Examining the Interplay of Social Support, Depression, and Blood Pressure: The Strong Heart Family Study

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Abstract

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Compared to the general US population, American Indian (AI) adults have disproportionately higher rates of mental health symptoms, including depression. In 2019, over 18% (n=260,000) of surveyed American Indians/Alaska Natives (AI/AN) 18 years of age or older experienced mental illness during the past year. Several cross-sectional studies have also shown that depression is common in individuals with uncontrolled hypertension (HTN) and may interfere with blood pressure control. To date, few studies have examined the association of symptoms consistent with depression with the development of HTN among AIs despite the high burden of HTN and depression in this population. The purpose of this analysis was to examine the association of depressive symptoms on incident HTN in a large cohort of AIs. As a secondary exploratory analysis, we also examined whether self-reported community and cultural engagement (CCE) impacted this relationship. Results from our analysis suggest that participants who reported depressive symptoms were more likely to develop HTN during a 3-to-8-year follow-up when compared to participants who did not report depressive symptoms. CCE did not appear to impact the observed association of depression and incident HTN. In conclusion, we found those who

experienced symptoms consistent with depression to be at increased risk of incident HTN, consistent with our hypothesis.

1. Introduction

The prevalence of hypertension (HTN) and depression are high in the general United States (US) population. It is estimated that in 2017-2020, 48% (120 million) of adults had prevalent HTN [1,2]. Additionally, approximately one in ten US adults (aged 18 and older) and one in five young adults (aged 18 to 25) experienced depression during the past 12 months[3]. Compared to the general US population, American Indian (AI) adults have disproportionately higher rates of cardiovascular risk factors and mental health issues, including HTN and depression. In 2019, over 18% (n=260,000) of surveyed American Indians/Alaska Natives (AI/AN) 18 years of age or older experienced mental illness during the past year[4]. In the Strong Heart Family Study (SHFS), the largest cohort study of cardio-metabolic health in AIs in the US, nearly 50% of participants reported depressive symptoms[5] at the baseline study examination. Of these participants, approximately 30% experienced moderate to severe symptoms of depression.

Established research has shown that depression is associated with HTN, and a meta-analysis of prospective cohort studies report depression as an independent risk factor for HTN[6]. Several cross-sectional studies have also shown that depression is common in individuals with uncontrolled HTN and may interfere with blood pressure control[6,7].To date, few studies have examined the association of depression with development of HTN among AIs[8] despite the high burden of HTN and depression in this population.

Prior research has shown that community and cultural engagement (CCE), such as participation in community arts, volunteering, or social groups, can support recovery from depression[9,10] and also lower blood pressure[11] in the general population. Numerous CCE-focused initiatives have been implemented to prevent HTN in diverse community contexts, including the use of churches and barbershops to monitor blood pressure, implement heart health education, and provide healthy diet/physical activity support groups[12]. However, few longitudinal studies have examined whether CCE might impact the association of depression with development of HTN. In a small pilot randomized trial (n=54), participants who received an enhanced intervention that included increased resources for social support demonstrated better blood pressure control and fewer depressive symptoms at follow-up when compared to participants who received a basic hypertension and depression management intervention (i.e., intervention that did not address social support)[13]. Unfortunately, the study focused exclusively on participants with co-morbid depression and HTN, and it is unknown whether CCE impacts the relationship of depressive symptoms with development of HTN.

The purpose of this analysis was to examine the relationship of depressive symptoms with incident HTN in a large cohort of AIs. As a secondary exploratory analysis, we also examined whether self-reported CCE impacts this relationship. We hypothesized that participants who reported a greater number of depressive symptoms were more likely to develop HTN than participants who reported fewer depressive symptoms. Additionally, we hypothesized that the magnitude of the association of depressive symptoms with HTN would be higher among participants who reported low levels of CCE.

2. Methods

2.1 Study design and data source

This analysis used data from the Strong Heart Family Study (SHFS), a family-based longitudinal study of cardiovascular disease (CVD) and its risk factors in 12 AI communities in Arizona, North Dakota, South Dakota, and Oklahoma. The study comprised of 2,756 AI individuals 14-93 years old from 92 multi-generational families. Participants completed two exams over an eight-year period: a baseline exam in 2001-2003 and a follow-up exam in 2006-2009. Each study examination included a personal interview, physical examination, medication review, and laboratory work-up. Details of the study design have been described in detail in previous publications [14]. The SHFS was approved by the institutional review board from each Indian Health Services and written informed consent was obtained from study participants at each study examination.

Of the 2,756 participants who completed the baseline examination, we excluded participants who were pregnant (n=3), had prevalent HTN (i.e., use of antihypertensive medications, diuretics, or betablockers; SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg) (n=713), did not complete the depression assessment (n=195), or reported taking antidepressant or antipsychotic medications at baseline (n=48). We also excluded participants who did not complete the follow-up exam (n=389). In total, 1,408 participants comprised the analytic sample.

2.2 Measures

Exposure of interest: symptoms consistent with depression

The exposure of interest for this study was experiencing symptoms consistent with clinical depression (yes/no). Depressive symptoms were assessed at baseline using the 20-item Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a valid and reliable instrument used to assess depressive symptoms experienced during the past week[15]. Symptoms assessed include, for example, feelings of guilt and hopelessness, feeling blue, experiencing insomnia, and inability to focus. For each question, response options were captured using a four-point Likert-scale ranging from 0 (none of the time/rarely) to 3 (most of the time). Responses to individual questions were summed after reverse coding of positively framed items per established CES-D guidelines (total possible score range: 0-60). A higher CES-D score is consistent with greater depressive symptomology, and scores above of 16 or higher have been found to be consistent with diagnoses of major depressive disorder[16]. As in previous SHFS analyses, CES-D scores were categorized as consistent with depression (CES-D >= 16) versus not consistent with depression (CES-D<16)[16,17].

Outcomes of Interest: Incident HTN and systolic and diastolic blood pressure

The primary outcome of interest for this study was incident HTN, and secondary outcomes were continuous measures of systolic and diastolic blood pressure, all measured at follow-up (2006-2009). At each study exam, blood pressure was measured 3 times on the right arm with a standard mercury sphygmomanometer after 5 minutes rest with the participant seated[18]. The average of the first 2 measurements taken at both the baseline and follow-up exams were used for these analyses. Incident HTN was defined as SBP ≥140 mm Hg, DBP ≥90 mm Hg, or use of HTN medications at follow-up.

Measurement of covariates

Detailed information on important confounding variables including demographic characteristics, diet and exercise, and other CVD risk factors (e.g., smoking status and prevalent diabetes) were collected at the baseline examination (2001-2003) using standardized interviews.

Past year diet was assessed using a Block 119-item food frequency questionnaire with ethnic foods supplement[19]. Diet quality was classified using the Alternative Healthy Eating Index (AHEI)[18]. Physical activity was captured using Accusplit AE120 pedometers[14]. Average steps per day for each participant were estimated as the mean steps per day across the 3-7 days that the pedometer was worn.

CCE was categorized dichotomously based on participants' response to the question: "Can you count on anyone to provide you with emotional support (talking over problems or helping you make a difficult decision)?" Only a sub-set of the study sample (n=332) completed the CCE assessment.

Anthropometric measures were obtained with the participant wearing light clothing and no shoes. Bodyweight was measured using a Tanita BWB-800 5 Adult Digital Scale. Height was measured using a vertical mounted ruler. Body mass index (BMI) was calculated as body weight divided by height-squared (kg/m^2)[20].

Blood samples were collected after a 12-hour overnight fast and were stored at -70 degrees Celsius. Plasma glucose, LDL cholesterol, and HDL cholesterol were measured using enzymatic methods[21]. Diabetes was defined based on 2003 ADA criteria[22], including use of insulin/oral anti-diabetic medication or fasting plasma glucose level greater than or equal to 126 mg/dL.

Statistical Analyses

For the primary analysis, two sequential generalized estimating equations (GEE) models were run to assess the association of symptoms consistent with depression on incident HTN. GEE was used to address potential familial correlation between participants within the data and were run with the assumption of an independent working correlation and specification of robust standard errors (SE). In total, there were 86 family clusters included in the analysis with a mean of 16 participants per family cluster (range: 1-57 participants per family cluster). Model 1 (minimally adjusted model) adjusted for age (years), sex (male or female), and site (Arizona, Oklahoma, North/South Dakota). Model 2 (primary model) further adjusted for CVD risk factors selected *a priori* based on potential associations with depression and blood pressure, including: (LDL cholesterol (mg/dL), HDL cholesterol (mg/dL), prevalent diabetes status (yes/no), smoking status (never/former/current), BMI (kg/m^2), AHEI (score), and physical activity (steps per day).

In secondary analyses, we examined the association of symptoms consistent with depression at baseline on systolic (and diastolic separately) blood pressure at the follow-up exam (i.e., 3-8 years later) by fitting the same 2 models described above with additional adjustment for baseline systolic and diastolic blood pressure, respectively. Statistical significance was based on Wald tests.

To better understand whether risk estimates for secondary analyses were driven by participants who developed HTN and started taking blood-pressure lowering medications between the baseline and follow-up exam, we repeated secondary analyses excluding participants who reported taking HTN medication at follow-up.

In the exploratory analyses, we examined potential interaction of depression and CCE on incidence of HTN by inclusion of an interaction term (depression*CCE) in the primary model and testing for significance using a Wald test.

Analyses were conducted using complete case analysis. All statistical analyses were performed in R Software.

3. Results

The median age of study participants was 33.5 years old (range: 14.1-86.0) and 40.5% of the analytic cohort identified as male. Baseline characteristics of study participants according to CES-D (<16 or >=16) are shown in Table 1. In total, 27.3% (n=385) of study participants reported symptoms consistent with depression at baseline (i.e., CES-D>=16). Participants who reported baseline symptoms consistent with depression were more likely to be female (74.0% versus 59.5%) and were slightly younger (32.6 years old versus 35.4 years old), had less education (11.5 years of education versus 12.4 years of education), higher BMI (31.2 versus 29.9), and reported less ambulatory activity (5,640 steps per day versus 6,690 steps per day) compared to participants with CES-D<16. There was no difference in diet quality based on CES-D.

During the follow-up period, 257 participants developed HTN. Table 2 describes baseline characteristics of study participants according to HTN status at follow-up. Participants who developed HTN were more likely to be older (42.0 years old versus 33.0 years old), male (44.7% versus 34.7%), and have prevalent diabetes at baseline (21.8% versus 6.6%), reported fewer steps per day (5,730 steps per day versus 6,540 steps per day), and had higher BMI (32.4 versus 29.8) than participants who did not develop HTN during follow-up. Additionally, participants who developed HTN were more likely to smoke (47.3% versus 36.7%) than participants who did not develop HTN. We observed no differences in education or diet quality based on HTN status.

In multivariable GEE analyses, those with baseline symptoms consistent with depression (CES-D >=16) had 56% higher odds of developing HTN during the 3-to-8-year follow-up (OR=1.54, 95% CI: 1.06, 2.23) compared to those with baseline symptoms not consistent with depression (CES-D <16) after adjustment for age, demographic, behavioral, and dietary factors (Table 3).

In secondary analyses, we did not observe an association of depressive symptoms at baseline with systolic or diastolic blood pressure at follow-up (assessed continuously) after adjustment for the primary model covariates (Table 4). Study results were not materially changed when participants who started blood pressure medication between baseline and follow-up (n=41) were excluded from secondary analyses.

There was also no statistically significant interaction of baseline depression status with CCE on risk of HTN, in a model adjusted for age, sex, education, center, baseline blood pressure measurement, HDL cholesterol, LDL cholesterol, smoking status, BMI, diabetes status, physical activity, diet index, sex, site, and prevalent diabetes (p-value= 0.35).

4. Discussion

In this large cohort study of AI adults, participants who reported symptoms consistent with depression at baseline were more likely to develop HTN when compared to participants who did not report symptoms consistent with depression. This finding supports the hypothesis that depression is associated with an increased risk of incident HTN.

The findings herein support findings from 5 prospective studies and one meta-analysis of 9 studies in non-AI populations that show a positive association of depressive symptoms with risk of HTN[6,23–26]. In these studies, participants who reported more depressive symptoms had poorer cardio-metabolic health outcomes, including higher risk of HTN[6,27,28]. Although these studies use a wide variety of instruments to assess depressive symptoms (e.g., 30-item General Health Questionnaire Depression subscale[26] , Center for Epidemiologic Studies Depression (CES-D-4 item) questionnaire[27–29], and Cohen Perceived Stress Scale (PSS) [27] (taken together)), these findings highlight a positive association of depressive symptoms and risk of HTN in diverse populations across a wide range of ages and geographical contexts.

Our findings are discordant with 4 studies that reported no (or inverse) associations of depressive symptoms with incident HTN[30–33]. Differences in study populations according to age and geography may account for contradictory findings across studies[33]. For instance, although it has not been extensively studied, it is possible that the etiology of depressive symptoms may be different in the elderly versus younger populations[34]. Additionally, access to quality healthcare (including mental health services) differs according to area of residence (e.g., urban versus rural; USA versus non-USA; AI reservation versus non-reservation). Finally, the lived experiences of AIs are different than non-AIs, including the impact of multi-generational historical trauma and structural racism on mental and physical health.

To our knowledge, no studies to date have examined the relationship of depression with the development of HTN in AIs. In one cross-sectional study among 500 older AI/AN adults who reside in urban areas in the Pacific Northwest, clinic patients with prevalent HTN were more likely to have depression than patients without HTN[35]. However, this cross-sectional study was unable to infer whether depression increased risk of HTN or vice versa. Our work complements findings from the SHFS that reported that participants with severe depressive symptoms (i.e., CES-D>=16) have a 71% higher risk of developing CVD when compared to participants who did not report symptoms consistent with depression, OR=1.71 (95% CI: 1.01, 2.91)[20].

Several studies in Indigenous populations point to high levels of depression and cardiovascular risk factors/diseases[36–38]. The high burden of depressive symptoms in AIs may be due at least in part to generations of oppression and historical trauma faced by AIs, including forced migration to reservations, abuse and neglect of AI youth at government-operated boarding schools, and near eradication of many Tribes' languages, spiritual practices, and cultures from society[39].

Historical trauma and present-day socioeconomic factors may also impact the availability, accessibility, and utilization of mental and physical health services by AI communities. Due to poor interactions with the US government historically, present-day AI communities may have lost trust in many institutional sources, including some healthcare settings[40]. Additionally, given the historical relationship between AI and US governmental authorities, many AIs may prefer to seek care from an AI healthcare providers, yet there is a scarcity of AI mental and physical healthcare providers available[41]. Coupled with limited access to healthy foods, opportunities for physical activity, and high rates of poverty in many AI communities, this may in part explain the high rates of depression and cardiovascular risk in many AI communities.

The mechanism by which depressive symptoms may influence risk of HTN is multi-faceted, and include stress, inflammation, and neurotransmission processes. Studies have shown that depression can increase the body's sympathetic tone and cortisol, which increase systemic inflammation, and lead to many cardio-metabolic risk factors, including HTN[42]. Established research has linked dopamine to depression as this neurotransmitter plays a vital role in an individual's ability to experience pleasure. Specifically, a dopamine deficit has been linked to anhedonia, the core feature of major depressive disorder[43]. Recent studies have shown that lack of dopamine at key brain sites can increase blood pressure[7]. Depression may also increase risk of key cardiovascular risk factors, including physical inactivity, obesity, poor dietary practices, and low social support[44].

Although we observed a statistically significant association of symptoms consistent with depression with incident HTN, we did not observe a statistically significant association of depressive symptoms with continuous measures of diastolic or systolic blood pressure at follow-up. This may in part be due the definition of HTN--which was based on a dichotomous threshold (SBP ≥140 mm Hg, DBP ≥90 mm Hg, or use of HTN medication at follow-up among participants without HTN at baseline) and did not account for trivial changes in blood pressure between baseline and follow-up for participants close to the cut point. It is also possible that participants free of HTN at baseline developed HTN at some point during the 3-to-8-year follow-up and started medications at that time. These participants would contribute to estimates of incident HTN but would have controlled blood pressure at follow-up due to medication usage. However, only 41 participants started HTN medications between baseline and follow-up and excluding these participants from analyses did not meaningfully change results. We also did not observe a statistically significant interaction of CCE with depression status on risk of incident HTN. This may be in part due to an incomplete measure of CCE (i.e., we only had one question on CCE) and/or limited power since this question was only collected on a sub-set of SHFS participants (n= 332). Future studies are needed that include a comprehensive measure of CCE to better assess whether CCE may mitigate the risk of symptoms consistent with depression on incident HTN.

This study has many strengths. To our knowledge, this is the first study to examine the association of depressive symptoms with incident HTN in a well-characterized multi-tribal cohort of AIs with detailed measures of depressive symptoms, HTN, and key covariates. This study is not without limitations. Although CES-D has been shown to be a valid and reliable measure of depressive symptoms in noninstitutionalized diverse populations[45,46], it is susceptible to social desirability bias. Residual confounding by unmeasured or poorly measured factors is possible. Finally, although these results are generalizable to those represented in the SHFS, it is unclear if findings are generalizable to other populations.

In conclusion, in this large study of AI adults, symptoms consistent with depression were found to be positively associated with incident HTN. This study adds to a growing body of evidence identifying mental health as a key determinant of CVD risk and suggests the need for mental health outreach programs that focus on prevention of depression to mitigate downstream effects on HTN.

Appendix 1. Tables

Table 1. Characteristics of Study Participants According to Baseline Depressive Symptoms

	CES-D score not consistent with depression (CES-D<16)	**CES-D score consistent with depression (CES-D >= 16)**	**Total Sample**
	(N=1023)	**(N=385)**	**(N=1408)**
Sex			
Male	414 (40.5%)	100 (26.0%)	514 (36.5%)
Female	609 (59.5%)	285 (74.0%)	894 (63.5%)
Age (years)			
Mean (SD)	35.4 (14.7)	32.6 (12.8)	34.6 (14.3)
Education (years)			
Mean (SD)	12.4 (2.19)	11.5 (2.17)	12.2 (2.23)
BMI (kg/m^(2))			
Mean (SD)	29.9 (6.88)	31.2 (8.28)	30.2 (7.31)
Diabetes			
Diabetes	89 (8.7%)	43 (11.2%)	132 (9.4%)
No diabetes	929 (90.8%)	339 (88.1%)	1268 (90.1%)
Current smoker			
Yes	375 (36.7%)	182 (47.3%)	557 (39.6%)
No	647 (63.2%)	202 (52.5%)	849 (60.3%)
AHEI			
Mean (SD)	43.4 (9.06)	43.2 (8.76)	43.3 (8.98)
Physical activity (continuous, steps per day)			
Mean (SD)	6690 (3980)	5640 (3510)	6400 (3880)

* missingness removed, therefore not all columns add up 100%
Center for Epidemiologic Studies Depression Scale (CES-D); Alternative Healthy Eating Index (AHEI)

Table 2. Demographic and health characteristics by HTN status at follow-up.			
	No HTN (N=1151)	**HTN (N=257)**	**Total (N=1408)**
Depression			
Not consistent with depression (CES-D<16)	844 (73.3%)	179 (69.6%)	1023 (72.7%)
Consistent with depression (CES-D >= 16)	307 (26.7%)	78 (30.4%)	385 (27.3%)
Sex			
Male	399 (34.7%)	115 (44.7%)	514 (36.5%)
Female	752 (65.3%)	142 (55.3%)	894 (63.5%)
Age (years)			
Mean (SD)	33.0 (13.6)	42.0 (14.9)	34.6 (14.3)
Education (years)			
Mean (SD)	12.1 (2.23)	12.4 (2.22)	12.2 (2.23)
BMI (kg/m^(2))			
Mean (SD)	29.8 (7.15)	32.4 (7.63)	30.2 (7.31)
Diabetes			
Diabetes	76 (6.6%)	56 (21.8%)	132 (9.4%)
No diabetes	1068 (92.8%)	200 (77.8%)	1268 (90.1%)
Current smoker			
Yes	446 (38.7%)	111 (43.2%)	557 (39.6%)
No	703 (61.1%)	146 (56.8%)	849 (60.3%)
AHEI			
Mean (SD)	43.1 (9.09)	44.5 (8.40)	43.3 (8.98)
Physical activity (continuous, steps per day)			
Mean (SD)	6540 (3870)	5730 (3870)	6400 (3880)

Center for Epidemiologic Studies Depression Scale (CES-D); Alternative Healthy Eating Index (AHEI)

Table 3. Odds of Incident HTN by depressive symptom exposure, all study centers.				
	Model 1 (n=1,408)		Model 2 (n=1,168)	
	OR	95% CI	OR	95% CI
Depressive symptom categories				
Not consistent with depression (CES-D<16)	1	Referent	1	Referent
Consistent with depression (CES-D >= 16)	1.54	1.12-2.11	1.54	1.06 – 2.23

Model 1: Adjusted only for age, sex, education, center.
Model 2: Further adjusted for HDL cholesterol, LDL cholesterol, smoking status, BMI, diabetes status, physical activity, diet index.

Table 4a. Changes in systolic blood pressure by depressive symptom exposure, all study centers.				
	Model 1 (n=1,166)		Model 2 (n=1,166)	
	β	95% CI	β	95% CI
Depressive symptom categories				
Not consistent with depression (CES-D<16)	0	Referent	0	Referent
Consistent with depression (CES-D >= 16)	0.5	-1.11 – 2.12	0.06	-1.59 – 1.72
Table 4b. Changes in diastolic blood pressure by depressive symptom exposure, all study centers.				
	Model 1 (n=1,166)		Model 2 (n=1,166)	
	β	95% CI	β	95% CI
Not consistent with depression (CES-D<16)	0	Referent	0	Referent
Consistent with depression (CES-D >= 16)	0.93	-0.29 – 2.14	1.08	-0.18– 2.34

Table 4a Model 1: Adjusted only for age, sex, education, center, baseline systolic blood pressure measurement.
Table 4a Model 2: Further adjusted for HDL cholesterol, LDL cholesterol, smoking status, BMI, diabetes status, physical activity, diet index.
Table 4b Model 1: Adjusted only for age, sex, education, center, baseline diastolic blood pressure measurement.
Table 4b Model 2: Further adjusted for HDL cholesterol, LDL cholesterol, smoking status, BMI, diabetes status, physical activity, diet index.

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