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EMPIRICAL PSYCHOLOGICAL MODELING OF CHEST PAIN: A COMPARATIVE STUDY

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Abstract—In this study the psychological profiles of 67 patients with noncardiac chest pain (NCA) and 47 patients with coronary artery disease (CAD) were analyzed to construct an empirical-psychological model that would be able to discriminate these two groups. All patients were suffering from chest pain at the time of referral by their general practitioner. The noncardiac patients were significantly younger, more often female, single, and nonsmokers. The two groups differed significantly on anxiety, somatization, obsessive compulsive behavior, psychoneuroticism, and hyperventilation. Logistic regression analysis on the variables jointly, showed that age, gender, anxiety, and hyperventilation contributed significantly to the model for discriminating between the two groups. Crossvalidation showed that the constructed model was stable.

Keywords: Anxiety; Chest pain; Hyperventilation; Normal coronary arteries; Quantitative model.

INTRODUCTION

Over the past years a considerable amount of research has been conducted on the relationship between chest pain with normal coronary arteries and psychological dysfunctioning [1]. Recent studies have shown that up to one-third of the patients with chest pain undergoing cardiac catherization or treadmill testing have normal or minimally diseased coronary arteries (NCA) [2–13]. These patients are relatively young, female, suffer from panic disorder, hyperventilate, are considered depressed and anxious, and have a higher prevalence of atypical chest pain. Frequently these patients are classified as cardiac phobics [2, 4, 6–8).

Although the prospects of survival for these patients are favorable [5, 10, 14–22], patients' symptoms tend to persist or even increase over the years. Ockene's study [16], for instance, showed that after an average follow-up period of 16 months, 70% of the patients with normal coronary angiograms, still complained of chest pain. Of these, 12% indicated that their chest pain had become even worse during follow-up, and many remained limited in their daily activities. Similarly, in a study by Wielgosz [20], of 548 noncardiac chest pain patients, 33% became pain free and 39% had less

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pain, but 28% continued to have similar or worse chest pain, whereas only 3 cardiac deaths occurred in the year following angiography.

It may be concluded that the present medical approach towards patients with chest pain and normal coronary arteries apparently does not suffice, and medical consumption and, as a consequence, costs remain high [23].

All of the studies mentioned above only signal the differences between the two groups of chest pain patients, but do not quantitatively relate them to a model in which the variables with differential potential are entered, thereby allowing for a quicker diagnosis and a more tailored treatment. In the present study, we will make an effort to fill this gap. The objective of this study was to construct a practical statistical model based on demographic and psychological variables that can, in an early stage, quantitatively discriminate between chest pain patients with diseased coronary arteries and patients with chest pain without a somatic cause.

METHODS

Eligible for this study were patients who had been referred to the outpatient cardiology clinic of the Rotterdam University Hospital for the first time between March 1991 and January 1993, with chest pain as a chief complaint. Exclusion criteria were insufficient proficiency in the Dutch language, age younger than 18 or older than 75 years, and a history of psychiatric illness. In addition, patients were screened to be sure that no further medical complications, such as myocardial infarction or by-pass surgery, had occurred between the time of referral and the onset of the study.

Patients who met these criteria were selected from medical records available at the Thoraxcentre of the Rotterdam University Hospital. All selected patients had undergone extensive cardiological testing in order to assess whether the chest pain was of a somatic nature.

In total, 163 patients were eligible for this study, 96 in the noncardiac group (NCA) and 67 in the group with coronary artery disease (CAD). After elimination of patients unwilling to participate ($n_{nca} = 26$; $n_{cad} = 15$) and inconclusive data ($n_{nca} = 3$; $n_{cad} = 5$), a total of 67 noncardiac patients (29 men, 38 women; mean age 48.5 years, SD 12.0) and 47 cardiac patients (36 men, 11 women; mean age 60.7 years, SD 9.0) were used for statistical analysis.

Procedure

The research group sent each patient a letter informing them about the study. After one week, potential subjects were phoned to make an appointment at the outpatient cardiology clinic to fill out psychological questionnaires. These appointments were generally one week later. The patients were allowed to take their time in completing the questionnaires, but usually this took no longer than 1 hour.

Psychological assessment

On the basis of earlier findings [2–11], psychological characteristics were measured with the following questionnaires, representing the constructs of relevance.

The Hospital Anxiety Depression Scale (HAD) [24] was used to assess anxiety and depression. The questionnaire consists of 14 questions, half concerning anxiety and half concerning depression. The possible answers indicate the intensity of the given mood; the sum of the individual scores give overall scores for anxiety (min 0; max 21) and for depression (min 0; max 21). Validity and reliability have been proven for British studies [4].

Psychopathology was measured with the General Health Questionnaire (GHQ-12). The 12 items of this self-rating questionnaire reflect a measure of severity of functional nonpsychotic psychopathology. The questions relate to unusual or unpleasant psychological experiences. Patients are requested to answer by indicating, on a 4-point scale, the difference between their present situation and their normal situation, choosing from *none, no more than usual, more than usual,* and *a lot more than usual.* The total scores (min 0; max 12) were obtained using the conventional scoring (0-0-1-1) [25]. Validity and reliability for the Dutch version have been demonstrated [26, 27].

The Symptom Checklist (SCL-90) [28] was used to assess agoraphobia (min 7; max 35), anxiety (min 10; max 50), depression (min 16; max 80), somatization (min 12; max 60), obsessive compulsive behavior (min 9; max 45), interpersonal sensitivity (min 18; max 90), hostility (min 6; max 30), sleeping problems (min 3; max 15), and the total of all subscales, including the residual items: psychoneuroticism (min 90; max 450). The SCL-90 is a self-report questionnaire that is widely used in medical research to categorize

Table I. – Demographic characteristics of noncardiac and cardiac patients

	NCA ($n=67$)	CAD ($n=47$)	p value
Age	48.49	60.65	$\ll 0.01$
mean (SD)	(12.02)	(9.02)	
Gender (male:female)	29:38	36:11	$\ll 0.01$*
Marital status (partner:single)	45:22	43:4	<0.05†
Full time employment (yes:no)	22:45	14:33	0.89
Smoking (yes:no:never)	15:23:29	12:27:8	<0.01‡

*$\chi^2 = 11.19$, df = 1.
†$\chi^2 = 7.95$, df = 1.
‡$\chi^2 = 9.79$, df = 2.

and quantify psychological distress. For each of 90 items, patients rate on a 5-point Likert scale (from 1, *not at all,* to 5, *extremely*) the degree of distress they have experienced in the preceding week. Validity and reliability have proven to be good for the Dutch population [29].

Hyperventilation was measured with the Nijmegen Questionnaire (NQ) [30]. This questionnaire consists of 16 complaints whose frequency of incidence can be indicated on a 5-point Likert scale (*never, rarely, sometimes, often* and *very frequently*). The complaints relate to different systems: (a) cardiovascular, for example, "palpitations"; (b) neurological, for example, "dizzy spells", "tingling fingers"; (c) respiratory, for example, "shortness of breath"; (d) gastrointestinal, for example, "bloated abdominal sensation"; (e) psychological, for example, "tense" and "anxious feeling". Total scores can range from 0 to 64. In Van Dixhoorn and Duivenvoorden's study [30], the sensitivity of the Nijmegen Questionnaire in relation to the clinical diagnosis was 91% and the specificity was 95%.

Hypochondria was assessed with the Maastricht hypochondria scale (MEGAH) [31]. Sixty-seven statements are divided into 5 subscales: "fear concerning own health" (min 12; max 60), "general health fear" (min 16; max 80), "illness belief" (min 7; max 35), "trust of doctors" (min 6; max 30), and "search for medical information" (min 3; max 15). The sum of the first 3 subscales indicates the amount of hypochondria (min 35; max 175). Subjects respond to the statements on a 5-point scale varying from 1, *strongly agree,* to 5, *strongly disagree*; a lower score is less favorable.

Displeasure (min 10; max 30) and disability (min 12; max 36) were assessed with subscales of the Heart Patients Psychological Questionnaire (HPPQ) [32]. The subscales consist of 10 and 12 items, respectively, which can be rated on a 3-point scale (*yes, ?,* or *no*). Validity and reliability for the Dutch population have proven to be sufficient [29].

Two subscales of the Fear Survey Schedule (FSS) [33–35] were used to assess "fear of bodily injury" and "social anxiety". The subscales consist of 12 and 13 items, respectively, which are rated on a 5-point Likert scale (from 1, *not at all,* to 5, *extremely*). Validity and reliability for the Dutch population have proven to be good.

State and trait anxiety were assessed by means of the State-Trait Anxiety Inventory (STAI) [36]. Each subscale entails 20 items. Items are scored on a 4-point Likert scale (state: 1, *not at all,* to 4, *very much*; trait: from 1, *almost never,* to 4, *almost always*). Reliability of this questionnaire has proven to be good for the Dutch population [29].

By means of the Profile of Mood States (POMS) [37], depression, anger, fatigue, vigor, and tension were measured. The subscales consist, respectively, of 8, 7, 6, 5, and 6 items, which are rated on a 5-point Likert scale varying from 0, *not at all,* to 5, *extremely*. Each item reflects a mood state that might have occurred during the preceding days. The total score of all items gives an indication of the patient's peevishness. Reliability in the Netherlands has proven to be good [37].

The Maastricht Questionnaire (MQ) [38] was used to measure vital exhaustion. This self-report questionnaire consists of 21 items which can be rated on a 3-point scale (*yes, ?,* or *no*). The total score can range from 0 to 42. Validity and reliability have been demonstrated [38].

Statistical analysis

Before the research questions were addressed, missing data were estimated for those variables for which the percentage missing was less than 15%. If the percentage missing was larger than 15% the variable was removed from analysis. For estimating the values of the missing data, the predicted mean matching method was used [39]. Other variables were utilized as predictors for the missing variables. Regression analysis, with the backwards elimination procedure, was used for this purpose. Only predictor variables that were significant at the 0.05 level were maintained in the regression model.

For the psychological variables, the means including the 95% confidence intervals and the 95% confidence intervals for the difference were calculated. The statistical significance is defined as whether the 95%

Table II. – Psychological characteristics of noncardiac and cardiac patients

Determinant	Noncardiac		Cardiac			
	$\bar{x}_n$	95% CI	$\bar{x}_n$	95% CI	Cohen's δ	95% CI
HAD						
Anxiety	7.61	6.55 to 8.67	5.82	4.72 to 6.92	0.43	0.23 to 3.35*
Depression	4.94	4.12 to 5.76	4.19	3.25 to 5.13	0.23	−0.51 to 2.01
GHQ						
Psychopathology	2.97	2.25 to 3.69	2.23	1.37 to 3.09	0.29	−0.24 to 1.72
SCL-90						
Agoraphobia	9.70	8.72 to 10.68	8.66	7.76 to 9.56	0.29	−0.34 to 2.42
Anxiety	18.32	16.64 to 20.00	14.79	13.45 to 16.13	0.58	1.23 to 5.83*
Depression	26.82	24.46 to 29.18	23.62	21.42 to 25.82	0.36	−0.16 to 6.56
Somatization	25.32	23.18 to 27.46	20.96	19.10 to 22.82	0.56	1.38 to 7.34*
Obsessive-compulsive	16.20	14.80 to 17.60	14.04	12.74 to 15.34	0.41	0.16 to 4.16*
Interpersonal sensitivity	27.03	24.69 to 29.37	24.67	22.19 to 27.15	0.26	−1.14 to 5.86
Hostility	8.11	7.55 to 8.67	7.63	6.85 to 8.41	0.20	−0.44 to 1.40
Sleep problems	6.77	5.87 to 7.67	5.98	5.20 to 6.76	0.24	−0.47 to 2.05
Psychoneuroticism	150.73	140.79 to 160.70	131.92	122.00 to 141.80	0.49	4.31 to 33.31*
NQ						
Hyperventilation	22.34	19.74 to 24.94	14.61	12.01 to 17.21	0.78	3.93 to 11.53*
MEGAH						
Fear for own health	48.97	46.79 to 51.15	50.55	47.85 to 53.25	−0.17	−5.02 to 1.86
Medical information	10.33	9.43 to 11.23	11.51	10.51 to 12.51	−0.33	−2.54 to 0.18
Trust doctors	21.67	20.51 to 22.83	23.25	21.75 to 24.75	−0.32	−3.46 to 0.30
Illness belief	26.84	25.56 to 28.12	27.11	25.49 to 28.73	−0.05	−2.31 to 1.77
General health	39.43	37.29 to 41.57	35.97	32.63 to 39.31	0.35	−0.32 to 7.24
Hypochondria index	115.37	110.83 to 119.90	113.62	107.30 to 119.90	0.09	−5.83 to 9.33
HPPQ						
Disability	23.83	22.21 to 25.45	24.69	22.65 to 26.73	−0.13	−3.44 to 1.72
Displeasure	15.42	14.30 to 16.54	14.72	13.38 to 16.06	0.15	−1.04 to 2.44
FSS						
Fear bodily injury	19.72	18.18 to 21.26	17.88	16.18 to 19.58	0.30	−0.48 to 4.16
Social anxiety	21.93	19.61 to 24.25	19.63	17.45 to 21.81	0.26	−1.02 to 5.62
STAI						
State anxiety	36.67	33.89 to 39.45	36.98	34.00 to 39.96	−0.03	−4.47 to 3.85
Trait anxiety	37.64	35.14 to 40.14	35.98	33.10 to 38.86	0.16	−2.18 to 5.50

POMS						
Depression	3.46	2.48 to 4.44	3.13	1.81 to 4.45	0.08	−1.27 to 1.93
Anger	4.35	3.37 to 5.33	3.87	2.27 to 5.47	0.10	−1.30 to 2.26
Fatigue	5.94	4.64 to 7.24	5.30	3.80 to 6.8	0.12	−1.36 to 2.64
Vigour	11.44	10.50 to 12.38	11.91	10.81 to 13.01	−0.12	−1.93 to 0.99
Tension	5.57	4.37 to 6.77	4.72	3.50 to 5.94	0.18	−0.91 to 2.61
Total mood disturbance	28.31	24.41 to 32.21	25.87	20.53 to 31.21	0.14	−4.00 to 8.88
MQ						
Vital exhaustion	15.88	13.44 to 18.32	13.93	11.11 to 16.75	0.20	−1.81 to 5.71

*Significant difference.

Table III. – Differential qualities for psychological determinants unadjusted and adjusted for gender and age

	β		exp β		SE		95% CI	
Determinant	Unadj	Adj	Unadj	Adj	Unadj	Adj	Unadjusted	Adjusted
Anxiety SCL-90	1.40	1.15	4.04	3.17	0.53	0.56	1.40 to 11.64*	1.03 to 9.81*
Hypoventilation	1.33	1.00	2.72	2.72	0.42	0.49	1.64 to 8.65*	1.02 to 7.23*
Medical information	−0.62	−0.30	0.74	0.74	0.27	0.31	0.31 to 0.92*	0.40 to 1.36
Hypochondria index	0.58	0.62	1.86	1.86	0.29	0.34	1.01 to 3.19*	0.95 to 3.65
Disability	−0.93	−0.44	0.64	0.64	0.32	0.36	0.21 to 0.74*	0.31 to 1.34
State anxiety	−0.77	−1.20	0.30	0.30	0.34	0.43	0.25 to 0.91*	0.13 to 0.71

*Significant at 0.05 level.

confidence interval of the difference includes the value 0.0 or not [40]. In addition, the magnitude of the difference between the two groups of patients is calculated using Cohen's delta [41].

Furthermore, all psychological variables, age, and gender were examined by means of a logistic regression analysis. With this multivariate modeling, an estimation of the probability of an event (cardiac or noncardiac) occurring can be made. Standardized scores of the variables were used in the analyses, in order to be able to more easily compare estimated coefficients (β). In the analyses, the backward elimination procedure was used. Here too, only predictor variables that were significant at the 0.05 level were maintained in the model.

The remaining variables were consequently put into a second logistic regression analysis to be able to adjust the model for age and gender. This was done by calculating the predicted probability using the same estimation coefficients for the psychological variables, but setting them to zero for age and gender.

Thereafter, a receiver-operator characteristic (ROC) curve was constructed for data adjusted for age and gender. The logistic model calculated the predicted probability of being a noncardiac patient for all subjects, and subsequently sensitivity and specificity were calculated. In the ROC curve, the true-positive rate (sensitivity) is plotted against the false-positive rate (1 minus specificity), and the discriminative ability of a test is shown by the position of the full curve: the farther upward and to the left the curve lies in the figure, the more optimal the test. Thus, the area under the ROC-curve reflects the performance of the model, in the sense that a larger surface area reflects a higher performance [42].

Finally, the model was crossvalidated by randomly assigning patients into 5 strata, making sure that each stratum contained the same proportion of noncardiac/cardiac and male/female patients as the total group. A model was constructed based on 4 of these strata, and the probabilities of the 5th stratum were then estimated based on the constructed model. This procedure was repeated 5 times for each combination. Consequently, the estimated probabilities were tested against the probabilities of the model based on all patients, using a regression analysis. All data were analyzed using the SPSS/PC program [43].

RESULTS

Table I shows the general characteristics of the two patient groups. Consistent with findings in earlier studies [2–11], the patients in the noncardiac group were significantly younger (95% CI_{diff} −16.29 to −8.01), more often female ($p \geq 0.01$), single ($p<0.05$), and a larger proportion had never smoked ($p<0.01$).

Table II shows the psychological characteristics for both groups. There is a significant difference between the two groups for HAD-anxiety (95% CI_{diff}, 0.23 to 3.35), SCL-anxiety (95% CI_{diff}; 1.23 to 5.83), somatization (95% CI_{diff}, 1.38 to 7.34), obsessive compulsive behavior (95% CI_{diff}, 0.16 to 4.16), psychoneuroticism (95% CI_{diff}, 4.31 to 33.31), and hyperventilation (95% CI_{diff}; 3.93 to 11.53).

Using the backward elimination, logistic regression method of analysis with the criterion variable cardiac (*yes/no*) and all psychological variables as the predictor variables, SCL-anxiety ($\beta = 1.40$), hyperventilation ($\beta = 1.33$), medical information seeking ($\beta = -0.62$), hypochondria index ($\beta = 0.58$), disability ($\beta = -0.93$), and state anxiety ($\beta = -0.77$) remained in the model, giving an overall correct classification of 75.4%. Taking the a priori probability of 58.8% into account, the model shows an improvement of 40% [(75.4 − 58.8)/(100 − 58.8)*100%]. In order to adjust for age and gender, these variables, together with age and gender, were subsequently put into a second logistic regression analysis, using the enter method. The estimation coefficients adjusted for age and gender can be found in Table III. Only SCL-anxiety (95% CI, 1.03 to 9.81) and hyperventilation (95% CI, 1.02 to 7.23) significantly contributed to the predictability of noncardiac chest pain.

In Figure 1 the ROC-curve for the adjusted model is shown. The area under the adjusted ROC-curve is 0.79 (95% CI, 0.70 to 0.87), indicating a high performance.

Figure 2 shows the predicted probability acquired by crossvalidation and the predicted probability acquired with the total model. As can be seen from the regression lines for cardiac ($\beta = 0.97$, $p<0.01$) and noncardiac ($\beta = 0.96$, $p<0.01$), the model

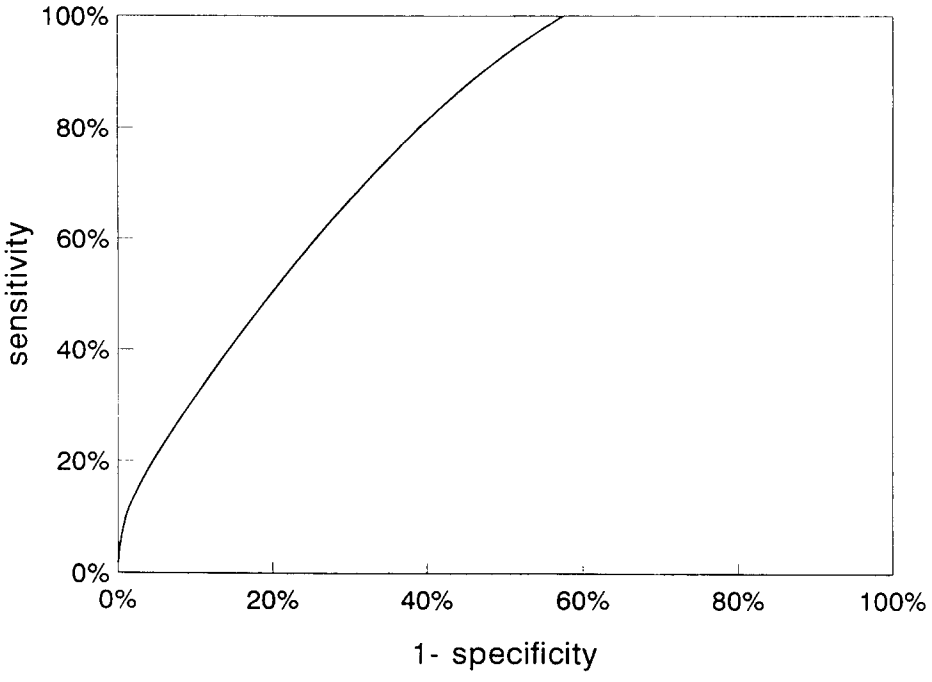

Fig. 1. Receiver Operator Characteristic Curve of the model, adjusted for age and gender.

acquired by crossvalidation highly resembles the model acquired with all of the data and is therefore stable. The intersections of the mean of the crossvalidated ($\bar{x}_{cad} = 0.34$, $SE_{cad} = 0.04$; $\bar{x}_{nca} = 0.76$, SEcad = 0.03) and total model ($\bar{x}_{cad} = 0.30$, $SE_{cad} = 0.04$; $\bar{x}_{nca} = 0.79$, $SE_{cad} = 0.03$) again clearly show the differentiation between noncardiac patients and patients with coronary artery disease.

DISCUSSION

In this study we have tried to construct a quantitative empirical-psychological model that can predict whether a patient's complaints of chest pain are of a cardiac or a noncardiac nature. Logistic regression analyses showed that, adjusted for age and gender, anxiety and hyperventilation are the foremost psychological variables that differentiate between the two groups. These findings are consistent with earlier studies [9, 44–50], in which noncardiac patients were found to suffer significantly more from hyperventilation and anxiety disorders than were cardiac patients. Moreyra and colleagues [49], for instance, found that of a group of 40 noncardiac patients, 91% of the women and 66% of the men suffered from hyperventilation. Similarly, results from a study by Bass and colleagues [9] suggested that hyperventilation might be one important mechanism involved in the production of noncardiac chest pain. In their study, 26% of the anxious or depressed patients suffered from hyperventilation. Almost half the patients with elevated anxiety and depression scores were hypocapnic at rest. In addition, patients with panic anxiety reported significantly more symptoms

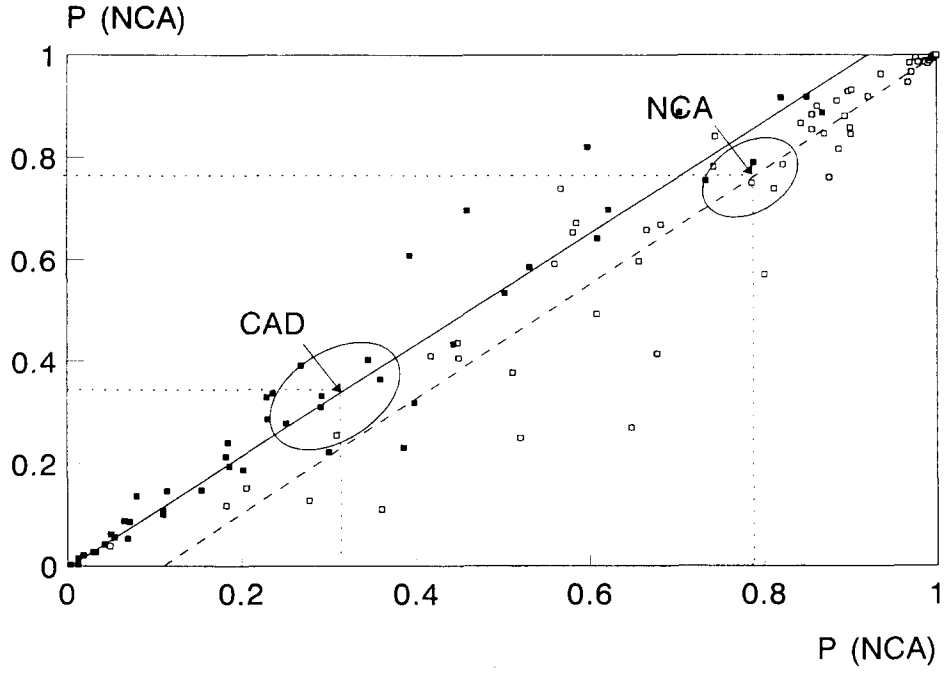

Fig. 2. The probability of being a noncardiac patient (NCA) for the total model set against the probability of being a noncardiac patient (NCA) for the model acquired by crossvalidation. (– –) depicts the regression line for the noncardiac patients (□). (—) depicts the regression line for the patients with coronary artery disease (■). The intersection of both means is surrounded by the standard error of the mean.

of breathlessness and other hyperventilation-related somatic complaints and developed hypocapnia on exercise more frequently than those without panic.

Additionally, however, our study has shown not only that noncardiac patients are more anxious and suffer more from hyperventilation, but also that in addition to age, gender, and questions regarding anxiety and hyperventilation, we were able to predict whether the complaints of patients with chest pain were cardiac or noncardiac, with an overall correct classification of 75.4%.

It should be clear, however, that the model constructed in this study should by no means replace diagnostic testing, but should be considered a helpful instrument, for doctors as well as for patients. In our view, all standard medical diagnostic testing should be done first to exclude coronary artery disease. Only if the cardiologic tests are inconclusive should the 26 questions significantly contributing to the model be utilized. In this way, one can trace the group of patients who are anxious and who hyperventilate and who are thus presumably noncardiac. Needless to say, standard diagnostic cardiologic testing, regardless of gender and age, is imperative. Applying the model in an early stage of diagnostic testing would most likely only enhance a policy of nonreferral, which is not desirable.

Once diagnosed as noncardiac, the patient can be adequately treated, as recent literature has shown [51–54]. Hegel and colleagues [54], for instance, successfully treated patients with noncardiac chest pain due to hyperventilation. The main focus of such therapies is on relaxation and breathing exercises.

We would also recommend that further research be conducted into the underlying characteristics of hyperventilation, such as the nature and/or origin of anxiety. Consideration might also be given to the variables for which both patient groups appeared to be different, even though these variables did not significantly contribute to the logistic regression model. These include such variables as somatization, obsessive compulsive behavior, and psychoneuroticism.

This study has shown that our model, in the form of 26 questions, can adequately distinguish cardiac from noncardiac chest pain patients. Implementation of the model, by completion of the short questionnaire, may help the treating cardiologist with the diagnosis of noncardiac chest pain in an early stage of diagnostic testing. This would be favorable because the noncardiac patient could be referred to a psychologist or psychiatrist more quickly for appropriate treatment. This will, in turn, most likely lead to a reduction in unnecessary medical consumption.

REFERENCES

1. Serlie AW, Erdman RAM, Passchier J, Trijsburg RW, Ten Cate FJ. Psychological aspects of noncardiac chest pain. Psychother Psychosom 1995;64:62–73.
2. Bass C, Wade C. Chest pain with normal coronary arteries: a comparative study of psychiatric and social morbidity. Psychol Med 1984;14(1):51–61.
3. Costa PT, Zonderman AB, Engel BT, Baile WF, Brimlow DL, Brinker J. The relation of chest pain symptoms to angiographic findings of coronary artery stenosis and neuroticism. Psychosom Med 1985;47(3):285–93.
4. Channer KS, Papouchado M, James MA, Rees JR. Anxiety and depression in patients with chest pain referred for exercise testing. Lancet 1985;2(8459):820–3.
5. Papanicolaou MN, Califf RM, Hlatky MA, et al. Prognostic implications of angiographically normal and insignificantly narrowed coronary arteries. Am J Cardiol 1986;58(13):1181–7.
6. Beitman BD, Basha I, Flaker G, DeRosear L, Mukerji V, Lamberti JW. Major depression in cardiology chest pain patients without coronary artery disease and with panic disorder. J Affect Disord 1987; 13(1):51–9.
7. Katon W, Hall ML, Russo J, et al. Chest pain: relationship of psychiatric illness to coronary arteriographic results. Am J Med 1988;84(1):1–9.
8. Cormier LE, Katon W, Russo J, Hollifield M, Hall ML, Vitaliano PP. Chest pain with negative cardiac diagnostic studies: relationship to psychiatric illness. J Nerv Ment Dis 1988;176(6):351–8.
9. Bass C, Chambers JB, Kiff P, Cooper D, Gardner WN. Panic anxiety and hyperventilation in patients with chest pain: a controlled study. Q J Med 1988;69(260):949–59.
10. Lantinga LJ, Sprafkin RP, McCroskery JH, Baker MT, Warner RA, Hill NE. One-year psychosocial follow-up of patients with chest pain and angiographically normal coronary arteries. Am J Cardiol 1988;62(4):209–13.
11. Herrmann C, Scholz KH, Kreuzer H. [Psychologic screening of patients of a cardiologic acute care clinic with the German version of the Hospital Anxiety and Depression Scale] Psychologisches Screening von Patienten einer kardiologischen Akutklinik mit einer deutchen Fassung der Hospital Anxiety and Depression (HAD)-Skala. Psychother Psychosom Med Psychol 1991;41(2):83–92.
12. Alexander PJ, Prabhu SG, Krishnamoorthy ES, Halkatti PC. Mental disorders in patients with noncardiac chest pain. Acta Psychiatr Scand 1994;89(5):291–3.
13. Mayou R, Bryant B, Forfar C, Clark D. Non-cardiac chest pain and benign palpitations in the cardiac clinic. Br Heart J 1994;72:548–53.
14. Proudfit WL, Bruschke AVG, Sones FM Jr. Clinical course of patients with normal or slightly or moderately abnormal coronary arteriograms: 10-year follow-up of 521 patients. Circulation 1980;62: 712–7.
15. Pasternak RC, Thibault GE, Savoia M, DeSanctis RW, Hutter AM. Chest pain with angiographically insignificant coronary arterial obstruction: clinical presentation and long-term follow-up. Am J Med 1980;68:813–7.
16. Ockene IS, Shay MJ, Alpert JS, Weiner BH, Dalen JE. Unexplained chest pain in patients with normal coronary arteriograms: a follow-up study of functional status. N Engl J Med 1980;303:1249–52.
17. Wilcox RG, Roland JM, Hampton JR. Prognosis of patients with chest pain ?cause. Br Med J 1981; 282:431–3.
18. Isner JM, Salem DN, Banas JS Jr, Levine HJ. Long-term clinical course of patients with normal

coronary arteriography: follow-up study of 121 patients with normal or nearly normal coronary arteriograms. Am Heart J 1981;102:645-53.
19. Bass C, Wade C, Hand D, Jackson G. Patients with angina with normal and near normal coronary arteries: clinical and psychosocial state 12 months after angiography. Br Med J Clin Res Ed 1983; 287(6404):1505-8.
20. Wielgosz AT, Fletcher RH, McCants CB, McKinnis RA, Haney TL, Williams RB. Unimproved chest pain in patients with minimal or no coronary disease: a behavioral phenomenon. Am Heart J 1984;108(1):67-72.
21. Kemp HG, Kronmal RA, Vlietstra RE, Frye RL. Seven year survival of patients with normal or near normal coronary arteriograms: a CASS registry study. J Am Coll Cardiol 1986;7(3):479-83.
22. Van Dorpe A, Piessens J, Willems JL, De Geest H. Unexplained chest pain with normal coronary arteriograms: a follow-up study. Cardiology 1987;74(6):436-43.
23. Faxon DP, McCabe CH, Kreigel DE, Ryan TJ. Therapeutic and economic value of a normal coronary angiogram. Am J Med 1982;73:500-5.
24. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67(6): 361-70.
25. Goldberg DP. The detection of psychiatric illness by questionnaire (vol 21). Oxford: Oxford University Press; 1972.
26. Ormel J, Koeter MW, Van den Brink W, Giel R. Concurrent validity of GHQ-28 and PSE as measures of change. Psychol Med 1989;19(4):1007-13.
27. Ormel J, Koeter MW, Van den Brink W. Measuring change with the General Health Questionnaire (GHQ): the problem of retest effects. Soc Psychiatry Psychiatr Epidemiol 1989;24(5):227-32.
28. Derogatis LR, Rickels K, Rock AF. The SCL-90 and the MMPI: a step in the validation of a new self-report scale. Br J Psychiatry 1976;128:280-9.
29. Evers A, Van Vliet-Mulder JC, Ter Laak J. [Documentation of tests and test reseach in the Netherlands] Documentatie van tests en testresearch in Nederland. Assen: Van Gorchum; 1992.
30. Van Dixhoorn J, Duivenvoorden HJ. Efficacy of Nijmegen Questionnaire in recognition of the hyperventilation syndrome. J Psychosom Res 1985;29(2):199-206.
31. Schmidt AJ, Lousberg R. [Health-attitude and hypochondrias: development of the MEGAH-scale] Gezondheidsattitude en hypochondrie. Ontwikkeling van de Maastrichter eigen gezondheidsattitude en hypochondrie-schaal. Gedrag en Gezondheid 1993;21(2):84-94.
32. Erdman RAM, Duivenvoorden HJ, Verhage F, Kazemier M, Hugenholtz PG. Predictability of beneficial effects in cardiac rehabilitation: a randomised clinical trial of psychological variables. J Cardiopulm Rehabil 1986;6: 206-13.
33. Wolpe J, Lang PJ. A fear survey schedule for use in behaviour therapy. Behav Res Ther 1964;2:27-30.
34. Arrindell WA. Dimensional structure and psychopathology correlates of the Fear Survey Schedule (FSS-III) in a phobic population: a factorial definition of agoraphobia. Behav Res Ther 1980;18(4): 229-42.
35. Arrindell WA, Zwaan EJ. [Phobic factors on the AZU-Fear Questionnaire (AZUV) and Wolpe and Lang's Fear Survey Schedule (FSS-III)] Fobische dimensies, de AZU-Vreesvragenlijst (AZUV) en Wolpe en Lang's Fear Survey Schedule (FSS-III). Ned Tijdschr Psychol 1982;37(4):225-39.
36. Van der Ploeg HM, Defares PB, Spielberger CD. [Manual for the State-Trait Anxiety Inventory (STAI)] Handleiding bij de Zelf-Beoordelings Vragenlijst (ZBV). Lisse: Swets & Zeitlinger; 1986.
37. Wald FDM, Mellenbergh GJ. [The shortened version of the Dutch translation of the Profile of Mood States] De verkorte versie van de Nederlandse vertaling van de Profile of Mood States. Ned Tijdschr Psychol 1990;45:86-90.38. Appels A, Hoppener P, Mulder P. A questionnaire to assess premonitory symptoms of myocardial infarction. 1987;17(1):15-24.
39. Little RJA. Missing-data adjustments in large surveys. J Bus Econ Stat 1988;6(3):287-96.
40. Gardner MJ, Altman DG. Statistics with confidence: confidence intervals and statistical guidelines. London: British Medical Journal; 1989.
41. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale: Erlbaum; 1988.
42. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143(1):29-36.
43. Statistical package for the social sciences. Chicago: SPSS-Inc.; 1990.
44. Chambers JB, Kiff PJ, Gardner WN, Jackson G, Bass C. Value of measuring end tidal partial pressure of carbon dioxide as an adjunct to treadmill exercise testing. Br Med J (Clin Res Ed) 1988;296(6632): 1281-5.
45. Chauhan A, Mullins PA, Taylor G, Petch MC, Schofield PM. Effect of hyperventilation and mental stress on coronary blood flow in syndrome X. Br Heart J 1993;69(6):516-24.
46. Mayou R. Invited review: atypical chest pain. J Psychosom Res 1989;33(4):393-406.
47. Bass C, Gardner WN, Jackson G. Abnormal breathing patterns associated with angina-like chest pain. Br J Clin Pract 1986;40(1):25-7.

48. Beck JG, Berisford MA, Taegtmeyer H. The effects of voluntary hyperventilation on patients with chest pain without coronary artery disease. Behav Res Ther 1991;29:611-21.
49. Moreyra AE, McGough WE, Hosler M, Kostis JB. Clinical improvement of patients with chest pain and normal coronary arteries after coronary arteriography: the possible role of hyperventilation syndrome. Int J Cardiol 1982;2:306-8.
50. Bass C, Chambers JB, Gardner WN. Hyperventilation provocation in patients with chest pain and a negative treadmill exercise test. J Psychosom Res 1991;35(1):83-9.
51. Fensterheim H, Wiegand B. Group treatment of the hyperventilation syndrome. Int J Group Psychother 1991;41(3):399-403.
52. Girotti LA, Crosatto JR, Messuti H, et al. The hyperventilation test as a method for developing successful therapy in Prinzmetal's angina. Am J Cardiol 1982;49(4):834-41.
53. Garssen B, Rijken H. Clinical aspects and treatment of the Hyperventilation syndrome. Behav Psychother 1986;14(1):46-68.
54. Hegel MT, Abel GG, Etscheidt M, Cohen-Cole S, Wilmer CI. Behavioral treatment of angina-like chest pain in patients with hyperventilation syndrome. J Behav Ther Exp Psychiatry 1989;20(1):31-9.