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Depressive Symptom Severity and Mortality in Older Adults Undergoing Percutaneous Coronary Intervention

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Depressive symptoms are frequently underdiagnosed and undertreated in patients with coronary artery disease (CAD), with prevalence rates up to 45% in patients with acute myocardial infarction (MI) (1-3). Previous studies describing the association between depression and outcomes commonly enrolled younger patients after acute MI (2,4,5); older adults, who often have greater prevalence and severity of ischemic heart disease, have been poorly studied. Consequently, the association of depressive symptoms and outcome in older adults undergoing percutaneous coronary intervention (PCI) remains unknown. We used the Center for Epidemiological Studies Depression (CES-D) scale to determine the prevalence of depression in older adults undergoing PCI and studied the relationship between depressive symptom severity and long-term outcomes.

This study was approved by the Mayo Clinic Institutional Review Board; all subjects provided written informed consent. We prospectively enrolled patients ≥ 65 years undergoing PCI for treatment of CAD at Mayo Clinic (Rochester, Minnesota; Franciscan Skemp Hospital, La Crosse, Wisconsin) from October 2005 through September 2008. The CES-D is a 20-item, self-report survey of the frequency of specific symptoms of depression and has been used to measure depressive symptoms in mortality studies (6,7). Frequency of depressive symptoms during the preceding week is assessed on a 4-point scale, where 0 = rarely or none of the time and 3 = most or all of the time (8). A CES-D score ≥ 16 has been used to identify individuals at risk for depression and is a predictor of adverse clinical outcomes, including death (6). The CES-D was administered to patients by trained research assistants after the index PCI.

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All subjects survived to hospital discharge. For outcomes assessment, patients were telephoned at 6 months and annually after the index PCI. Each time, study personnel reviewed the presence and severity of anginal symptoms, behavioral lifestyle changes (eg, smoking status, exercise habits), and medications. Data regarding major adverse cardiovascular events, including MI, target lesion revascularization (TLR), and cause-specific mortality were recorded. Death certificates were requested to confirm date and cause of death through the Rochester Epidemiology Project Minnesota Death Certificate data and via review of the electronic medical record. Standard descriptive statistics were applied and continuous variables were summarized as mean (SD) and categorical variables were presented as frequency (percentage). Missing items from the CES-D questionnaire were imputed using the average score of the completed items, with appropriate corrections for items with reverse-scoring order. Cox regression models were used to estimate the unadjusted association of baseline covariates to outcomes. Significance was declared at $P < .05$.

Baseline clinical characteristics, categorized by CES-D scores, were generally similar across groups (Table 1). Regarding in-hospital event rates or length of stay, we observed no difference when stratifying patients by CES-D scores. In unadjusted analyses, patients with moderate/severe depressive symptoms (CES-D score, >21) had significantly higher risk of death compared with patients with none/mild depressive symptoms (CES-D score, <16) (hazard ratio [HR], 2.00; 95% CI, 1.10-3.63; $P = .02$). Other covariates that were significantly associated with death in univariate analyses were age, comorbidity (Charlson comorbidity index), diabetes mellitus, multivessel coronary disease, and chronic kidney disease. During a median follow-up of 3.0 years, 74 patients died. Noncardiovascular deaths occurred in 49 patients (66%); cardiovascular deaths were attributed to MI ($n=6$), heart failure ($n=5$), stroke ($n=4$), and other causes ($n=10$).

After multivariable adjustment, patients with moderate/severe depressive symptom severity had significantly greater risk of all-cause mortality than patients with none/mild symptom severity (adjusted HR, 1.90; 95% CI, 1.02-3.53; $P = .04$) (Table 2). Patients with moderate depressive symptoms (CES-D score, 16-21) had nearly a 50% increased risk of death compared with the reference group (CES-D score, <16), but this difference was not statistically significant (adjusted HR, 1.50; 95% CI, 0.79-2.85; $P = .22$). Depression level was not significantly associated with the composite incidence of death, MI, or TLR during follow-up. More than one-fifth of patients in our cohort had clinically important depressive symptoms (22.7% with CES-D score ≥ 16), and those with moderate/severe depressive symptom severity (CES-D score, >21) had significantly higher adjusted risk of mortality. In addition, we observed that the estimated effect of depression on all-cause mortality in those with high depressive scores was similar to that of a decade increase in age, a known prognostic factor in PCI-treated patients.

A systematic review of the prevalence of depression in patients with cardiovascular disease reported ranges from 16% to 23% (2), with differences likely related to methodologic approaches, ascertainment of depression at varying times during hospitalization, and differences in study populations. In one study, the prevalence of depressive symptoms (defined by a cutoff score of ≥ 2 on the 2-item Patient Health Questionnaire) was 30% in a

population of middle-aged patients undergoing PCI; depression was associated with adverse clinical outcomes (death or nonfatal MI) (9). However, the prevalence was lower when the Patient Health Questionnaire cutoff score was increased to 3, likely reflecting decreased sensitivity as a result of greater specificity for depression.

Our report represents a large prospective study of long-term outcomes in older adults treated with PCI who were screened for depressive symptoms at baseline. We observed that greater depressive symptom severity was associated with higher mortality rates after adjusting for confounders, which supports the current recommendations of the American Heart Association that screening for depression in patients with coronary heart disease should not be missed, with referral for professional depression treatment as appropriate. The results of this study support ongoing research to further evaluate interventions for depression in patients with CAD undergoing revascularization (10).

The CES-D was administered after PCI during the index hospital admission; these circumstances might have influenced responses to the questionnaire and the prevalence of depression, although long-term mortality was unlikely to be affected. Other limitations include missing information regarding depression history, including antidepressant use. Our findings may have been susceptible to bias from unmeasured confounders such as socioeconomic status or substance use. However, our observation that objectively measured depressive symptoms were independently associated with long-term mortality in older adults undergoing PCI has important implications in the assessment and management of depressive symptoms among older cardiac patients.

Given the high prevalence and worse outcomes of depression in older adults with CAD, further research is needed to understand potential benefits of depression screening in the older adult population undergoing revascularization.

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Table 1

Baseline Characteristics, Stratified by CES-D Score

Variable	Overall (N=596)	CES-D <16 (n=461)	CES-D 16-21 (n=67)	CES-D >21 (n=68)	P Value
Age, mean (SD), y	74.7 (6.4)	74.7 (6.5)	74.5 (5.7)	74.9 (6.3)	.68
Women, No. (%)	188 (32)	140 (30)	23 (34)	25 (37)	.24
Charlson comorbidity index, mean (SD)	3.5 (3.3)	3.6 (3.4)	3.0 (3.0)	3.1 (2.7)	.86
Seattle Angina Questionnaire, mean (SD)					
Physical limitation	69.5 (21.1)	72.3 (20.0)	58.0 (21.8)	61.9 (22.5)	.27
Anginal stability	51.0 (39.2)	53.8 (39.3)	40.9 (34.8)	42.5 (40.4)	.82
Anginal frequency	71.2 (25.5)	73.3 (25.3)	65.4 (22.9)	63.2 (26.9)	.62
History of congestive heart failure, No. (%)	92 (15)	69 (15)	11 (16)	12 (18)	.48
Canadian Cardiovascular Society angina scale III, No. (%)	291 (49)	216 (47)	40 (60)	35 (51)	.18
History of myocardial infarction, No. (%)	183 (31)	140 (30)	22 (33)	21 (31)	.72
Hypertension, No. (%)	478 (80)	369 (80)	53 (79)	56 (82)	.70
Diabetes mellitus, No. (%)	180 (30)	133 (29)	23 (34)	24 (35)	.21
History of cholesterol >240 mg/dL, No. (%)	465 (78)	370 (80)	48 (72)	47 (69)	.002
Chronic kidney disease, No. (%)	77 (13)	58 (13)	8 (12)	11 (16)	.49
Prior PCI, No. (%)	219 (37)	176 (38)	22 (33)	21 (31)	.18
Previous coronary artery bypass graft, No. (%)	152 (26)	115 (25)	15 (22)	22 (32)	.32
Current smoker, No. (%)	34 (6)	21 (5)	8 (12)	5 (7)	.09
Body surface area, mean (SD), m ²	2.0 (0.2)	2.0 (0.2)	2.0 (0.2)	2.0 (0.3)	.71
Multivessel disease, No. (%)	356 (60)	275 (60)	40 (60)	41 (60)	.36
Left main coronary artery 70% stenosis, No. (%)	59 (10)	46 (10)	6 (9)	7 (10)	.83
Left ventricular ejection fraction, mean (SD), %	53.3 (13.1)	53.1 (13.1)	55.4 (11.7)	52.5 (14.3)	.26
Urgency of PCI, No. (%)					.12
Elective	198 (33)	157 (34)	16 (24)	25 (37)	
Urgent	280 (47)	214 (46)	35 (52)	31 (46)	
Emergent	115 (19)	87 (19)	16 (24)	12 (18)	
Myocardial infarction within 24 h before PCI, No. (%)	187 (31)	145 (31)	22 (33)	20 (29)	.89

Abbreviations: CES-D, Center for Epidemiological Studies Depression; PCI, percutaneous coronary intervention.

Table 2
Multivariable Model of Factors Associated With Long-Term Mortality and the Composite Outcome of Death, MI, or TLR in Older Adults Treated with PCI^a

Variable	Death			Death, MI, or TLR		
	Adjusted Hazard Ratio (95% CI)	P Value		Adjusted Hazard Ratio (95% CI)	P Value	
Moderate/severe depressive symptoms (CES-D score, >21) ^b	1.90 (1.02-3.53)	.04		1.10 (0.69-1.75)		.70
Moderate depressive symptoms (CES-D score, 16-21) ^b	1.50 (0.79-2.85)	.22		1.13 (0.71-1.80)		.60
Age (per decade increase)	1.88 (1.31-2.68)	<.001		1.32 (1.03-1.69)		.03
Charlson comorbidity index (per unit increase)	1.08 (1.02-1.15)	.01		1.02 (0.97-1.06)		.53
Diabetes mellitus	2.04 (1.26-3.30)	.004		1.24 (0.89-1.72)		.21

Abbreviations: CES-D, Center for Epidemiological Studies Depression; MI, myocardial infarction; PCI, percutaneous coronary intervention; TLR, target lesion revascularization.

^aOther variables included in the model adjustment included the Seattle Angina Questionnaire physical limitation score, chronic kidney disease, and multivessel disease.

^bReferent was none/mild depressive symptoms (CES-D score, <16).