Relationship Between Optimism and Outcomes in Patients With Chronic Angina Pectoris

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Greater optimism regarding recovery from chronic illness is associated with improved quality of life and clinical outcomes. We performed a post-hoc analysis on the association between optimism and outcomes in Ranolazine in Patients with Incomplete Revascularization after Percutaneous Coronary Intervention (RIVER-PCI), a randomized trial in patients with chronic angina pectoris who had incomplete revascularization following percutaneous coronary intervention. At baseline, patients answered how much they agreed with the phrase, "I am optimistic about my future and returning to a normal lifestyle." We evaluated the association between baseline optimism and time to ischemia-driven hospitalization or revascularization using a Cox model, and the association between baseline optimism and change in frequency of angina pectoris using a mixed measures model. Of 2,389 patients, 782 (33.2%) were very optimistic ("strongly agree"), 1,000 (42.4%) were optimistic ("agree"), 451 (19.1%) were neutral ("undecided"), and 123 (5.2%) were not optimistic ("disagree" or "strongly disagree"). Very optimistic patients had a lower prevalence of co-morbidities and less severe angina at baseline than less optimistic patients. The rate of ischemia-driven revascularization or hospitalization was higher in neutral and not optimistic patients compared with very optimistic patients; this finding persisted after adjustment for co-morbidities and baseline angina frequency (hazard ratio 1.42, 95% confidence interval 1.14 to 1.77 for neutral vs very optimistic; hazard ratio 1.38, 95% confidence interval 0.98 to 1.94 for not optimistic vs very optimistic). Neutral and not optimistic patients also had less improvement in angina than very optimistic patients. In conclusion, in patients with angina, those with more self-reported optimism had better health status outcomes. Whether structured interventions targeting optimism improve outcomes in these patients warrants further study.   © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1399−1405)

Chronic angina afflicts an estimated 8.7 million people in the United States,[1] and contributes to lower quality of life and higher rates of healthcare utilization.[2,3] In patients with chronic angina, there are strong associations between depression, severity of self-reported symptoms, and clinical outcomes. However, depressive symptoms comprise only part of the psychosocial aspect of chronic illness, and are distinct from expectations regarding recovery (i.e. optimism).[4] Expectations regarding recovery are associated with quality of life and health status in patients with some acute and chronic illnesses, but not others,[4−7] and it is uncertain whether expectations for recovery are associated with quality of life and healthcare utilization in patients with chronic angina pectoris. If lower optimism is associated with worse clinical outcomes and quality of life independent of standard prognostic factors, it may be a useful marker for physicians to recognize and consider as a potential therapeutic target. We, therefore, performed a secondary analysis of RIVER-PCI (Ranolazine in Patients with Incomplete Revascularization after Percutaneous Coronary Intervention) to evaluate associations between baseline optimism, quality of life, and use of healthcare resources in patients with symptomatic coronary artery disease (CAD).

Methods

RIVER-PCI was a multicenter, randomized, double-blind, placebo-controlled trial conducted in 245 centers in 15 countries; the design and primary results have been published, as have the effects on angina frequency and quality of life.[8−10] Briefly, the trial randomized patients with a history of chronic angina who had incomplete revascularization after percutaneous coronary intervention (PCI) to receive ranolazine 1000 mg twice daily or placebo. Chronic

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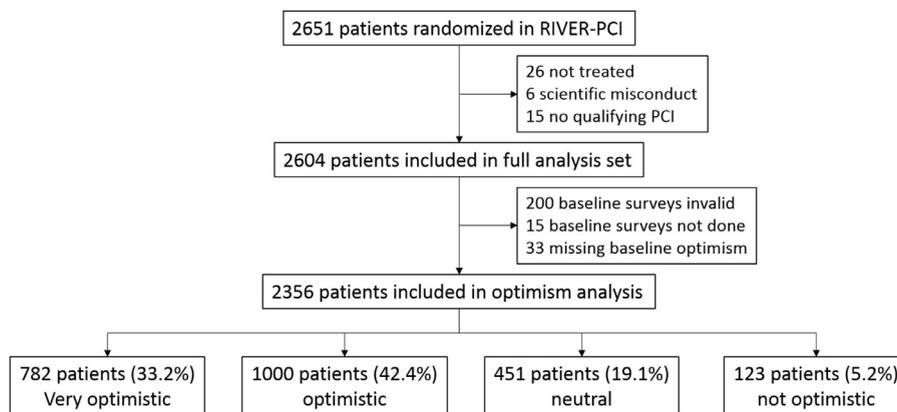*E-mail address:* alexander.fanaroff@duke.edu (A.C. Fanaroff).

Figure 1. Study flow.

angina was defined as ≥2 episodes of typical angina, with episodes occurring on ≥2 separate days between 30 days and 1 year before PCI. The qualifying PCI could be due either to an acute coronary syndrome (ACS) or stable angina. Incomplete revascularization was defined as the presence of at least 1 lesion with ≥50% diameter stenosis in a coronary artery ≥2.0 mm in diameter, whether in a PCI-treated or nontreated vessel. In patients with previous coronary artery bypass grafting surgery, incomplete revascularization was defined as at least 1 ≥50% diameter stenosis in a nonbypassed coronary artery ≥2.0 mm in diameter, or at least 1 ≥50% diameter stenosis in a bypass graft supplying an otherwise nonrevascularized territory.

Patients completed a survey at baseline, 1, 6, and 12 months to evaluate disease-specific health status and quality of life. Optimism was assessed using a single question from the 18-question Expectations for Coping Scale at each study visit.[4] Patients were asked to indicate on a 5-point Likert scale how much they agreed with the statement, "I am optimistic about my future and returning to a normal lifestyle." For this study, patients were divided into groups based on self-reported optimism at baseline. Patients selecting "strongly agree" were defined as "very optimistic," those selecting "agree" were defined as "optimistic," and those selecting "undecided" were defined as "neutral." Patients selecting "disagree" and "strongly disagree" were pooled into a single group defined as "not optimistic."

Quality of life indicators were derived from the Seattle Angina Questionnaire (SAQ), Duke Activity Status Index, European Quality of Life 5 Dimension 3-Level Scale (EuroQol-5D-3 L; a 5-item instrument assessing specific domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), Rose Dyspnea Scale, and the 5-question Mental Health Inventory (MHI-5) from the 36-item Short Form Health Survey (SF-36).

The primary outcome of this secondary analysis was centrally-adjudicated ischemia-driven revascularization or hospitalization. Ischemia-driven revascularization was defined as any PCI or coronary artery bypass graft surgery for angina or angina equivalent symptoms, with or without objectively documented ischemia. Ischemia-driven hospitalization was defined as any hospital admission, emergency department visit with stay >23 hours, or coronary angiography for angina or angina equivalent symptoms, with or without

objectively documented ischemia. The secondary outcome was change in angina frequency over time. Angina was assessed using the SAQ at baseline and at 1, 6, and 12 months. The SAQ angina frequency score is determined from 2 questions about angina frequency and nitroglycerin usage; scores range from 0 to 100, with 100 representing no angina and 0 representing very frequent angina.[11]

RIVER-PCI randomized 2,651 patients; of these, 2,604 who had a qualifying PCI and received at least 1 dose of study drug were included in the full efficacy analysis. For this analysis, we excluded 215 patients that had a missing or invalid baseline survey, and 33 patients with missing response to the baseline optimism question (Figure 1). Baseline characteristics were reported by optimism groups (very optimistic, optimistic, neutral, not optimistic), with categorical variables reported as number (%) and continuous variables reported as median (25th, 75th percentile). Categorical variables were compared between groups using the Chi-square test and continuous variables using the Kruskal-Wallis test.

To evaluate the association between optimism and time to first occurrence of ischemia-driven revascularization or hospitalization, we used Cox proportional hazards regression modeling to estimate the relation (hazard ratio, HR) of time to ischemia-driven revascularization or hospitalization for optimistic, neutral, and not optimistic patients, with very optimistic patients as the reference. Covariates for adjustment were chosen based on clinical judgment and included demographic and clinical variables, including details of the index PCI. The full list of covariates is listed in the Supplemental Methods. We repeated the analysis, including baseline MHI-5 score in the list of covariates in order to adjust for a measure of baseline anxiety and depression.

To evaluate the association between baseline optimism and angina frequency, we generated descriptive statistics for SAQ angina frequency score at baseline, 1, 6, and 12 months, as well as change from baseline data at each time point, for each optimism group. Using a repeated measures model with a compound symmetric covariance structure, we tested the association between optimism group and least-squares mean change from baseline SAQ angina frequency score at 1, 6, and 12 months. We first performed this analysis including only terms for baseline

angina frequency, treatment group, optimism group, visit, and optimism-by-visit interaction (unadjusted), and then repeated the analysis adjusting for the same baseline characteristics included in the analysis of the association between optimism and ischemia-driven hospitalization or revascularization described above. The response vectors were taken to be multivariate normal. Only patients with all covariates measured were included in the analysis, but they were permitted to have missing responses at 1 or 2 of the 3 timepoints. The model was fit using maximum likelihood estimation.

The investigators had full access to all of the data. Faculty and staff statisticians at the Duke Clinical Research Institute performed all analyses using SAS version 9.4 (Cary, North Carolina).

Results

Of 2,356 patients, 782 (33.2%) were very optimistic, 1,000 (42.4%) were optimistic, 451 (19.1%) were neutral, and 123 (5.2%) were not optimistic. Compared with optimistic patients, not optimistic patients had a higher prevalence of most co-morbidities, including previous MI, chronic kidney disease, and peripheral artery disease (Table 1). Index PCIs for not optimistic patients were less likely to be for an ACS indication. Compared with very optimistic patients, not optimistic patients had more daily or weekly angina, and a higher residual SYNTAX score following index PCI. Not optimistic patients also had lower functional capacity, as measured by the Duke Activity Status Index, and lower overall quality of life, as measured by the EuroQOL visual analog scale compared with more optimistic patients.

Optimism declined slightly during follow-up, with the proportion of patients reporting they were very optimistic dropping from 33% at baseline to 30% at 1, 28% at 6, and 25% at 12 months (Figure 2). Individual levels of self-reported optimism also shifted over time (Supplemental Figure 1). In very optimistic patients at baseline, 46% remained very optimistic at 12 months, 37% were optimistic, 12% were neutral, and 5% were not optimistic; in patients that were not optimistic at baseline, 32% remained not optimistic at month 12, 28% were neutral, 29% were optimistic, and 11% were very optimistic.

Of patients that were very optimistic, 24.4% (191/782) had an ischemia-driven hospitalization or revascularization over 1-year follow-up, compared with 25.8% of (258/1000) optimistic patients, 32.8% of neutral patients (148/451) and 35.0% (43/123) of not optimistic patients. After adjustment for baseline characteristics and SAQ angina frequency, differences between optimism groups were attenuated, but neutral and not optimistic patients remained at higher risk of ischemia-driven revascularization or hospitalization, although this result was significant only for neutral patients (hazard ratio 1.42, p = 0.002 for neutral vs very optimistic; hazard ratio 1.38, p = 0.07 for not optimistic vs very optimistic; Figure 3). After adjusting for baseline characteristics, SAQ angina frequency, and MHI-5, differences were further attenuated, but neutral and not optimistic patients remained at higher risk.

Compared with more optimistic patients, less optimistic patients had more angina (lower SAQ angina frequency score) at baseline (SAQ angina frequency score 59.6 for not optimistic, 64.5 for neutral, 68.6 for optimistic, 72.1 for very optimistic; p <0.001). By protocol, all patients enrolled in RIVER-PCI underwent PCI at baseline and most reported improvement in self-reported angina frequency at 1 month (Figure 4). After adjusting for baseline characteristics and angina frequency, neutral patients improved by 3.4 points less than very optimistic patients (95% confidence interval [CI] 1.2 to 5.6) and not optimistic patients by 5.7 points less than very optimistic patients (95% CI 2.1 to 9.3) at 1 month follow-up; improvement in angina frequency was not significantly different between optimistic and very optimistic patients (Supplemental Table 1). Adding MHI-5 to the list of covariates used for adjustment did not substantially change the results.

Between 1 and 12 months, angina frequency remained relatively stable in all groups. By 12 months, optimistic patients had improved by 19.0 points on the SAQ angina frequency scale, and very optimistic patients by 20.3 points, but not optimistic patients had improved by 15.0 points and neutral patients by 15.1 points. After adjustment, neutral patients improved by 4.6 points less than very optimistic patients (95% CI 2.3 to 6.9, p <0.001) and not optimistic patients improved by 4.2 points less than very optimistic patients (95% CI 0.4 to 8.1, p = 0.03) from baseline to 12-month follow-up. At the end of 12 months' follow-up, patients that were not optimistic at baseline had the most severe angina (SAQ angina frequency score 82.5 for not optimistic, 83.0 for neutral, 87.9 for optimistic, 89.9 for very optimistic).

Discussion

We found that most patients with chronic angina and incomplete revascularization after PCI enrolled in a clinical trial reported being optimistic or very optimistic about returning to a normal lifestyle, and that optimism was associated with better recovery of health status and better outcomes over time. The majority of patients who were optimistic at baseline remained so at 12 months. Even after adjusting for co-morbidities and baseline angina frequency, optimistic patients were less likely to have an ischemia-driven revascularization or hospitalization than neutral and not optimistic patients, and had more improvement in angina frequency over time. This observational analysis sets the stage for randomized studies evaluating the effect of interventions that improve optimism on long-term health outcomes in patients with angina.

The psychosocial contribution to outcomes in patients with ACSs and stable angina are well-recognized,[4,5,12–14] but recommendations for screening and treatment are largely focused on anxiety and depression.[15,16] Although expectations for recovery are correlated with, and may be causally related to, depressive symptoms, they are conceptually distinct. Expectations for recovery are part of the way in which patients cognitively process the experience of illness; to the extent that depression and anxiety are caused by situational factors like illness, they are downstream consequences of the psychological reaction to illness.[17]

In patients with clinically significant CAD, higher levels of optimism are associated with a lower risk of both

Table 1
Baseline characteristics by optimism level

Variable	Very optimistic (n = 782)	Optimistic (n = 1,000)	Neutral (n = 451)	Not optimistic (n = 123)	p Value
Demographic characteristics and medical history					
Age (years)	63 (56, 70)	64 (56, 71)	63 (56, 71)	63 (56, 73)	0.25
Men	628 (80%)	819 (82%)	335 (74%)	99 (81%)	0.010
Non-white	58 (7%)	65 (7%)	29 (6%)	11 (9%)	0.68
BMI (kg/m^2)	29 (26, 32)	29 (26, 32)	29 (26, 32)	29 (27, 32)	0.36
Prior MI	351 (45%)	457 (46%)	245 (54%)	74 (60%)	<0.001
Prior resuscitated sudden cardiac death	12 (2%)	9 (1%)	5 (1%)	3 (2%)	0.39
Hypertension*	661 (85%)	858 (86%)	396 (88%)	112 (91%)	0.15
Hyperlipidemia*	655 (84%)	856 (86%)	391 (87%)	105 (85%)	0.53
Chronic kidney disease	50 (6%)	87 (9%)	36 (8%)	22 (18%)	<0.001
Atrial fibrillation/flutter	62 (8%)	77 (7%)	37 (8%)	14 (11%)	0.57
Cerebrovascular disease	58 (7%)	104 (10%)	57 (13%)	13 (11%)	0.023
Peripheral artery disease	68 (9%)	122 (12%)	62 (14%)	23 (19%)	0.002
Diabetes mellitus	248 (32%)	322 (32%)	152 (34%)	48 (39%)	0.41
Current alcohol use	143 (18%)	213 (21%)	97 (22%)	30 (24%)	0.24
Symptomatic heart failure[†]	98 (13%)	129 (13%)	85 (19%)	18 (15%)	0.010
Details of the index PCI					
CCS angina level					0.010
No angina pectoris	32 (4%)	36 (4%)	20 (4%)	4 (3%)	
I	120 (15%)	136 (14%)	45 (10%)	10 (8%)	
II	418 (54%)	508 (51%)	224 (50%)	56 (46%)	
III	178 (23%)	275 (27%)	134 (30%)	44 (36%)	
IV	31 (4%)	40 (4%)	26 (6%)	9 (7%)	
Index PCI for ACS	297 (38%)	339 (34%)	156 (35%)	28 (23%)	0.008
Baseline SYNTAX score	15 (10, 22)	15 (11, 21)	16 (11, 23)	16 (11, 22)	0.35
Residual SYNTAX score	8 (5, 13)	9 (5, 14)	9 (5, 15)	10 (6, 15)	0.02
Incomplete revascularization due to lesion complexity[‡]	234 (30%)	305 (30%)	164 (36%)	45 (37%)	<0.001
Baseline quality of life					
SAQ angina frequency	80 (60, 90)	70 (50, 90)	70 (50, 80)	60 (40, 80)	<0.001
SAQ angina frequency category					<0.001
No angina (SAQ AF = 100)	160 (20%)	158 (16%)	46 (10%)	13 (11%)	
Angina monthly (SAQ AF = 61−99)	342 (44%)	431 (43%)	187 (41%)	42 (34%)	
Angina weekly (SAQ AF = 31−60)	214 (27%)	318 (32%)	163 (36%)	47 (38%)	
Angina daily (SAQ AF = 0−30)	64 (8%)	90 (9%)	55 (12%)	21 (17%)	
Duke Activity Status Index	19 (10, 35)	15 (7, 26)	11 (6, 18)	7 (5, 19)	<0.001
SF-36 MHI-5	75 (60, 85)	65 (55, 80)	55 (45, 70)	50 (40, 70)	<0.001
EuroQOL VAS	75 (65, 82)	70 (55, 80)	60 (50, 70)	55 (40, 66)	<0.001
Rose dyspnea scale					<0.001
0 (No Dyspnea)	255 (33%)	231 (23%)	83 (18%)	20 (16%)	
1	182 (23%)	272 (27%)	103 (23%)	21 (17%)	
2	106 (14%)	172 (17%)	100 (22%)	25 (20%)	
3	95 (12%)	164 (16%)	77 (17%)	23 (19%)	
4	133 (17%)	149 (15%)	78 (17%)	31 (25%)	
Global Health Utility					<0.001
Excellent	32 (4%)	15 (1%)	1 (0%)	0 (0%)	
Very Good	156 (20%)	92 (9%)	21 (5%)	3 (2%)	
Good	386 (49%)	557 (56%)	170 (38%)	50 (41%)	
Fair	191 (24%)	297 (30%)	227 (50%)	51 (41%)	
Poor	17 (2%)	33 (3%)	30 (7%)	19 (15%)	
Work/regular physical activity					<0.001
Mainly sedentary	150 (19%)	158 (16%)	62 (14%)	16 (13%)	
Predominantly walking on one level	239 (31%)	332 (33%)	158 (35%)	39 (32%)	
No heavy lifting	22 (3%)	24 (2%)	11 (2%)	1 (1%)	
Mainly walking including climbing stairs/walking uphill/lifting objects	176 (23%)	211 (21%)	81 (18%)	15 (12%)	
Heavy physical labor	49 (6%)	55 (5%)	21 (5%)	5 (4%)	
Do not work	140 (18%)	207 (21%)	115 (25%)	43 (35%)	

* As reported by the patient;

[†] HF with NYHA class II, III, or IV symptoms;

[‡] Defined as operator report that either "PCI of lesion would have a low likelihood of acute success," "PCI of lesion would have a low likelihood of long-term success," "PCI of lesion would have a high complication rate," or "PCI of lesion failed during index procedure.
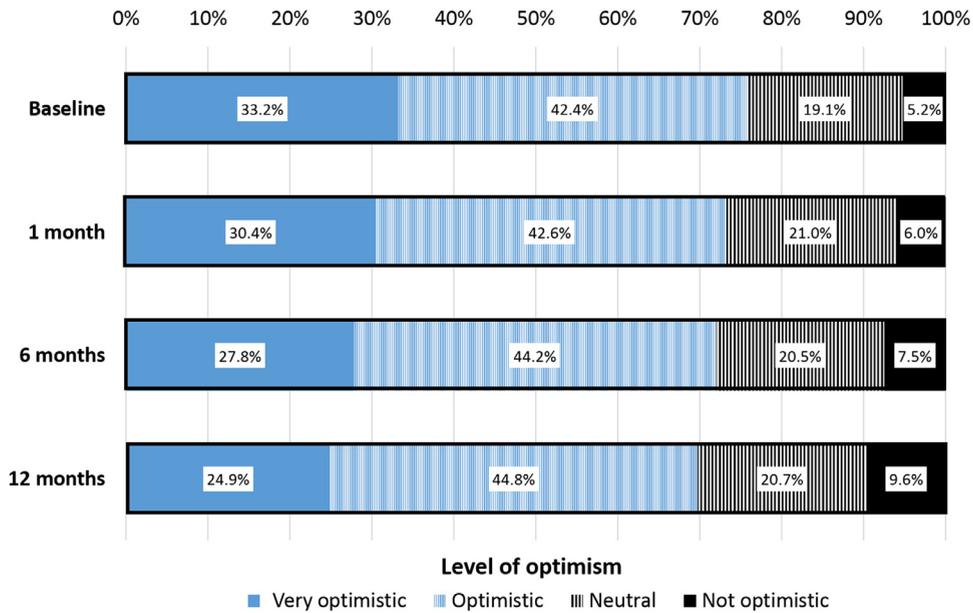
Figure 2. Proportion of patients reporting each optimism level at each time point.
Overall, the proportion of patients reporting that they were optimistic or very optimistic decreased over time, but the majority of patients remained either optimistic or very optimistic throughout follow-up.
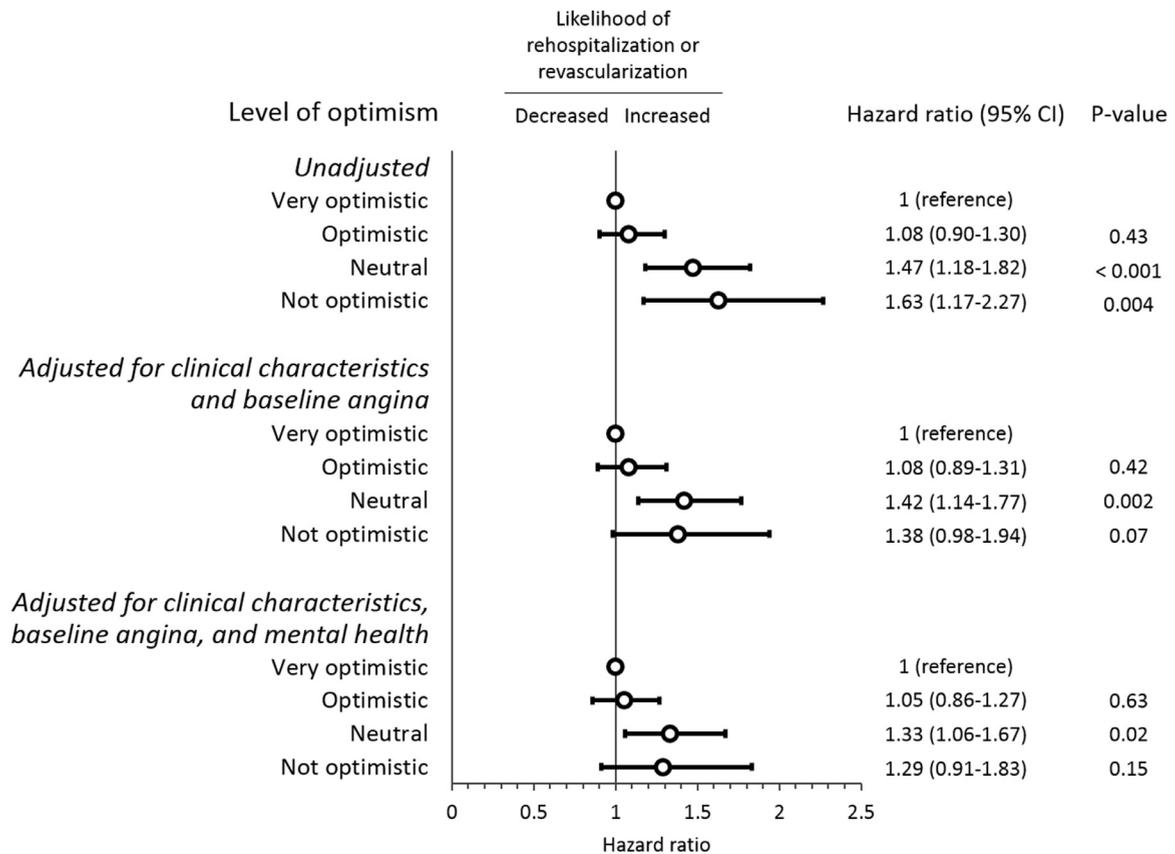

Figure 3. Association between baseline optimism and ischemia-driven revascularization or hospitalization.
Compared with very optimistic patients, neutral and not optimistic patients had a higher likelihood of ischemia-driven hospitalization or revascularization over the course of follow-up. This association was attenuated by the addition of baseline characteristics, but remained statistically significant for neutral patients.
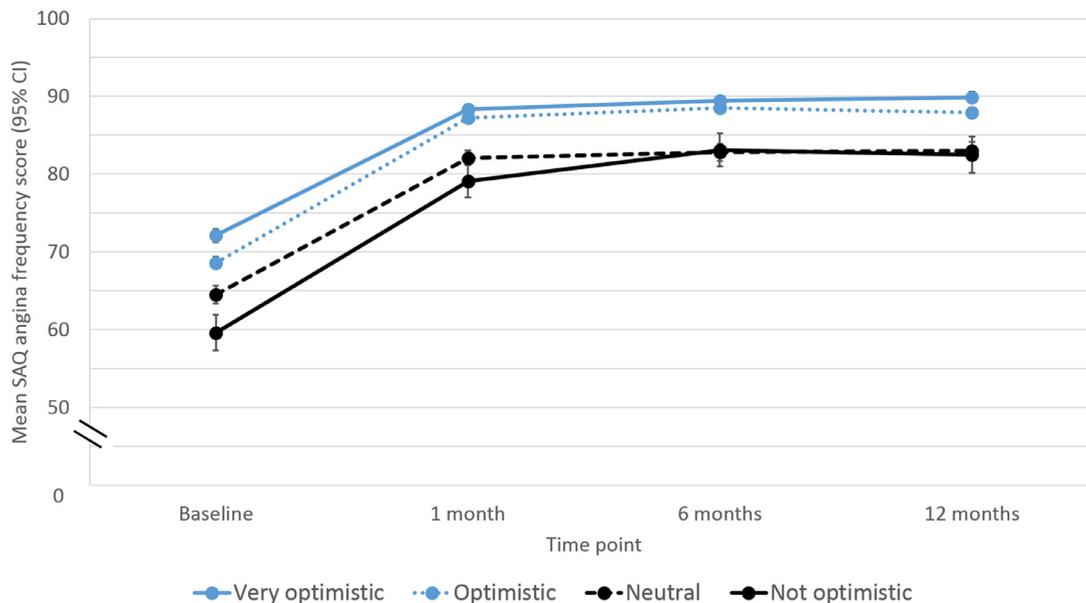
Figure 4. Association between baseline optimism and change in angina frequency over time.
Angina frequency decreased substantially (SAQ AF score increased) for patients between baseline and 1 month follow-up regardless of baseline optimism level, during which time all patients underwent a protocol-mandated PCI procedure. Angina frequency remained relatively stable from 1 to 12 months in all groups of patients. Compared with very optimistic patients, neutral and not optimistic patients had less improvement in angina frequency, which persisted after adjustment for baseline characteristic. PCI = percutaneous coronary intervention.

cardiovascular and all-cause mortality over 15-year follow-up.[4] Similarly, post-myocardial infarction (MI) patients with less stress and better coping self-efficacy have lower 2-year mortality.[18] The mechanism by which optimism affects mortality in patients with CAD is uncertain; however, a separate mechanism is likely to underlie the link we observed between patient-reported symptoms of angina and subsequent revascularization and hospitalization. Angina is an intrinsically variable condition, often only weakly correlated with objective myocardial ischemia, and healthcare utilization for angina is driven largely by patient-perceived symptom burden.[10,19,20] In patients with CAD, observed negative mood is more predictive of chest pain during exercise testing than ST segment depression,[21] and greater perceived risk of MI is more strongly associated with self-reported angina during activities of daily living than ischemia on stress imaging.[22] More broadly, individuals differ in their readiness to attribute symptoms to chronic illness, versus attributing symptoms to psychological factors or transient conditions.[23] If patients believe they will return to normal functioning, they may be less likely to attribute somatic symptoms to angina, and be less likely to present to medical attention. In this way, our results parallel studies in patients with MI showing that greater expectations for recovery were associated with a higher likelihood of return to work and better functional status.[5,18] The association we observed between optimism and improvement in angina frequency may also explain some of the difficulty untangling symptomatic benefit of PCI from the placebo effect.[24]

MI patients' expectations and beliefs about illness can be changed through brief interventions focused on explaining the pathophysiology of MI, exploring and challenging negative beliefs regarding recovery, and developing written action plans for reducing cardiovascular risk factors and recovering normal physical functioning.[25] These interventions improve rates of return to work, with a signal toward improvements in angina pain and exercise habits.[25,26] These interventions may also be useful in patients with chronic angina, but should be formally tested in this population. Until then, healthcare providers caring for patients with chronic angina should routinely ask patients how optimistic they are about returning to normal functioning. They should remind those with low levels of optimism that their prognosis for returning to a normal level of functioning may be quite good.

Our study does have a number of limitations. This is an observational study, and is subject to unmeasured confounding. Specifically, low expectations for recovery may reflect patients' accurate assessment of their prognosis, rather than a modifiable target for intervention, or it may be a marker of social isolation or low educational or socioeconomic status. Even if this is true, however, the prognostic information contained in the simple measure we employed did not appear to be accounted for by any of the standard measures of baseline risk and therefore might be useful as a novel risk marker even if "optimism" itself is not directly modifiable. Furthermore, RIVER-PCI did not systematically capture objective evidence of ischemia in patients with ischemia-driven hospitalization or revascularization, and so we cannot determine the association between optimism and objectively-defined ischemia-driven hospitalization or revascularization. In addition, clinical trials typically enroll a selected population, and patients that choose to enroll in a clinical trial may have different expectations for recovery than those who do not. Patient-level factors that may affect level of optimism, including uncertainty about prognosis and lack of disease-specific knowledge were not assessed. Finally, patients answered only 1 question from the 18-question Expectations for Coping Scale, and the performance and psychometric properties of this 1 question for assessing optimism has not been described.

In this study of patients with angina pectoris and incomplete revascularization after PCI, we found that optimism was associated with a fewer ischemia-driven revascularizations and hospitalizations during follow-up, and less angina. The association between self-reported optimism and better outcomes suggests an important role for health outlook and coping in patients with symptomatic CAD.

Disclosures

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi:10.1016/j.amjcard.2019.01.036.

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