

Association of Panic Disorder and Panic Attacks with Hypertension

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PURPOSE: Previous studies of the association between hypertension and panic disorder were uncontrolled or involved small numbers of patients.

PATIENTS AND METHODS: We compared the prevalence of panic disorder and panic attacks in 351 patients with documented hypertension who were randomly selected from all hypertensive patients registered in one primary care practice with age- and gender-matched normotensive patients from the same practice and with hypertensive patients attending a hospital clinic. All three groups completed questionnaires for panic disorder based on standard criteria, as well as the Hospital Anxiety and Depression scale.

RESULTS: The prevalence of current (previous 6 months) panic attacks was significantly greater in primary care patients with hypertension (17%, $P < 0.05$) and hospital-based hypertensive patients (19%, $P < 0.01$) than in normotensive patients

(11%). Similar results were seen for lifetime panic attacks (35% versus 39% versus 22%; both P for comparisons with normotensive patients < 0.001). The prevalence of panic disorder was significantly greater in primary care patients with hypertension (13%) than normotensive patients (8%, $P < 0.05$). Anxiety scores were significantly higher in both hypertensive groups than in normotensive patients. Depression scores were significantly higher in hospital-based hypertensive patients than in the other two groups. The reported diagnosis of hypertension antedated the onset of panic attacks in a large majority of patients ($P < 0.01$).

CONCLUSIONS: Physicians caring for patients with hypertension should be aware of the significantly greater prevalence of panic attacks in these patients. *Am J Med.* 1999;107:310-316. ©1999 by Excerpta Medica, Inc.

Panic disorder was recognized as a clinical entity in 1980 (1), is common in the population (2-4), and even more common in hospital-based clinics (5, 6). An association between panic disorder and hypertension has been suggested. Hypertension was more common in patients with panic disorder than in controls in two small studies (7, 8). In an uncontrolled study of African-Americans with hypertension, at least 36% had panic attacks, and 10% fulfilled the diagnostic criteria for panic disorder (9). Recently, Kaplan described anxiety-related hyperventilation—a common feature of panic attacks—in a prospective but uncontrolled study of patients referred to a tertiary care clinic with hypertension that was difficult to manage (10). Of 300 consecutive patients, 35% had symptoms suggestive of hyperventilation, and in 29% of the 300 the symptoms were repro-

duced by forced hyperventilation. He suggested that hyperventilation made blood pressure control more difficult and noted that episodic hypertension provoked by hyperventilation led to multiple, often unhelpful, investigations. Others (11, 12) have described episodic hypertension related to panic attacks in patients with hypertension. Hyperventilation has a significant pressor effect, causing an increase in blood pressure of about 9 mm Hg in normotensive subjects (13).

Like Kaplan (10) and others (14-16), we suspected that panic might contribute to refractory hypertension. We previously studied patients with refractory hypertension attending a hospital-based clinic, and confirmed that they had a substantial prevalence of panic attacks (33%) and panic disorder (12%) (17). Panic attacks (39%) and panic disorder (14%) were also common in patients with well-controlled hypertension (17). The prevalence of panic disorder was greater in both groups of hypertensive patients than anticipated from population studies (2-4). However, we could not determine whether the prevalence of panic disorder was unique to hospital-based clinic patients as a consequence of selective referral. The purpose of the present study was to determine whether there is a relation of panic attacks and panic disorder to hypertension, and if so, whether this is true for all hypertensive patients.

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Manuscript submitted January 6, 1999, and accepted in revised form June 23, 1999.

MATERIAL AND METHODS

Study Design

We used self-administered questionnaires to measure the prevalence of panic disorder, panic attacks, anxiety, and depression in hypertensive patients in primary care, hypertensive patients attending a hospital-based clinic, and normotensive patients matched for age and gender from the same primary care practice. Recruitment from primary care was chosen to represent a population-based sample, as a substantial proportion of residents in the area studied were registered with a general practitioner.

Patients

Primary care hypertensive patients. A random sample of 351 patients was selected from all hypertensive patients who were registered in a single general practice in February 1996. Hypertensive patients had been identified by systematic screening and were identified on computerized problem lists. All patients were on antihypertensive treatment or had a recent blood pressure measurement 160/90 mm Hg.

Primary care normotensive patients. For each hypertensive patient, one patient was identified from the same practice register who did not have hypertension or blood pressure 160/90 mm Hg on the computerized record. These patients were matched for age (same decade) and gender, and had the next highest registration number. Two additional (reserve) normotensive patients were identified by subsequent registration numbers. Those on antihypertensive medications were excluded unless the drugs were for other conditions (eg, diuretics for heart failure, beta-blockers for angina); they were replaced by reserve patients. Patients with no blood pressure noted in the computerized records were included if blood pressure was recorded below 160/90 mm Hg within 5 years in the written records. Forty patients had no blood pressure record within 5 years, and were asked to consent to blood pressure measurement after completion of the questionnaires. Four were unwilling, 1 died before measurement, and 6 had blood pressure >160/90 mm Hg. These 11 patients were excluded without replacement.

Hospital-based clinic hypertensive patients. Hospital-based clinic hypertensive patients were matched with the primary care hypertensive patients for age (same decade) and gender. We randomly selected 520 patients with hypertension from all those attending the Sheffield Hypertension Clinic between January and September 1995. Eighty-two who had participated in another study on panic disorder (17) were excluded. From the 438 remaining patients, each primary care hypertensive patient was matched to a hospital-based hypertensive patient by age,

Table 1. Criteria for Panic Attacks and Panic Disorder

A *panic attack* is a discrete period of intense fear or discomfort involving at least four of the following symptoms:

1. Shortness of breath (dyspnea) or smothering sensations
2. Dizziness, unsteady feelings, or faintness
3. Palpitations or accelerated heart rate (tachycardia)
4. Trembling or shaking
5. Sweating
6. Choking
7. Nausea or abdominal distress
8. Depersonalization or derealization
9. Numbness or tingling sensations (paresthesias)
10. Hot flushes or chills
11. Chest pain or discomfort
12. Fear of dying
13. Fear of going crazy or doing something uncontrolled

A diagnosis of *panic disorder* requires either four attacks within a 4-week period, or one or more attacks followed by at least a month of persistent fear of having another attack. Some attacks must be spontaneous, and must have developed suddenly and increased in intensity within 10 minutes of the onset of the first symptom. There must be no medical or drug-related cause.

gender, and next highest registration number. Three hundred and forty-two hospital-based hypertensive patients were eventually matched to the 351 primary care patients with hypertension.

Questionnaires for Panic, Anxiety and Depression

All three groups were mailed a covering letter, a questionnaire for panic attacks and panic disorder (17), a Hospital Anxiety and Depression Scale (18), and supplementary questions on medications and the age at diagnosis of hypertension. Those not responding within 2 months were sent a second questionnaire; they were deemed nonresponders if they had not replied within a further 6 weeks. The questionnaire for panic attacks and panic disorder is based on the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (*DSM-III-R*) diagnostic system (19) and derived from the relevant section of the Structured Clinical Interview for *DSM-III-R* (20). It provides information on the severity and frequency of attacks, panic symptoms experienced, whether attacks were ever spontaneous, whether an attack had occurred in the last 6 months, and age at the first attack. The Hospital Anxiety and Depression Scale (18) is a self-administered instrument that provides separate scores for anxiety and depression. For both subscales, a score of 11 or more indicates a high probability of suffering from the disorder.

Definitions

A *panic attack* was defined as a discrete period of intense fear or discomfort during which 4 or more of 13 panic

Table 2. Characteristics and Response Rates of the Three Groups of Patients

	Primary Care Normotensive Patients	Primary Care Patients with Hypertension	Hospital-based Clinic Patients with Hypertension
	Number (percent) or mean \pm SD		
Questionnaires sent	350	351	342
Questionnaires returned and analyzable	271 (78%)	312 (89%)	307 (90%)
Male gender	112 (41%)	129 (41%)	135 (44%)
Age (years)	67 \pm 12	67 \pm 12	67 \pm 12
Systolic blood pressure (mm Hg)	134 \pm 13	149 \pm 17	159 \pm 24
Diastolic blood pressure (mm Hg)	76 \pm 8	83 \pm 8	86 \pm 11
Number of antihypertensive agents	—	1.4 \pm 0.7	2.4 \pm 1.0

symptoms (Table 1) were experienced. We defined panic attacks as current if the last one occurred within 6 months. Spontaneous panic attacks occurred in the absence of a recognized stimulus or situation (eg, public speaking). The severity of the worst attack was rated on a five-point scale, from very mild to unbearable; moderate, severe, or unbearable attacks were considered separately from mild or very mild attacks. The diagnosis of *panic disorder* required that attacks peaked within 10 minutes, at least one was spontaneous, at least four panic attacks occurred per month or one attack was followed by a month of persistent fear of further attack, and medical or drug related causes were absent. These criteria resemble those of the *DSM-III-R* (19).

Statistical Analysis

We estimated that a sample size of 280 patients in each group would detect a 7% difference in the prevalence of panic disorder (13% in hypertensive patients and 6% in normotensive patients) with a power of 80% at an alpha of 0.05 (two-sided) (21). Anticipating that 20% of patients would fail to respond, we aimed for 350 patients in each group. Groups were compared with the chi-square test or Student's *t* test. The temporal relation between the reported onset of panic and the reported diagnosis of hypertension was examined using the sign test. It was envisaged that matching would be disrupted substantially by nonrespondents, as had occurred previously (17), and we specified in advance that the main analysis would use unpaired methods. Analyses of matched pairs were performed to confirm the findings in unmatched analyses.

RESULTS

Of the 1,043 questionnaires sent, 916 (88%) were returned. Twenty-five respondents were excluded (11 normotensive patients [see Methods] and 14 with uninterpretable or invalid responses). The 891 analyzable responses included 313 primary care patients with hypertension (89% response), 271 normotensive patients

(77% response), and 307 hospital-based hypertensive patients (90% response). There were 244 age- and gender-matched pairs of respondents for the primary care hypertensive and normotensive groups, 240 matched pairs for the hospital-based clinic and primary care normotensive groups, and 276 matched pairs for the primary care hypertensive and hospital-based hypertensive groups.

As expected, mean age and gender were similar in the three groups, and primary care hypertensive patients had greater mean blood pressure than normotensive patients (Table 2). Hospital-based clinic hypertensive patients had a greater mean blood pressure and were taking more treatment than the primary care hypertensive patients.

Panic Attacks and Panic Disorder

The lifetime prevalence of panic attacks in the primary care hypertensive patients was 35%, compared with 22% in normotensive patients ($P < 0.001$) (Figure). The lifetime prevalence of panic attacks in hospital-based clinic hypertensive patients was 39%, also significantly greater than in normotensive patients ($P < 0.001$). The prevalences of panic attacks in hospital-based clinic and primary care hypertensive patients were not significantly different.

The prevalence of spontaneous panic attacks was significantly greater in primary care hypertensive patients (30%) than in normotensive patients (19%, $P < 0.01$). The prevalence in hospital-based clinic hypertensive patients was 31%, significantly greater than in normotensive patients ($P < 0.001$), and similar to the primary care hypertensive patients. The severity of panic attacks was rated as moderate or worse by 22% of primary care hypertensive patients and 12% of normotensive patients ($P < 0.01$). Attacks rated moderate or worse had a prevalence of 28% among the hospital-based clinic hypertensive patients, again significantly greater than in normotensive patients ($P < 0.001$), and similar to that in primary care hypertensive patients.

The prevalence of current panic attacks was 11% in normotensive patients and 17% in primary care hyper-

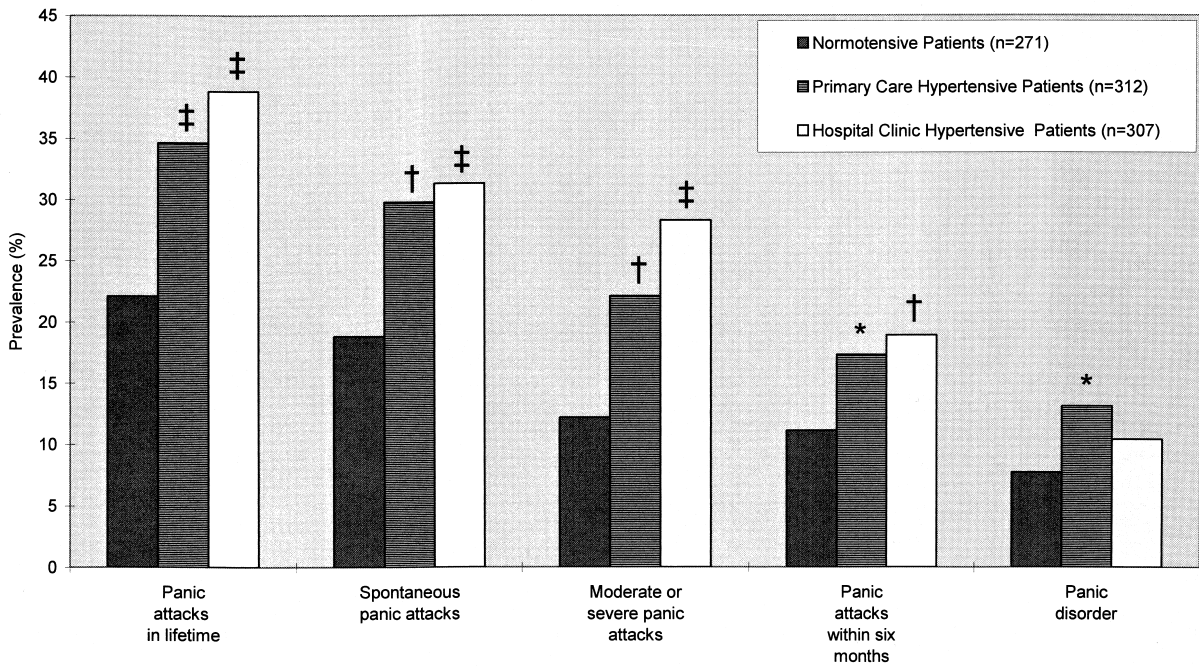


Figure. Prevalence of panic attacks and panic disorders in the three groups of patients. * $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$ compared with normotensive patients.

tensive patients ($P < 0.05$). The prevalence in hospital-based clinic hypertensive patients (19%) was also significantly greater than in normotensive patients ($P < 0.01$). The difference between primary care and hospital-based hypertensive patients was not significant.

The criteria for the diagnosis of panic disorder were fulfilled by 13% of primary care hypertensive patients and 8% of normotensive patients ($P < 0.05$). The prevalence in hospital-based clinic patients (10%) did not differ significantly from that in normotensive patients or primary care hypertensive patients. Matched pair analyses confirmed all of the findings in the unmatched analyses.

Temporal Relation of Panic and Hypertension

Of the 197 hypertensive patients in both groups who had experienced panic attacks and who recalled their ages at the first panic attack and when hypertension was diagnosed, the diagnosis of hypertension preceded panic attacks in 95 patients, panic attacks preceded the diagnosis of hypertension in 53 patients, and the ages coincided for 49 patients. A diagnosis of hypertension preceded panic attacks more often than vice-versa ($P < 0.01$, sign test).

Anxiety and Depression

Anxiety scale scores were significantly higher in both groups of hypertensive patients than in normotensive patients ($P < 0.05$) (Table 3). The difference between primary care and hospital clinic hypertensive patients was not significant. Depression scores were significantly higher in hospital-based clinic hypertensive patients than

in primary care hypertensive patients ($P < 0.05$) and primary care normotensive patients ($P < 0.01$). The difference between the two primary care groups was not significant. The matched analysis confirmed these findings, except that the difference in depression scores between hospital-based clinic and primary care hypertensive patients was no longer statistically significant.

Relation of Panic Attacks to Age and Gender

The excess prevalence of panic attacks in hypertensive patients was observed in both men ($P < 0.01$ for lifetime, $P < 0.05$ for current panic attacks) and women ($P < 0.001$ for lifetime, $P < 0.05$ for current panic attacks). In relative terms, the excess was somewhat larger in men (2.8-fold for lifetime panic) than in women (1.6-fold for lifetime panic). In absolute terms, lifetime and current panic attacks were more common in women than men in all three groups. The prevalence of panic symptoms was not related to age in either hypertensive group. In normotensive patients, the prevalence of lifetime panic attacks was significantly greater in patients aged 65 years or less than in patients aged 66 to 75 years.

Antihypertensive Drug Use and Panic Disorder

Among patients with hypertension, there were no significant differences in antihypertensive drug use when patients with panic disorder were compared with patients who had never experienced panic attacks for either diuretics (73% versus 76%), beta-blockers (42% versus 46%), angiotensin-converting enzyme inhibitors (32%

Table 3. Hospital Anxiety and Depression Scores in the Three Groups of Patients

	Normotensive Patients (n = 271)	Primary Care Patients with Hypertension (n = 312)	Hospital-based Clinic Patients with Hypertension (n = 307)	Primary Care Hypertensive Patients—Normotensive Patients	Hospital-based Clinic Hypertensive Patients—Normotensive Patients	Primary Care Hypertensive Patients—Hospital Clinic Hypertensive Patients
Anxiety score	6.0 ± 4.4	6.8 ± 4.3	7.0 ± 4.3	+0.8 (+0.01 to +1.5)*	+1.0 (+0.2 to +1.7)*	-0.2 (-0.9 to +0.5)
Depression score	4.6 ± 4.0	4.9 ± 3.7	5.7 ± 4.0	+0.3 (-0.3 to +1.0)	+1.1 (+0.4 to +1.7)†	-0.8 (-1.4 to -0.1)*
				Difference (95% Confidence Interval)		

* $P < 0.05$.

† $P < 0.01$.

versus 31%), or calcium channel blockers (29% versus 31%).

DISCUSSION

This study supports previous suggestions (7–12,14,17) that there is an association between panic symptoms and hypertension. Hypertensive patients in primary care had a significantly greater prevalence of panic than did normotensive patients. This was true for lifetime, current, spontaneous, and moderate to severe panic attacks, and for symptoms fulfilling the criteria for panic disorder. Hypertensive patients attending a hospital-based clinic also had a substantial prevalence of panic attacks, suggesting that the previously reported prevalence of panic attacks and panic disorder in these patients (17) is not a consequence of selective referral. Bias is unlikely to account for these findings. Although some normotensive subjects were excluded because they declined a blood pressure check, the number excluded (4 of 275 patients) was too small to have a substantial influence.

In this study, panic attacks and panic disorder were assessed by a standardized questionnaire. The remarkable agreement among studies of the prevalence of panic attacks and panic disorder in hypertensive patients appears to be independent of the method used to identify the psychological disorder. Panic attacks have been reported in 35% of patients in primary care (this study), 39% of hospital-based clinic patients (this study), 33% of patients with refractory hypertension (17), 39% of patients with controlled hypertension (17), and 36% of African-Americans with hypertension (9). Furthermore, anxiety-related hyperventilation and other symptoms of panic were reported in 35% of patients with treatment-resistant hypertension (10). The prevalence of panic disorder varied from 10% to 14% in these studies.

In this study, panic symptoms were more common in both men and women with hypertension. In absolute terms, however, panic disorder was much more common in women than in men, whether or not they had hypertension. The greater prevalence of panic symptoms in women mirrors Kaplan's description of anxiety-related hyperventilation in 45% of women and 16% of men with hypertension (10).

Although panic disorder has features in common with generalized anxiety disorder, they are different entities. We also found an association between anxiety and hypertension that was significant both in primary care and hospital-based hypertensive patients. However, the mean difference in anxiety scores was less than one point between hypertensive and normotensive patients. Patients with any form of anxiety disorder may be more likely to have hypertension (22), and high levels of anxiety may be an independent predictor of subsequent hypertension

(23,24). A link between depression and hypertension has been suggested (24,25), but our findings were less clear cut. Hypertensive patients attending a hospital-based clinic had significantly higher depression scores than patients in primary care. There may be selective referral of hypertensive patients with depression to hospital clinics, or hypertension that is severe or difficult enough to require referral to a specialist may cause depression.

Why are panic symptoms and hypertension associated? We can suggest several possible mechanisms. Panic symptoms could increase the chance of hypertension being diagnosed through greater medical contact. This is unlikely to explain our findings, however, because ascertainment of hypertension was nearly complete in the primary care patients studied. Panic symptoms may prompt the initiation of antihypertensive treatment that otherwise might be withheld. If so, the association would be between panic and treated hypertension, and not with hypertension per se. Some common factor may relate to both panic and hypertension. Pheochromocytoma causes symptoms akin to panic and is an obvious candidate (26), but it is too rare to explain the association. Other factors common to panic and hypertension might be comorbidity, such as the vascular complications of hypertension, or subjective side effects of antihypertensive drugs. An intriguing possibility is that panic may actually cause hypertension, as panic attacks (11,12) and hyperventilation (13) have a distinct pressor effect. Finally, the diagnosis or treatment of hypertension may cause panic symptoms through a "labelling" effect. Hypertensive patients with panic attacks reported that their hypertension was diagnosed before the onset of panic significantly more often than the reverse sequence. This evidence is weak because it depends on recall, which may be unreliable. Nevertheless, labelling people as hypertensive can have an important adverse effect on psychological well-being (27).

What are the practical implications of these observations? It has been suggested that panic and other psychiatric disorders may be important contributory factors in whether hypertension is resistant to therapy (10,14). However, we did not confirm this possibility in our previous study that compared patients with resistant and treatable hypertension (17). Nevertheless we believe that Kaplan (10) is correct to suggest that panic symptoms make management of hypertension more difficult. Patients and doctors alike often attribute panic symptoms incorrectly to hypertension itself, or to antihypertensive therapy, so that drugs are discontinued inappropriately. The symptoms of panic commonly prompt unnecessary investigations (6,10) or referral to other specialties. Above all, panic disorder is unpleasant, readily amenable to treatment (28), and present in 10% to 13% of hypertensive patients. It ought to be identified and managed appropriately. In the Kaplan (10) series, the true cause of

the symptoms had been recognized in fewer than 10% of patients.

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