ORIGINAL RESEARCH

Psychosocial Well-Being and Progression of Coronary Artery Calcification in Midlife Women

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BACKGROUND: Prevention of cardiovascular disease (CVD) is a public health priority. The combination of physical activity, a healthy diet, and abstaining from tobacco plays an important role in prevention whereas aspects of psychosocial well-being have largely been examined separately with conflicting results. This study evaluated whether the combination of indices of psychosocial well-being was associated with less progression of coronary artery calcium (CAC).

METHODS AND RESULTS: Participants were 312 women (mean age 50.8) from the SWAN (Study of Women's Health Across the Nation) ancillary Heart Study, free of clinical CVD at baseline. A composite psychosocial well-being score was created from 6 validated psychosocial questionnaires assessing optimism, vitality, life engagement, life satisfaction, rewarding multiple roles, and positive affect. Subclinical CAC progression was defined as an increase of ≥10 Agatston units over 2.3 years measured using electron beam tomography. Relative risk (RR) regression models examined the effect of well-being on CAC progression, progressively adjusting for sociodemographic factors, depression, healthy lifestyle behaviors, and standard CVD risk factors. At baseline, 42.9% had a CAC score >0, and progression was observed in 17.6%. Well-being was associated with less progression (RR, 0.909; 95% CI, 0.843–0.979; *P*=0.012), which remained significant with adjustment for potential confounders, depression, and health behaviors. Further adjustment for standard CVD risk factors weakened the association for the total sample (RR, 0.943; 95% CI, 0.871–1.020; *P*=0.142) but remained significant for the 134 women with baseline CAC>0 (RR, 0.921; 95% CI, 0.852–0.995; *P*=0.037).

CONCLUSIONS: Optimum early prevention of CVD in women may result from including the mind side of the mind-heart-body continuum.

Key Words: coronary calcium ■ health behaviors ■ midlife women ■ protective factors ■ psychosocial factors

More than 50% of US women over the age of 40 have cardiovascular disease (CVD), translating into annual medical costs of $318 billion.[1] Because CVD develops progressively over decades, an optimal approach to prevention would begin early by targeting midlife women undergoing the menopausal transition and identifying independent predictors of progression at that time of life. Coronary artery calcium (CAC) is a quantifiable, subclinical marker of atherosclerotic burden, worsening atherosclerosis, incident atrial fibrillation, and future CVD events in both younger and middle-aged individuals.[2–8] Thus it provides an excellent benchmark for the identification of early risk and protective factors.

It is now widely accepted that engaging in regular physical activity, abstaining from smoking, and maintaining a diet high in fruits, vegetables, and fiber but low in sugar, sodium, and fat prevent clinical coronary disease.[9] When examined in combination as a marker of a healthy lifestyle, composite health behavior scores

Nonstandard Abbreviations and Acronyms

SWAN   Study of Women's Health Across the Nation

have been associated with lower levels of intima-media thickness and adventitial diameter,[10] CAC,[11] and CAC progression[12] in both men and women.

Less is known about psychosocial risk and protective factors in midlife women. When single psychosocial risk factors (eg, hostility, anger, anxiety, cynicism, stress) are examined, they are generally unrelated to CAC level or progression.[13–16] The only exception is for depression, which predicts both CAC and CAC progression, particularly when it is recurrent.[17–19] Single psychosocial protective factors (eg, optimism, purpose in life) have not been significantly associated with CAC level.[13–15] Having rewarding social roles in midlife, however, is related to less CAC progression over 2.3 years.[20]

Unlike the emerging practice of examining health behaviors as a composite index that reflects a general healthy lifestyle, few studies examine psychosocial factors as a composite index that reflects general well-being. The only study to date, conducted in older,

postmenopausal women, found that a composite of psychosocial risk factors predicted CAC progression whereas a composite of positive psychosocial factors did not.[21] In midlife women, there have been no studies of the impact of general well-being, measured by a composite index of psychosocial protective factors, on progression of subclinical cardiovascular disease.

A recent scientific statement from the American Heart Association encouraged in-depth exploration of how psychosocial health and well-being can prevent the development of clinical CVD.[22] If positive psychosocial factors can reduce the risk of early CAC progression in healthy midlife women, they represent new targets for early prevention with potentially high patient acceptability.

The SWAN (Study of Women's Health Across the Nation) Heart Study, an ancillary to the parent SWAN study, features assessments of a variety of psychosocial factors measuring well-being defined broadly, and repeated measures of subclinical CAC, in midlife women. Thus, it provides an excellent opportunity to investigate the hypothesis that psychosocial well-being in midlife women is a novel target for early prevention of clinical cardiovascular disease.

METHODS

Transparency and Reproducibility

SWAN provides access to public use data sets that include data from SWAN screening, baseline, and follow-up visits (https://agingresearchbiobank.nia.nih.gov/). To preserve participant confidentiality, some, but not all, of the data used for this article are contained in the public use data sets. A link to the public use data sets also is located on the SWAN website: http://www.swanstudy.org/swan-research/data-access/. Investigators requiring assistance accessing the public use data set may contact the SWAN Coordinating Center by email at swanaccess@edc.pitt.edu. Data came from the SWAN Heart Study, an ancillary study of SWAN. The aim of the parent SWAN study, which started in 1996 to 1997, was to conduct annual assessments of a variety of risk and protective factors for the purpose of better understanding the natural history of the menopausal transition. SWAN included 3302 women from 5 ethnic backgrounds who were recruited from 7 geographic sites in the United States.[23] The SWAN Heart Study, conducted only at the Chicago and Pittsburgh sites, recruited only non-Hispanic White and Black participants and added an additional set of predictive variables and 2 CAC scans conducted 2.3 years apart. The institutional review boards at each site approved all protocols. All women provided written informed consent.

SWAN Heart began in 2001 to 2003, at the time of the SWAN visit 4 or 5. A total of 362 participants (33% Black) free of clinical CVD were recruited and completed 2 CAC scans. The analytic sample for the current report included 312 (86.2% of 362) participants. Exclusions were for incomplete psychosocial assessments (N=45) or missing health behavior assessments (N=5). Excluded participants were more likely to have CAC progression but did not differ from participants in the analysis on any other variables listed in Table 1.

Measures
Outcome

CAC at each time point was measured by electron beam computed tomography in 2 passes. The first provided landmarks and the second provided the coronary artery images. A total of 30 to 40 contiguous 3-mm-thick transverse images from the level of the aortic root to the apex of the heart were obtained during maximal breath holding. ECG triggering was used so that each 100-millisecond exposure was obtained during the same phase of the cardiac cycle (60% of the RR interval). Calcification, using the method established by Agatston,[24] was present if at least 3 contiguous pixels showed >130 Hounsfield units. The calcium score was the sum of scores for each of the 4 major epicardial coronary arteries categorized as 0 (none), 1–10 (minimal), or ≥10 (moderate).[25] Two scans were performed over an average of 2.3 years.

Psychosocial Well-Being

Psychosocial well-being was assessed as a composite of 6 scales: optimism (Life Orientation Test[26]), life engagement (Purpose in Life scale[27]), life satisfaction (Satisfaction with Life scale[28]), rewards from multiple roles (a modified version of the Multiple Roles Questionnaire[20,29]), positive affect (Positive and Negative Affect scale[30]), and vitality (Short Form Health Survey-36[31]). Life engagement, life satisfaction, vitality, and rewards from multiple roles were assessed at the SWAN Heart baseline visit. Optimism was assessed at SWAN visit 1 and is thought to be a stable personality trait.[32] Positive affect was assessed at SWAN visit 6 and has been shown to have long-term stability.[33] All scales have excellent internal consistency and reliability and are scored such that higher scores indicate higher levels of psychosocial well-being. All psychosocial scales were significantly positively correlated with each other (range: 0.23 to 0.47) and loaded on the same factor in a principal component analysis.

The psychosocial well-being score was modeled similarly to the established summary scores of health behaviors and of traditional CVD risk factors. As there are no established cut points for poor, intermediate,

Table 1. Baseline Characteristics in the Total Sample and by CAC Progression (Δ CAC≥10)

		Progression	
	Total	Yes	No
N (%)	312	55 (17.6)	257 (82.4)
Race			
White	214 (68.6)	39 (70.9)	175 (68.1)
Black	98 (31.4)	16 (29.1)	82 (31.9)
Age, y, mean (SD)	50.8 (2.7)	52.0 (2.8)	50.6 (2.6)[§]
Financial strain, n (%)	96 (30.8)	15 (27.3)	81 (31.5)
Menopausal status, n (%)			
Surgically menopausal	7 (2.2)	2 (3.6)	5 (1.9)
Postmenopausal	77 (24.7)	17 (30.9)	60 (23.3)
Late perimenopausal	32 (10.3)	6 (10.9)	26 (10.1)
Early perimenopausal	151 (48.4)	25 (45.5)	126 (49.0)
Premenopausal	27 (8.7)	4 (7.3)	23 (8.9)
Undetermined due to hormone therapy use	18 (5.8)	1 (1.8)	17 (6.6)
Psychosocial well-being composite*, mean (SD)	6.6 (3.1)	5.6 (3.0)	6.8 (3.1)[‖]
Health behavior composite[†], mean (SD)	3.4 (1.3)	3.2 (1.2)	3.4 (1.4)
Cardiovascular disease risk factor composite[‡], mean (SD)	5.6 (1.6)	4.4 (1.4)	5.8 (1.6)[§]
Depression, n (%)	36 (11.5)	10 (18.2)	26 (10.1)
CAC at baseline, n (%)			
=0	178 (57.1)	9 (16.4)	169 (65.8)[§]
>0	134 (42.9)	46 (83.6)	88 (34.2)

Study variables are presented as mean (SD) or n (%).
CAC indicates coronary artery calcium.
*Composite score of optimism, life engagement, life satisfaction, rewards from multiple roles, positive affect, and vitality; range 0–12; higher=better well-being.
[†]Composite score of physical activity, smoking, and diet; range 0–6; higher=better health behaviors.
[‡]Composite score of body mass index, blood pressure, cholesterol, and diabetes; range 0–8; higher=fewer risk factors.
[‖]$P<0.05$.
[§]$P<0.001$.

and ideal levels of the psychosocial measures that we included, we divided the score distribution for each scale into equal tertiles and assigned 0 points to the bottom, 1 point to the middle, and 2 points to the top tertile, corresponding to low, moderate, and high levels of the psychosocial well-being. Points from each of the 6 questionnaires were added, producing a composite score ranging from 0 to 12, with higher scores reflecting greater well-being.

Covariates

Healthy lifestyle behaviors were assessed at SWAN Heart baseline or earlier and included self-reported smoking status (assessed using standard questions

from the American Thoracic Association[34]), physical activity (assessed from the sports and exercise questions of the Kaiser Physical Activity Survey),[35,36] and diet (assessed by the 1995 Block Food Frequency Questionnaire[37,38]). Each health behavior was categorized into 3 levels (poor=0 points, intermediate=1 point, ideal=2 points), according to American Heart Association specifications[9] (Table S1). The sum of the scores ranged from 0 to 6 with higher scores indicating healthier behavior.

CVD risk factors were measured at the SWAN Heart baseline and included body mass index, cholesterol, blood pressure, and glucose. Each factor was categorized into 3 levels (poor=0 points, intermediate=1 point, ideal=2 points), according to American Heart Association specifications[9] (Table S1). The sum of the scores ranged from 0 to 8 with a higher score indicating fewer CVD risk factors and lower CVD risk. Age was calculated from self-reported date of birth and exam date. Race was self-reported as Black or White. Financial strain, a measure of socioeconomic status, was dichotomized as very or somewhat hard to pay for basics versus not hard at all.[39] Depressive symptoms were assessed in SWAN with the 20-item Center for Epidemiologic Studies Depression Scale[40] The 20-item scale measures the frequency of being bothered by depressive symptoms in the previous week on a scale of 0 (rarely) to 3 (most or all of the time). Item responses are summed for a total score (range 0–60); higher scores indicate more depressive symptomatology. A score of ≥16 is typically used to identify potential clinical depression.

Statistical Analysis

Participant characteristics were summarized using the mean and SD for continuous measures and N (%) for categorical measures. CAC progression was defined as an increase of ≥10 Agatston units since the first CAC assessment. For healthy midlife women, an increase by 10 units is clinically significant[41]; this cutoff has been used previously in studies of asymptomatic subjects to identify significant CAC progression.[20,21,42] Because calcium change ≥10 Agatston units was not rare in our sample, occurring in 17.6% of participants, and logistic regression could overestimate risk, we used relative risk (RR) regression[43] to model the probability of CAC progression. Log-binomial models with robust standard errors were used to estimate relative risk and CIs. When models did not converge, log-Poisson models[44] were used. The 5 models of the well-being composite were (1) unadjusted; (2) adjusted for CAC presence at baseline (CAC>0), time between scans, and potential sociodemographic confounders (baseline age [centered at the mean of 50.8], race, financial strain); (3) further adjusted for depressive symptoms; (4) further

adjusted for the health behavior composite, and (5) further adjusted for the CVD risk factor composite. In additional preplanned analyses, we restricted the sample to women with a positive CAC score at baseline, as that might reflect better pure progression. Analyses were conducted in SAS 9.4.

RESULTS

Table 1 presents a description of the cohort of 312 women at baseline, overall, and separated by CAC progression. On average, women were 50.8 years of age (SD=2.7, range 46–58), 98 (31.4%) were Black, and 96 (30.8%) reported financial strain. Prevalent CAC, defined as a calcium score >0, was detected in 134 (42.9%) of the women. CAC progression, defined as an increase ≥10 Agatston units over mean of 2.3 years (SD=0.4), occurred in 55 women (17.6%). Progression was more likely in women who were older, had CAC>0 compared with CAC=0 at baseline (P<0.001), a lower psychosocial well-being score, or a lower CVD risk factor score. Progression was not associated with race, financial strain, depressive symptoms, menopausal status, or the health behavior score.

Table 2 presents a series of relative risk regression models showing the association between the psychosocial well-being composite and CAC progression with progressive adjustment for covariates. In all models, the psychosocial well-being score was inversely related to relative risk of CAC progression. The unadjusted relative risk of CAC progression for the psychosocial well-being composite was estimated as RR, 0.909; 95% CI, 0.843–0.979; P=0.012. Progressive adjustments for CAC presence at baseline, sociodemographic confounders, depressive symptoms, and the health behavior composite did not change this association. Further adjustment for the CVD risk factor composite reduced this association to nonsignificance, RR, 0.943; 95% CI, 0.871–1.020; P=0.142. As the CI for CAC presence at baseline is rather wide, the adjustment for CAC presence might yield biased estimates for other parameters. We therefore reran models 2 to 5 without this indicator. Estimates for other parameters were only minimally affected, and conclusions did not change. Behavioral factors may mediate the relation between psychosocial well-being or depression and CAC progression. We therefore tested for interactions of the health behavior score with well-being and with depression, but none of the interactions was statistically significant.

A second set of analyses was limited to the subgroup of 134 women with CAC >0 at baseline. The association between the psychosocial well-being score and progression of CAC was similar but stronger than in the overall sample, and remained significant in the

Table 2. Association of the Well-Being Composite and CAC Progression With Progressive Adjustment for Covariates: N=312

	Model 1	Model 2	Model 3	Model 4	Model 5
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Intercept	0.317 (0.198–0.506)	0.069 (0.019–0.244)	0.067 (0.019–0.241)	0.083 (0.021–0.318)	0.285 (0.047–1.744)
Well-being composite	0.909 (0.843–0.979)*	0.914 (0.854–0.977)*	0.917 (0.853–0.986)*	0.922 (0.855–0.995)*	0.943 (0.871–1.020)
CAC>0 at baseline		6.344 (3.227–12.473)*	6.318 (3.219–12.402)*	6.289 (3.208–12.329)*	4.719 (2.208–10.090)*
Age, y, centered		1.406 (1.106–1.786)*	1.406 (1.106–1.787)*	1.419 (1.117–1.804)*	1.365 (1.068–1.743)*
Black		0.719 (0.444–1.165)	0.729 (0.445–1.194)	0.711 (0.427–1.182)	0.692 (0.416–1.152)
Financial strain		0.706 (0.418–1.193)	0.704 (0.416–1.19)	0.693 (0.410–1.170)	0.683 (0.394–1.183)
Time between scans, y		1.196 (0.770–1.859)	1.191 (0.767–1.848)	1.184 (0.765–1.835)	1.112 (0.718–1.720)
Depression			1.091 (0.669–1.781)	1.120 (0.684–1.833)	1.048 (0.621–1.767)
Health behavior composite				0.936 (0.792–1.106)	0.925 (0.781–1.095)
Cardiovascular disease risk factor composite					0.823 (0.710–0.954)*

Model 1: unadjusted.
Model 2: adjusted for confounders.
Model 3: additionally adjusted for depression.
Model 4: additionally adjusted for health behavior composite.
Model 5: additionally adjusted for cardiovascular risk factor composite.
CAC indicates coronary artery calcium; and RR, relative risk.
*All variables significantly ($P<0.05$) related to CAC progression.

fully adjusted model when the CVD risk factor composite was added (RR, 0.921; 95% CI, 0.852–0.995; P=0.037; Table 3).

DISCUSSION

In this population of midlife women without clinical CVD, we found a significant burden of subclinical disease: 42.9% had CAC>0, consistent with other studies in younger women[6,45,46] Progression of CAC occurred in 17.6% overall: 5.1% of those with CAC=0 at baseline, and 34.3% in those with CAC>0 at baseline. This supports the potential importance of early preventive interventions for women at midlife as they enter the menopausal transition, lose their estrogen protection, and begin to increase cardiovascular risk.

Psychosocial well-being is not simply the absence of negative psychological states such as depression but exerts an independent association with cardiovascular outcomes above and beyond them.[22] The psychosocial well-being score studied here was a composite that included the established psychosocial factors of optimism, life engagement, life satisfaction, rewarding social roles, positive affect, and vitality. It was associated with less CAC progression and was not accounted for by the negative psychological state of depression.

Psychosocial well-being predicted CAC progression but a composite of the established health behaviors of smoking, diet, and physical activity did not. The reasons for this result are unclear. Deleterious health behaviors were well represented in the sample, so a bias toward the null from a low-risk population seems unlikely. The health behavior score categorized risk based upon cut points drawn from clinical guidelines, and so the categories would not appear to be insensitive to increased risk. These self-reports were from questionnaires all of which have been validated, so measurement imprecision, although possible, seems unlikely.

The association between psychosocial well-being and CAC progression was weakened only when the standard CVD risk factor composite of blood pressure, cholesterol, glucose, and body mass index was entered into the model. This suggests that psychosocial well-being may contribute to CAC progression through its influence on these standard CVD risk factors. However, in the subsample of women with prevalent CAC at baseline, the association of psychosocial well-being and CAC progression was stronger and not affected by adjustment for CVD risk factors. As CAC progresses, other, nontraditional pathways between

Table 3. Association of the Well-Being Composite and CAC Progression for Women With CAC>0 at Baseline With Progressive Adjustment for Covariates: N=134

	Model 1	Model 2	Model 3	Model 4	Model 5
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Intercept	0.547 (0.363–0.825)	0.429 (0.131–1.404)	0.400 (0.124–1.292)	0.484 (0.140–1.670)	0.762 (0.168–3.453)
Well-being composite	0.923 (0.860–0.990)*	0.897 (0.836–0.961)*	0.907 (0.843–0.975)*	0.911 (0.846–0.981)*	0.921 (0.852–0.995)*
Age, y, centered		1.297 (1.028–1.636)*	1.296 (1.025–1.639)*	1.309 (1.037–1.651)*	1.289 (1.016–1.635)*
Black		0.802 (0.488–1.318)	0.842 (0.501–1.415)	0.822 (0.483–1.399)	0.811 (0.478–1.375)
Financial strain		0.597 (0.342–1.040)	0.587 (0.336–1.027)	0.578 (0.333–1.006)	0.579 (0.329–1.019)
Time between scans, y		1.282 (0.814–2.021)	1.254 (0.802–1.963)	1.251 (0.803–1.950)	1.207 (0.766–1.902)
Depression			1.283 (0.781–2.109)	1.323 (0.806–2.171)	1.268 (0.763–2.106)
Health behavior composite				0.939 (0.781–1.128)	0.934 (0.778–1.121)
Cardiovascular disease risk factor composite					0.915 (0.796–1.053)

Model 1: unadjusted.
Model 2: adjusted for confounders.
Model 3: additionally adjusted for depression.
Model 4: additionally adjusted for health behavior composite.
Model 5: additionally adjusted for cardiovascular risk factor composite.
CAC indicates coronary artery calcium; and RR, relative risk.
*All variables significantly (P<0.05) related to CAC progression.

psychosocial well-being and CAC progression may be activated.

These data were drawn from a well-characterized cohort of Black and White women similar on socio-economic background, free of clinical CVD, and assessed longitudinally on a variety of CVD risk factors, health behaviors, and psychosocial factors using well-validated scales. An important feature is that our study went beyond the common practice of examining single risk or protective factors in isolation and instead created composite scores that provide a broader perspective on the psychosocial milieu, the health behavior milieu, and CVD risk. This made it possible to go beyond, for example, studying optimism to studying well-being, beyond studying physical activity to studying a healthy lifestyle. This approach is gaining popularity in the hope that a more comprehensive assessment of the whole person will translate into stronger associations with CVD outcomes.

A limitation of this study is its reliance upon self-reports for assessment of health behaviors, which may have the undesired effect of underestimating their effect on CAC progression. However, any bias in self-reported measures is shared across the well-being and health behavior composites, and it does not, therefore, weaken the argument that the whole person approach to CVD prevention should include psychosocial well-being. The association between psychosocial well-being and CAC progression was consistent and difficult to eliminate with progressive adjustments.

CONCLUSIONS

The significance of these findings is their implication for optimum prevention of cardiovascular disease in midlife women. They suggest that early preventive efforts would be more effective if they focused on not only health behaviors but also general well-being. The implications for clinical practice include considering the value of a brief screen for assessment of psychological health, a brief query to understand the psychosocial context within which the patient lives, and referrals to providers that focus on the mind side of the mind-heart-body continuum.

Supplemental Material

Table S1

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Supplemental Material

Table S1. Definition of ideal, intermediate, and poor Health Behaviors and CVD Risk Factors.

	Poor = 0 points	Intermediate = 1 point	Ideal = 2 points
Health Behaviors			
Smoking	Current	Former	Never
Physical Activity	< once/month	≥ once/month, but not ideal	≥ 2 hours/week, ≥ 9 months/year with at least a moderate increase in heart rate and breathing
Diet	0 components *	1 component	≥ 2 components
CVD Risk Factors			
BMI (kg/m^2)	≥ 30	25 − 29.9	< 25
Blood pressure (mmHg)	SBP ≥ 140 or DBP ≥ 90	< 120/80, treated or SBP 120 − 139 & DBP 80 − 89, untreated	< 120/80, untreated
Total cholesterol (mg/dL)	≥ 240	< 200, treated or 200 − 239, untreated	< 200, untreated
Glucose (mg/dL)	≥ 126	< 100, treated or 100 − 125, untreated	< 100, untreated

*Components of the diet score were defined as: fiber ≥25 g; sodium <1.1 g/1000 kcal; trans fat <1% kcal; ratio of poly + monounsaturated fats (gm) to saturated fats (gm) >2.5; fruits and vegetables ≥5 servings; dairy ≥1.3 cups/1000 kcal; grains ≥3 oz/1000 kcal; and added sugar <2.5% total kcal.

CVD indicates cardiovascular disease; BMI body mass index; DBP diastolic blood pressure; SBP systolic blood pressure.