic Disorder or No Panic Disorder at Baseline

	Baseline Panic Disorder N = 44 N (%)	Baseline Nonfearful Panic Disorder N = 11 N (%)	Baseline No Panic Disorder N = 95 N (%)
Follow-up			
Current panic disorder	12 (27.3)	2 (18.2)	9 (9.5)
History of panic disorder	15 (34.1)	5 (45.5)	8 (8.34
Current nonfearful panic disorder	0	0	0
History of nonfearful panic disorder	0	0	0
No panic disorder	17 (38.6)	4 (36.3)	78 (82.1)

TABLE 3. Comorbid Axis I Disorders at Follow-Up in Patients Diagnosed at Baseline with Panic Disorder, Nonfearful Panic Disorder or No Panic Disorder

	Panic Disorder N = 44 N (%)	Nonfearful Panic Disorder N = 11 N (%)	No Panic Disorder N = 95 N (%)	p-value Chi-square Df = 2[a]	p-value Chi-square Df = 1[a]
Agoraphobia	6 (13.6)	1 (9.1)	5 (5.3)	p = 0.236	
Generalized anxiety disorder	8 (18.2)	2 (18.2)	11 (11.6)	p = 0.532	
Social phobia	3 (6.8)	0 (0)	8 (8.4)	p = 0.591	
Simple phobia	9 (20.5)	2 (18.2)	11 (11.6)	p = 0.366	
Any anxiety disorder	16 (36.4)	4 (36.4)	23 (24.2)	p = 0.284	
Somatization disorder	1 (2.3)	1 (9.1)	5 (5.3)	p = 0.569	
Somatoform pain disorder	8 (18.2)	3 (27.3)	11 (11.6)	p = 0.279	
Hypochondriasis	4 (9.1)	0	0	p = 0.007	1 vs 2 p = 0.299 1 vs 3 p = 0.003 2 vs 3 -
Any somatoform disorder	11 (25.0)	4 (36.4)	12 (12.6)	p = 0.054	1 vs 2 p = 0.449 1 vs 3 p = 0.068 2 vs 3 p = 0.037
Current major depression	15 (34.1)	1 (9.1)	10 (10.5)	p = 0.002	1 vs 2 p = 0.102 1 vs 3 p = 0.001 2 vs 3 p = 0.883
History depression	14 (31.8)	6 (54.5)	25 (26.3)	p = 0.147	
Any depressive disorder	24 (54.5)	6 (54.5)	32 (33.7)	p = 0.044	1 vs 2 p = 1.000 1 vs 3 p = 0.020 2 vs 3 p = 0.172
Lifetime alcohol abuse	6 (13.6)	0 (0.0)	2 (2.1)	p = 0.014	1 vs 2 p = 0.194 1 vs 3 p = 0.007 2 vs 3 p = 0.627
Any psychiatric disorder	35 (79.5)	6 (54.5)	40 (42.1)	p < 0.001	1 vs 2 p = 0.089 1 vs 3 p < 0.001 2 vs 3 p = 0.431

[a] Df = Degrees of freedom.

TABLE 4. Self-Reported Symptoms of Anxiety, Somatization, Depression, Agoraphobia and Chest Pain at Follow-Up in Patients with Panic Disorder, Nonfearful Panic Disorder and No Panic Disorder at Baseline

	Panic Disorder N = 41 Mean (SD)	Nonfearful Panic Disorder N = 10 Mean (SD)	No Panic Disorder N = 89 Mean (SD)	p-value[a]
Anxiety				
Symptom Checklist-90 Anxiety	0.69 (0.73)	0.17 (0.15)	0.35 (0.59)	1 vs 2 p = 0.001
				1 vs 3 p = 0.007
				2 vs 3 p = 0.768
Somatization				
Symptom Checklist-90	1.20 (0.82)	0.75 (0.58)	0.62 (0.61)	1 vs 2 p = 0.107
Somatization				1 vs 3 p < 0.001
				2 vs 3 p = 0.532
Depression				
Symptom Checklist-90	0.98 (0.81)	0.45 (0.27)	0.53 (0.65)	1 vs 2 p = 0.001
Depression				1 vs 3 p = 0.002
				2 vs 3 p = 0.498
Agoraphobia				
Agoraphobia Cognitions	1.34 (0.37)	1.10 (0.11)	1.14 (0.28)	1 vs 2 p = 0.001
Questionnaire				1 vs 3 p = 0.005
				2 vs 3 p = 0.574
Mobility Inventory of	1.45 (0.60)	1.22 (0.39)	1.29 (0.53)	1 vs 2 p = 0.269
Agoraphobia				1 vs 3 p = 0.145
Unaccompanied				2 vs 3 p = 0.685
McGill Pain Questionnaire [b]				
Total sensory intensity score	10.04 (5.24)	8.33 (7.99)	5.98 (5.79)	1 vs 2 p = 0.523
				1 vs 3 p = 0.005
				2 vs 3 p = 0.512
Total affective intensity score	4.04 (2.15)	2.83 (2.48)	2.00 (2.98)	1 vs 2 p = 0.240
				1 vs 3 p = 0.003
				2 vs 3 p = 0.474
Total intensity score	14.08 (6.76)	11.17 (10.15)	7.98 (8.42)	1 vs 2 p = 0.397

				1 vs 3 p = 0.003
				2 vs 3 p = 0.489
Pain intensity	49.0 (18.7)	55.2 (17.0)	39.9 (18.8)	1 vs 2 p = 0.474
VAS (0-100)				1 vs 3 p = 0.072
				2 vs 3 p = 0.067

[a] Student's *t* test or Mann–Whitney *U* test used as appropriate.

[b] Scores on McGill Pain Questionnaire for those patients who had chest pain last month (N = 89).

TABLE 5. Somatic Disorders at Follow-Up in Patients Diagnosed at Baseline with Panic Disorder, Nonfearful Panic Disorder or No Panic Disorder

	Panic disorder N = 40 N (%)	Nonfearful panic disorder N = 8 N (%)	No panic disorder N = 89 N (%)	p-value Chi-square Df = 2[a]	p-value Chi-square Df = 1[a]
Coronary artery disease	7 (17.5)	2 (22.2)	26 (28.9)	p = 0.377	
N = 139					
Asthma	11 (27.5)	1 (12.5)	12 (13.5)	p = 0.147	
N = 137					
Migraine	7 (18.4)	1 (14.3)	9 (10.1)	p = 0.432	
N = 134					
Fibromyalgia	4 (10.5)	1 (14.3)	4 (4.5)	p = 0.338	
N = 133					
Musculoskeletal	14 (35.0)	2 (28.6)	24 (27.3)	p = 0.673	
N = 135					
Dyspepsia	19 (47.5)	3 (42.9)	23 (26.1)	p = 0.051	1 vs 2 p = 0.820
N = 135					1 vs 3 p = 0.017
					2 vs 3 p = 0.340
Peptic Ulcer	7 (17.9)	3 (37.5)	5 (5.7)	p = 0.006	1 vs 2 p = 0.218
N = 135					1 vs 3 p = 0.029
					2 vs 3 p = 0.002
Hyperthyroidism	0	0	0		
N = 137					
Hypothyroidism	4 (10.0)	2 (25.0)	4 (4.5)	p = 0.075	1 vs 2 p = 0.242
N = 137					1 vs 3 p = 0.230
					2 vs 3 p = 0.021
Any somatic disorder	32 (84.2)	5 (83.3)	59 (67.8)	p = 0.138	
Number of somatic					
disorders	1.74 (1.25)	1.00 (0.63)	1.18 (1.14)		1 vs 2 p = 0.044
(mean, SD, *t* test)					1 vs 3 p = 0.017
					2 vs 3 p = 0.697

[a]Df = Degrees of freedom.

TABLE 6. Comparison of Mean (SD) Short Form-36 Scores at Follow-Up for Patients with Panic Disorder, Nonfearful Panic Disorder and No Panic Disorder at Baseline

Note: a higher score indicates a better health state.

Short Form 36 Subscales	Panic Disorder N = 44 Mean (SD)	Nonfearful Panic Disorder N = 11 Mean (SD)	No Panic Disorder N = 95 Mean (SD)	p-value *t* test
Physical functioning	72.3 (23.4)	67.1 (27.0)	81.7 (18.1)	1 vs 2 p = 0.524 1 vs 3 p = 0.012 2 vs 3 p = 0.020
Role physical	38.4 (42.0)	52.3 (41.0)	65.7 (41.8)	1 vs 2 p = 0.330 1 vs 3 p = 0.001 2 vs 3 p = 0.315
Bodily pain	49.8 (26.2)	45.7 (27.4)	63.5 (26.9)	1 vs 2 p = 0.661 1 vs 3 p = 0.006 2 vs 3 p = 0.050
General health	52.2 (21.2)	48.4 (23.3)	67.2 (21.1)	1 vs 2 p = 0.599 1 vs 3 p < 0.001 2 vs 3 p = 0.007
Vitality	42.9 (23.2)	49.1 (23.1)	54.7 (23.1)	1 vs 2 p = 0.430 1 vs 3 p = 0.006 2 vs 3 p = 0.449
Social functioning	68.0 (24.7)	75.0 (24.4)	80.9 (23.7)	1 vs 2 p = 0.407 1 vs 3 p = 0.004 2 vs 3 p = 0.442
Role emotional	51.2 (41.7)	69.7 (45.8)	67.4 (38.8)	1 vs 2 p = 0.205 1 vs 3 p = 0.030 2 vs 3 p = 0.854
Mental health	66.8 (20.5)	76.7 (23.4)	77.2 (18.8)	1 vs 2 p = 0.170 1 vs 3 p = 0.004 2 vs 3 p = 0.944