# Prevalence and Predictors of Depression and Anxiety Among Survivors of Myocardial Infarction Due to Spontaneous Coronary Artery Dissection

Jackson J. Liang, DO; Marysia S. Tweet, MD; Sarah E. Hayes, BA; Rajiv Gulati, MD, PhD; Sharonne N. Hayes, MD

■ **PURPOSE:** Depression and anxiety after myocardial infarction (MI) are common and associated with increased morbidity and mortality. The epidemiology and pathophysiology of MI due to spontaneous coronary artery dissection (SCAD) differs substantially from atherosclerotic MI, and rates of mental health comorbidities after SCAD are unknown. We aimed to determine the prevalence and predictors of depression/anxiety in SCAD survivors.

■ **METHODS:** In this cross-sectional study, 158 SCAD survivors (97% women; mean age, 45.5 ± 9.3 years) were screened for depression/anxiety via surveys, including the Patient Health Questionnaire Depression Scale (PHQ-9) and Generalized Anxiety Disorder 7-Item Scale (GAD-7), a mean 3.7 ± 4.7 years after SCAD. Comorbidities and environmental, socioeconomic, and clinical cardiovascular characteristics were obtained from the surveys.

■ **RESULTS:** Since their initial SCAD MI, 51 (33%) patients had received treatment with medications or counseling for depression and 57 (37%) for anxiety. When surveyed, 46 (31.7%) were taking antidepressant or anxiolytic medications. Overall, mean PHQ-9 (4.1) and GAD-7 (4.7) scores suggested borderline mild depression/anxiety (normal range: 0-4). Younger age was associated with higher PHQ-9 ($P = .04$) and GAD-7 ($P = .02$) scores. The 19 (12%) patients with peripartum SCAD had higher mean PHQ-9 (6.7 vs 3.7; $P < .0005$) and GAD-7 (8.1 vs 4.3; $P = .003$) scores. Patients treated with percutaneous coronary intervention had lower PHQ-9 (1.5; $P = .02$) and GAD-7 (2.4; $P = .004$) scores.

■ **CONCLUSIONS:** Symptoms of depression/anxiety are common in patients with MI due to SCAD, particularly younger women and those with peripartum SCAD. The PHQ-9 and GAD-7 assessments may detect depression/anxiety in SCAD survivors who do not self-report these disorders, suggesting a role for routine screening in these patients.

Depression and anxiety are common following myocardial infarction (MI), particularly in young women, and may adversely affect quality of life as well as short- and long-term survival.[1,2] Spontaneous coro-nary artery dissection (SCAD) is an increasingly rec-ognized cause of acute MI that most frequently afflicts younger women with few cardiovascular risk factors.[3] Unlike MI due to acute plaque rupture in the

setting of coronary artery atherosclerosis, individuals with SCAD rarely have significant coronary artery disease. Although the underlying pathophysiology and etiology of SCAD remains undefined, it has been associated with peripartum status, underlying systemic vasculopathies such as fibromuscular dysplasia, and several genetic mutations. Unlike in MI due to atherosclerosis, optimal acute and long-term management of SCAD is not well established, and to date, no effective therapies to prevent recurrence have been identified. Because of these uncertainties, high and unpredictable recurrence risk, and female predominance,[3] SCAD patients may be predisposed to develop depression and anxiety. To our knowledge, these disorders have not been examined in patients with MI due to SCAD. The aim of our study was to quantify the prevalence of depression and anxiety in SCAD survivors and to identify medical, environmental, or socioeconomic factors that may predict their development.

## METHODS

This cross-sectional study was approved by the Mayo Foundation institution review board, and a signed, written consent was obtained from all patients for use of their records for research. Participants were recruited from the Mayo Clinic SCAD Clinic population, non-Mayo physician- and self-identified SCAD patients, and from referrals from members of 2 SCAD-specific online social networking Web sites.[4] In all patients, the diagnosis of SCAD was confirmed by a senior interventional cardiologist who reviewed all coronary angiograms before study entry.

### Data Collection

Between September 2011 and February 2013, survey materials were mailed to participants. In addition to data collected about each SCAD event, study participants provided demographic information, a personal health narrative, current and past symptoms and treatments, current health status, and medical comorbidities. The Patient Health Questionnaire Depression Scale (PHQ-9)[5] and Generalized Anxiety Disorder 7-Item Scale (GAD-7),[6] 2 well-validated self-report questionnaires, were used to screen for depression and anxiety, respectively. Data from the 158 patients who returned the materials were included for analysis.

### Statistical Analysis

Statistical analysis was performed with JMP version 9.0.0 (SAS Institute, Cary, NC). Continuous data were summarized as mean (standard deviation), and univariate comparisons were performed with a Student $t$ test. Discrete variables were expressed as frequencies or percentages, and univariate comparisons were performed with a $\chi^2$ test. A value of $P < .05$ was considered statistically significant.

## RESULTS

Participant characteristics are reported in the Table.

### Depression and Anxiety

All 158 (100%) patients completed the PHQ-9, and 155 (98%) completed the GAD-7, a mean $3.7 \pm 4.7$ years after their initial SCAD. The overall mean PHQ-9 score was $4.1 \pm 3.9$, with 13 (8%) patients scoring 10 or higher, consistent with at least moderate depression. The mean GAD-7 score was $4.7 \pm 5.1$, and 25 (16%) patients scored 11 or higher, suggesting at least moderate anxiety. The PHQ-9 and GAD-7 scores were higher in those patients who indicated that SCAD affected quality of life and stress levels. Since their SCAD, 51 (33%) patients reported receiving pharmacological or behavioral treatment for depression and 57 (37%) for anxiety, and 46 (31.7%) were still taking prescription antidepressant/anxiolytic medications. Time from SCAD to survey completion was inversely related to GAD-7 scores ($P = .02$), and patients who completed their GAD-7 temporally closer to their SCAD were more likely to report having stress related to SCAD that was high enough to affect their lives ($P = .03$). For instance, those who completed the survey within 6 months of their SCAD event (n = 25) had a mean GAD-7 score of 7 and a mean PHQ-9 score of 6, compared with a mean GAD-7 score of 4 and a mean PHQ-9 score of 4 among the others ($P = .02$, $P = .03$, respectively).

Age was inversely related to PHQ-9 ($P = .04$) and GAD-7 ($P = .018$) scores; younger patients more frequently had GAD-7 scores consistent with severe anxiety ($P = .02$) and were more likely to report past or current treatment of depression ($P = .01$) and anxiety ($P = .004$). The 19 (12%) patients whose SCAD occurred during the peripartum period had higher mean PHQ-9 (6.7 vs 3.7; $P < .0005$) and GAD-7 (8.1 vs 4.3; $P = .0026$) scores than nonperipartum SCAD patients, and they were more likely to have scores consistent with moderate or severe depression (PHQ-9: 10.5 vs 1.5%; $P = .02$) and severe anxiety (GAD-7: 26.3 vs 6.7%; $P = .005$). Neither gender nor recurrent chest pain or dyspnea correlated with GAD-7/PHQ-9 scores. The 76 (49%) patients treated with percutaneous coronary intervention (PCI)

## Table • Baseline Characteristics of SCAD Survivors

| Characteristics at time of survey completion, n (%) | |
|---|---|
| Time from SCAD to survey, median ± SD, mo | 44.4 ± 56.6 |
| Female gender | 154 (97) |
| Caucasian | 145 (95) |
| Married | 132 (86) |
| Living in own home/apartment | 149 (97) |
| Yearly household income >$50 000 | 131 (87) |
| Yearly household income >$80 000 | 99 (66) |
| Completed high school | 152 (100) |
| Completed 4 years of college | 107 (70) |
| Employed, working full-time | 73 (48) |
| SCAD recurrence | 24 (15) |
| Hypertension | 44 (28) |
| Hyperlipidemia | 37 (23) |
| Diabetes mellitus | 2 (1) |
| Any smoking history | 42 (27) |
| Migraines | 49 (32) |
| **Characteristics of initial SCAD event, n (%)** | |
| Age at initial SCAD event, mean ± SD, y | 45.2 ± 9.3 |
| Peripartum | 19 (12) |
| Percutaneous coronary intervention | 76 (49) |
| Coronary artery bypass surgery | 19 (12) |
| Fibrinolytics | 18 (12) |
| Cardiac rehabilitation | 118 (77) |
| Number of CR sessions attended, mean ± SD | 18.2 ± 11.2 |
| **Medications at time of survey, n (%)** | |
| Any cardiac medication | 143 (92) |
| Aspirin | 133 (86) |
| Thienopyridine/ticagrelor | 71 (46) |
| Statin | 80 (52) |
| β-blocker | 96 (62) |
| ACE-inhibitor or angiotensin receptor blocker | 46 (30) |
| Ranolazine | 9 (6) |
| Warfarin | 3 (2) |
| Any depression/anxiety medication | 46 (32) |
| Benzodiazepine | 16 (11) |
| Selective serotonin reuptake inhibitor | 26 (18) |
| Serotonin-norepinephrine reuptake inhibitor | 8 (5) |
| Bupropion | 5 (3) |
| Trazodone | 2 (1) |
| Tricyclic antidepressant | 4 (3) |
| Buspirone | 1 (1) |

Abbreviations: ACE, angiotensin-converting enzyme; CR, cardiac rehabilitation; SCAD, spontaneous coronary artery dissection.

at SCAD presentation had significantly lower mean PHQ-9 (1.5; $P = .02$) and GAD-7 (2.4; $P = .0035$) scores and were less likely to have severe anxiety ($P = .032$). Compared with PCI or medical management, PHQ-9 and GAD-7 scores were no different in those treated with coronary artery bypass graft surgery (CABG), but in the subset of patients with severe anxiety, CABG had been a more frequent intervention ($P = .005$). There was no correlation of PHQ-9 or GAD-7 score with race, education level, income, cardiac rehabilitation participation, or frequency or duration of exercise.

## Self-Perception of Depression and Anxiety

A history of depression and anxiety at any point during life was reported by 61 (38.8%) and 60 (38.5%) patients, respectively. At the time of survey completion, 32 (20.5%) SCAD survivors reported depression and 46 (30.5%) reported anxiety. The PHQ-9 scores in the 124 patients who denied current depression were consistent with mild depression in 31 (25%) and moderate or higher depression in 7 (5.7%) patients. Among the 105 patients not reporting current anxiety, GAD-7 suggested mild anxiety in 23 (21.9%), moderate anxiety in 6 (5.7%), and severe anxiety in 2 (1.9%) patients.

## DISCUSSION

Spontaneous coronary artery dissection tends to occur in young, otherwise healthy women, without the cardiac risk factors typically present in women with classic atherosclerotic MI.[3]

Following MI, younger women (age, <60 years) have higher inhospital and postdischarge mortality than age-matched men.[7] The reason for the increased risk in younger women has not been fully elucidated, although depression and anxiety may be contributing factors. Young women also have the highest prevalence of depression immediately after MI, with 40% of women younger than 60 years being affected.[8] The presence of depressive symptoms, regardless of whether they resolve, persist, or develop in the first month after MI hospitalization, is associated with higher rates of mortality, angina, physical limitations, and worse quality of life,[9] and depression has thus been proposed as a conventional cardiovascular disease risk factor.[2] Patients with post-MI depression are less likely to adhere to recommendations for diet, exercise, stress management, and increasing social support.[10]

Several studies have demonstrated the association of depression in acute coronary syndromes and an approximate 3-fold increase in mortality risk in the

months and years after the acute event, with the degree of risk positively correlated with depression severity. Even minor depressive symptoms are associated with a 50% to 100% increase in cardiovascular disease risk in a "dose dependent" manner as measured by standard depression assessment tools.[2]

Major depressive disorder occurs in 15% to 18% of patients in the first 2 to 42 days after MI, with 17% to 47% of patients experiencing depressive symptoms.[1] We demonstrate a similar prevalence of self-reported depression (33%) requiring medical or behavioral therapy among SCAD survivors. Diagnosing depression and anxiety in women with cardiovascular disease can be challenging, despite clear diagnostic criteria. Frequent overlap exists between the symptoms of acute or chronic cardiovascular disease and those of depression, with fatigue, poor appetite, and sleep disturbances common to both conditions. Clinicians must have a high index of suspicion if depression is to be accurately identified in these high-risk women. Although, in our study, the true prevalence of "major depressive disorder" after SCAD cohort could not be ascertained by survey assessment alone, one-third of SCAD survivors reported having received treatment with medications and/or counseling for symptoms of depression since their SCAD, suggesting that efforts to identify depressive symptoms are warranted.

Anxiety frequently occurs in women with coronary artery disease, with 1 study showing a greater than 70% lifetime prevalence of anxiety disorders in women (average age, 60 years) with coronary heart disease.[11] In our study, 37% of patients reported having ever been treated with medications or counseling for anxiety. Anxiety has been linked to increased cardiovascular mortality, and while the exact mechanism for the increased cardiovascular risk is unclear, research has associated both anxiety/depression with increased inflammatory and coagulation markers in healthy individuals, which may increase risk for cardiac events.[12]

The increased prevalence and severity of depression and anxiety in patients with SCAD that occurred while pregnant or postpartum are of interest. The volatile hormonal shifts in the peripartum period may be a contributory factor, and acute stress during the postpartum period may predispose patients to depression. The process of childbirth itself may cause symptoms of posttraumatic stress and anxiety,[13] and the additional stress of an SCAD MI in this vulnerable period may potentiate the risk of subsequent anxiety.

Optimal management for SCAD is unclear at this time, but patients treated conservatively with medical management have similarly favorable long-term outcomes compared with those treated with an initial interventional approach (PCI or CABG).[3,14] The observation that patients treated with PCI had lower rates of depression and anxiety following SCAD is intriguing. One may hypothesize that these patients may be less apt to worry about SCAD recurrence, given their initial culprit vessel was successfully intervened upon. As may be expected given the invasiveness of CABG compared with PCI, those treated with CABG were more likely to have severe anxiety. They may perceive themselves as having more severe disease and are concerned about the need for repeat major surgery with its associated postsurgical recovery period. Recovery from CABG is more challenging for women than for men, as manifested by higher rates of hospital readmission, worse physical function, and more depressive symptoms, particularly in younger women.[15]

The risk of development of depression and anxiety in SCAD survivors may be heightened by the disease's relative rarity, unclear pathogenesis, and uncertain optimal acute and long-term management and because patients often feel isolated in their recovery because of young age and female gender. In contrast to atherosclerotic MI, where numerous proven-effective interventions for secondary prevention of recurrent MI are available, including statins, aspirin, and lifestyle modification, no medical or lifestyle interventions have been identified that prevent recurrence of MI due to SCAD. In fact, statins, a mainstay of secondary prevention in atherosclerosis, may be associated with an increased risk of recurrent SCAD.[3] With a reported 10-year SCAD recurrence rate of up to 21%, the prognostic uncertainty combined with the lack of proven therapies to reduce recurrence risk may increase anxiety levels. As such, future studies examining the usefulness of developing psychological interventions focused on building resiliency among SCAD survivors may augment the effects of traditional interventions in the management of depression and anxiety.

To more comprehensively and accurately differentiate true depressive and anxiety disorders (versus situational reactions to an SCAD event), future studies could use evidence-based assessment measures such as the Minnesota Multiphasic Personality Inventory–II,[16] which could help differentiate somatic complaints and depression/anxiety, the Personality Assessment Inventory,[17] and the Structured Clinical Interview of Disorders,[18] although these assessments carry significant cost and time burden.

## Limitations

As SCAD is uncommon and underrecognized, the small sample size in our study is the major limitation. The low number of male subjects (n = 4) limited our ability to perform matched gender comparison.

Furthermore, our predominantly white patient cohort had relatively high education and income levels compared with the general population. These patient demographics may affect accessibility to mental health care and medications, which may have impacted the prevalence of diagnosed depression and anxiety and prior treatment of these disorders. Because this was a cross-sectional study, we are able to describe only associations and causality cannot be implied. The long time delay between SCAD event and survey completion may have resulted in recall bias. Furthermore, because the PHQ-9 and GAD-7 questionnaires were given at a single point in time, the scores were likely higher before treatment in those patients whose depression and anxiety was being adequately managed. The results of this study should be considered hypothesis-generating.

# CONCLUSIONS

Our results demonstrate high rates of depression and anxiety after MI due to SCAD, consistent with rates in non-SCAD MI survivors, despite differences in pathogenesis and baseline clinical characteristics. Young women are at highest risk for development of these symptoms, particularly those with peripartum SCAD. On the basis of these high rates of depression and anxiety found in SCAD MI survivors, we concur with recommendations for screening all MI survivors for depression[19] and would further suggest that screening for anxiety be considered. As this study was cross-sectional, we were unable to determine whether depression and anxiety affected outcomes. Further prospective studies should focus on determining the prognostic implications of these psychiatric disorders after MI due to SCAD.

## References

1. Ziegelstein RC. Depression in patients recovering from a myocardial infarction. *JAMA.* 2001;286:1621-1627.
2. Hayes SN. Broken-hearted women: the complex relationship between depression and cardiovascular disease. *Womens Health (Lond Engl).* 2009;5:709-775.
3. Tweet MS, Hayes SN, Pitta SR, et al. Clinical features, management, and prognosis of spontaneous coronary artery dissection. *Circulation.* 2012;126:579-588.
4. Tweet MS, Gulati R, Aase LA, Hayes SN. Spontaneous coronary artery dissection: a disease-specific, social networking community-initiated study. *Mayo Clin Proc.* 2011;86:845-850.
5. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. *J Gen Intern Med.* 2001;16:606-613.
6. Spitzer RL, Kroenke K, Williams JW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med.* 2006;166:1092-1097.
7. Vaccarino V, Krumholz HM, Yarzebski J, Gore JM, Goldberg RJ. Sex differences in 2-year mortality after hospital discharge for myocardial infarction. *Ann Intern Med.* 2001;134:173-181.
8. Mallik S, Spertus JA, Reid KJ, et al. Depressive symptoms after acute myocardial infarction: evidence for highest rates in younger women. *Arch Intern Med.* 2006;166:876-883.
9. Parashar S, Rumsfeld JS, Spertus JA, et al. Time course of depression and outcome of myocardial infarction. *Arch Intern Med.* 2006;166:2035-2043.
10. Ziegelstein RC, Fauerbach JA, Stevens SS, Romanelli J, Richter DP, Bush DE. Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from a myocardial infarction. *Arch Intern Med.* 2000;160:1818-1823.
11. Todaro JF, Shen B-J, Raffa SD, Tilkemeier PL, Niaura R. Prevalence of anxiety disorders in men and women with established coronary heart disease. *J Cardiopulm Rehabil Prev.* 2007;27:86-91.
12. Pitsavos C, Panagiotakos DB, Papageorgiou C, Tsetsekou E, Soldatos C, Stefanadis C. Anxiety in relation to inflammation and coagulation markers, among healthy adults: the ATTICA Study. *Atherosclerosis.* 2006;185:320-326.
13. Czarnocka J, Slade P. Prevalence and predictors of post-traumatic stress symptoms following childbirth. *Br J Clin Psychol.* 2000;39(pt 1):35-51.
14. Alfonso F, Paulo M, Lennie V, et al. Spontaneous coronary artery dissection: long-term follow-up of a large series of patients prospectively managed with a "conservative" therapeutic strategy. *JACC Cardiovasc Interv.* 2012;5:1062-1070.
15. Vaccarino V, Lin ZQ, Kasl SV, et al. Gender differences in recovery after coronary artery bypass surgery. *J Am Coll Cardiol.* 2003;41:307-314.
16. Butcher JN, Dahlstrom WG, Graham JR, Tellegen AM, Kreammer B. *The Minnesota Multiphasic Personality Inventory-2 (MMPI-2) Manual for Administration and Scoring.* Minneapolis, MN: University of Minneapolis Press; 1989.
17. Morey L, Ambwani S. The Personality Assessment Inventory. In: Boyle G, Matthews G, Saklofske D, eds. *The SAGE Handbook of Personality Theory and Assessment: Volume2—Personality Measurement and Testing.* London, England: SAGE Publications Ltd; 2008:626-646.
18. First MB, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P).* New York, NY: Biometrics Research, New York State Psychiatric Institute; 2002.
19. Lichtman JH, Bigger JT, Blumenthal JA, et al. Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association. *Circulation.* 2008;118:1768-1775.