

Panic Attacks May Be an Independent Risk Factor for Cardiovascular Disease

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October 8, 2007 — A new analysis of data from a substudy of the Women's Health Initiative Observational Study suggests panic attacks may be an independent risk factor for cardiovascular morbidity and mortality.

Postmenopausal women in this study who reported having had a panic attack in the previous 6 months had a 4-fold increased risk for coronary heart disease (CHD) and a 3-fold increased risk for the combined endpoint of CHD and stroke for approximately 5 years of follow-up. The risk persisted after controlling for known cardiovascular risk factors and was similar in magnitude to other established risk factors.

"Although it was quite a significant increase in relative risk, the absolute numbers of women who had those outcomes was still relatively small," first author Jordan W. Smoller, MD, ScD, from Harvard Medical School and Massachusetts General Hospital in Boston, told *Medscape Psychiatry*.

"On the clinical side, this may identify a subgroup of women who warrant additional monitoring or assessment of their overall cardiac risk," Dr. Smoller said.

The report appears in the October issue of the *Archives of General Psychiatry*.

Depression, Phobic Anxiety, Panic Attacks

The new findings related to panic attacks are consistent with previous studies that have implicated negative emotional states and psychological symptoms in cardiovascular outcomes, Dr. Smoller said. For example, previous work has shown an association between depression and phobic anxiety and cardiovascular morbidity and mortality. "This is the first large prospective study to look at panic attacks in particular," he said.

Panic attacks involve sudden episodes of fear, anxiety, or extreme discomfort accompanied by 4 or more associated cognitive or autonomic symptoms, the study authors write. Panic attacks may occur sporadically or as a feature of several anxiety disorders, including panic disorder, social anxiety disorder, and specific phobias.

The present report, called the Myocardial Ischemia and Migraine Study (MIMS), is an ancillary study of the Women's Health Initiative Observational Study, an ongoing, multicenter prospective survey of risk factors for heart disease, cancer, fractures, and other causes of morbidity and mortality among 93,676 postmenopausal women.

MIMS was carried out at 10 of the 40 centers that participated in the Women's Health Initiative. Included were 3369 community-dwelling, generally healthy postmenopausal women aged 51 to 83 years. They were enrolled between 1997 and 2000 and completed a questionnaire about the occurrence of panic attack within the last 6 months.

The study authors report that 10% of women reported full-blown panic attacks. "It was surprising how common it was," Dr. Smoller said. "We had a somewhat broad definition of panic attacks, but previous studies had suggested the frequency would not be as high as 10%, but closer to 1% or 2%."

A 6-month history of panic attack was associated with a 4-fold increase in CHD, as well as an increased risk for the combined endpoint of CHD and stroke. After excluding those with a history of cardiovascular and cerebrovascular events, there was still an increased risk for all-cause mortality associated with panic attacks.

Table. MIMS: Risk for Cardiovascular Outcomes Associated With Panic Attack in the Previous 6 Months*

Endpoint	Hazard Ratio	95% CI
Coronary heart disease	4.20	1.76 - 9.99
Coronary heart disease and stroke	3.08	1.60 - 5.94
All-cause mortality	1.75	1.04 - 2.94

*MIMS indicates Myocardial Ischemic and Migraine Study; CI, confidence interval.

"The study doesn't really address whether this is a direct effect of anxiety on the cardiovascular system or whether panic attacks were a proxy for some other risk factor, although we controlled for known risk factors and it did not seem due to those," Dr. Smoller said. It is possible that because panic attacks have symptoms that overlap with cardiovascular and pulmonary disease, these symptoms may represent unrecognized symptoms of underlying disease, he noted.

However, there is evidence from previous studies that physiologic aspects of panic attacks have effects on the cardiovascular system. For example, panic attacks can reduce heart rate variability. Stress hormones that accompany panic attacks can have adverse effects on the cardiovascular system or increase cardiac ischemia, "but again, at this level, it's just a hypothesis because we were not able to look directly at that," Dr. Smoller said.

"We also don't know from this study whether treating panic has any effect on cardiac outcomes, and that would obviously be an important question for follow-up studies," he noted.

Finally, Dr. Smoller pointed out that because the question asked was simply whether these women had had a panic attack in the last 6 months, those who said they had would include both those with a single panic attack and those with chronic, severe, recurrent panic disorder. "So we can't look at the effect of frequency or severity of the panic in the association here. For example, panic attacks can occur as part of a number of psychiatric conditions including anxiety disorders and depression, or sometimes be related to medical conditions, or substances, or medications, and we couldn't really tease that apart."

The Women's Health Initiative program is funded by the National Heart, Lung, and Blood Institute, US Department of Health and Human Services. Glaxo Wellcome (now GlaxoSmithKline) has funded the MIMS. Dr. Smoller has disclosed receiving honoraria from Hoffman-La Roche, Inc; has served on an advisory board for Roche Diagnostics Corp; and may receive an honorarium for a lecture he may give to an Eli Lilly and Co Advisory Board in the near future. The complete list of disclosures is available in the original article.

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Learning Objectives for This Educational Activity

Upon completion of this activity, participants will be able to:

1. Describe the association between full-blown panic attacks and myocardial infarction, stroke, and all-cause mortality in postmenopausal women.
2. Describe the association between limited-symptom panic attacks and all-cause mortality in postmenopausal women.

Clinical Context

The MIMS study population was part of a larger Women's Health Initiative Observation Study described in the February 1998 issue of *Controlled Clinical Trials*. According to results from the MIMS reported by Smoller and colleagues in the September 22, 2003, issue of the *Archives of Internal Medicine* and the November-December 2006 issue of *Psychosomatic Medicine*, 18% of postmenopausal women reported full-blown or limited-symptom panic attacks in the previous 6 months, and full-blown panic attacks were associated with ischemic and nonischemic chest pain.

Panic attack refers to an attack of sudden fear, anxiety, or extreme discomfort. A full-blown attack is accompanied by at least 4 symptoms of panic attack, whereas a limited-symptom attack is accompanied by 1 to 3 symptoms of panic attack.

This prospective, cohort survey of the MIMS study population evaluates whether panic attacks in postmenopausal women are associated with myocardial infarction, stroke, and all-cause mortality.

Study Highlights

- 3369 postmenopausal women aged 51 to 83 years (mean age, 65.9 years) were enrolled.
- Exclusion criteria were enrollment in hormone therapy or diet modification clinical trials, expected survival of less than 3 years because of illness, and substance use or depression preventing participation in the study.
- Subjects answered 2 screening questions about "sudden attack of feeling frightened, anxious, or extremely uncomfortable" and "sudden episode of rapid or irregular heartbeats" leading to questions about 12 panic attack symptoms in the past 6 months.
- 330 women had full-blown panic attacks.
- 273 women had limited-symptom panic attacks.
- 126 women with indeterminate panic attacks, defined as only rapid or irregular heartbeats and at least 4 symptoms of panic attack, were excluded from the analysis.
- 2640 women in the comparison group had neither full-blown nor limited-symptom panic attacks.
- Depression was assessed with use of 6 items about depressive symptoms in the past 2 weeks from the Center for Epidemiologic Studies Depression Scale and 2 items about depressive symptoms in the past 2 years from the Diagnostic Interview Schedule.
- Primary outcome measures of fatal or nonfatal myocardial infarction, stroke (acute onset of neurologic deficit resulting from obstruction or rupture of arterial system lasting > 24 hours or demonstrated by computed tomography or magnetic resonance imaging), combined CHD or stroke, and all-cause mortality were assessed annually for a mean follow-up of 5.3 years.
- Self-reported outcome measures were confirmed by records.
- The full-blown panic attack group vs the no panic attack group had younger age (49% aged 50 - 59 years vs 46% aged 60 - 69 years), different race composition (9% vs 18% Asian; 8% vs 5% black; 4% vs 2% Hispanic), lower education (44% post-high school vs 48% college degree), lower income, more current vs past smoking (10% vs 5%), more alcohol use in the past vs present alcohol use (26% past drinker vs 24% present drinkers, 1 - 6 drinks per week), higher body mass index, higher likelihood of diabetes treatment (6% vs 3%), depression (31% vs 7%), history of CHD (8% vs 3%), history of CHD or stroke (9% vs 4%), and atrial fibrillation (7% vs 3%).
- Statistical analysis took into account variables that differed between the full-blown panic attack group and the no panic attack group and variables known to be linked to cardiovascular outcomes (hormone use, hypercholesterolemia requiring medication, hypertension status, and physical activity).
- CHD (fatal and nonfatal myocardial infarction) occurred in 41 women: 1.1% in the no panic attack group vs 1.5% in the limited-symptom panic attack group vs 2.4% in the full-blown panic attack group.
- Stroke occurred in 40 women: 1.1% in the no panic attack group vs 1.8% in the limited-symptom group vs 1.8% in the full-blown panic attack group.
- All-cause mortality occurred in 147 women: 4.2% in the no panic attack group vs 5.5% in the limited-symptom group vs 6.7% in the full-blown group.

- Full-blown panic attack was associated with CHD (hazard ratio [HR], 4.20; 95% confidence interval [CI], 1.76 - 9.99), combined CHD or stroke (HR, 3.08; 95% CI, 1.60 - 5.94), and all-cause mortality (HR, 1.75; 95% CI, 1.04 - 2.94).
- Full-blown panic attack and risk for stroke alone were not significant.
- Limited-symptom panic attack and risk for combined CHD or stroke had an HR of 2.05 (95% CI, 0.99 - 4.23).
- Limited-symptom panic attack and risks for stroke alone, CHD alone, and all-cause mortality were not significant.
- There was no relationship between depression and death or combined CHD or stroke.

Pearls for Practice

- Postmenopausal women with full-blown panic attacks have an almost 4-fold increased risk for fatal or nonfatal myocardial infarction, almost 3-fold increased risk for combined CHD and stroke, 1.75-fold increased risk for all-cause mortality, and no significant association with the risk for stroke alone.
- Postmenopausal women with limited-symptom panic attacks have an increased HR of 2.05 for combined CHD and stroke but no significant increase in the risk for CHD alone, stroke alone, or all-cause mortality.