Title page

a. Title: Diabetes-specific food insecurity is associated with impaired heart rate variability independent of glycemic control: Exploratory findings among Latinos with type 2 diabetes

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d. Footnotes to the title disclosing:

(i) Links to supporting data deposited in repositories such as Dryad or figshare, as well as the DOI for the data deposit;

Not applicable

(ii) A list of abbreviations and their definitions for all abbreviations used in the text if there are 3 or more;

HRV, Heart rate variability

ECG, electrocardiogram

SDNN, standard deviation of the R-R interval

FI, Food insecurity

T2DM, type 2 diabetes

CALMS-D, Community health educators Assisting Latinos Manage Stress and Diabetes

A1C, glycated hemoglobin concentrations

VLF, very low frequency

LF, low frequency

HF, high frequency

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Abstract

Background. Food insecurity (FI), diabetes prevalence, and poor diabetes outcomes all disproportionately affect Latinos in the U.S. Heart rate variability (HRV) is reflects autonomic tone and is associated with glycemic control and predicts mortality in type 2 diabetes. It is unknown whether food insecurity is related to HRV and, if so, whether glycemic control accounts for this association.

Objective. This exploratory, cross-sectional study examined FI and HRV among U.S. Latinos with type 2 diabetes.

Methods. Participants reported demographics, socioeconomic status, and FI including the 6-item USDA food security module and a one-item measure of diabetes-specific food security. Participants wore an ambulatory electrocardiogram monitor for 24 hours. In the time domain, HRV was assessed with the standard deviation of the R-R interval (SDNN). In the frequency domain, the power spectrum was integrated over three frequency bands-very low frequency (VLF), low frequency (LF), and high frequency (HF), and then natural log transformed. Unadjusted ANOVA and ANCOVA adjusting for age, gender, A1c, and indicators of socioeconomic status compared food security groups on HRV.

Results. Participant mean age was 59.7 (SD=10.9) years and 73% were women. Of the n=94 participants, 63 reported FI according to the USDA food security module and 46 reported FI according to the diabetes-specific measure. Mean A1c was 8.6% (SD=1.7) and was marginally higher among those reporting diabetes-specific FI than those reporting diabetes-specific food security. Participants who reported diabetes-specific FI had lower SDNN, VLF, LF, and HF HRV with effect sizes in the small-to-medium range.

Differences remained significant even after controlling for age, gender, socioeconomic hardship, and A1c. The 6-item USDA food security module was not associated with HRV. Conclusions. Diabetes-specific FI may be a unique risk factor for poor health outcomes among U.S. Latinos. Efforts to address FI could benefit diabetes outcomes.

Keywords

Food insecurity, heart rate variability, type 2 diabetes, Latinos

Introduction

Food insecurity (FI) is the limited or uncertain ability to acquire nutritionally adequate and safe foods (1). FI is associated with increased risk for type 2 diabetes mellitus (T2DM) (2) and, among persons with diabetes it is associated with poor glycemic control (3). In 2015, 12.7 percent of U.S. households (15.8 million households) were food insecure, and the prevalence was higher for Latino households (19.1 percent) than for non-Hispanic White households (10.0%) (4). Prospective studies have shown that FI hastens mortality in the general population and among and medically compromised persons in North America (5, 6).

The mechanisms through which FI hastens mortality are unknown. Heart rate variability (HRV) is one putative mechanism. HRV quantifies the beat-to-beat changes in heart rate caused by changes in autonomic activity and reflects autonomic tone. Low HRV is an early finding in diabetic cardiac autonomic neuropathy (7) and may be present as early as at diabetes diagnosis (8). Poor glycemic control is associated with lower HRV (9). Low HRV is a strong predictor of mortality in the setting of diabetes (10).

Patients with diabetes are asked to follow specific nutritional guidelines. Patients may have food security, i.e., access to nutritionally adequate and safe foods, yet still be financially unable to select foods the types of foods recommended for their diabetes management. Several validated scales are used to measure FI, most of which largely measure the ability to acquire *enough* food (11, 12). That is, they assess food security as it pertains to food quantity. And, whereas the commonly used 6-item USDA scale does make reference to the ability to acquire “the types of foods desired”, it does not

reference the ability to acquire the healthy foods typically recommended for diabetes management, e.g., high fiber, low fat foods such as whole grains and vegetables.

The objective of this exploratory, cross-sectional analysis among low-income Latinos with T2DM was to examine the relationships among the 6-item USDA food insecurity measure, diabetes-specific FI, and HRV and to determine whether glycemic control accounts for any association.

Materials and Methods

We analyzed cross-sectional baseline data from the Community Health Educators Assisting Latinos Manage Stress and Diabetes (CALMS-D) trial, registered at clinicaltrials.gov as NCT01578096 (13, 14). Participants were recruited from an inner-city clinic if they were adult residents of Hartford, CT, Latino/Hispanic, Spanish-speaking, with T2DM ≥ 6 months, and glycosylated hemoglobin concentrations (A1C) ≥ 7.0%. Patients were excluded for: medical instability or intensive medical treatment; bipolar disorder or thought disorder; suicide attempt or psychiatric hospitalization in the past 2 years; alcohol problems; or enrollment in another research study.

The CALMS-D trial was approved by the institutional review boards involved and all participants provided written informed consent. At a morning home visit, participants provided informed consent, provided a fasting venous blood sample, answered questionnaires that were verbally administered by interviewers in preferred language (English or Spanish) and were compensated $10. Next, participants were instrumented with 7-lead, 3-channel ambulatory ECG monitors (Holters), GE Medical (Milwaukee, WI) Marquette Series 8500 direct (amplitude-modulated) recorders. Participants were de-instrumented after 24 hours.

Measures

Food Insecurity.

We measured diabetes-specific FI with the question, “In the past year, has it happened to you that you did not have enough money to buy the food you should eat for your diabetes?” We defined a “yes” response as diabetes-specific FI and a “no” response as diabetes-specific food security. This question was designed specifically for this study. The English and Spanish CALMS-D survey questions were piloted and revised in an iterative fashion with the target community. The final questions demonstrated excellent content and face validity as previously reported (13).

We also measured FI using the 6-item USDA Food Security Module (15, 16). A raw score of 0-1 indicates high or marginal food security, 2-4 indicates low food security, and 5-6 indicates very low food security. We also used scores of 0 vs >0 to dichotomize participants as either food secure or food insecure (17). Finally, we also calculated a total sum score for a continuous measure of food security.

Heart Rate Variability.

HRV was assessed as in our previous studies (18). Holter recordings were scanned by an experienced technician. As described in the literature (19), each tape was manually processed and edited and then analyzed with customized software. The R-R interval data file was edited to remove ectopics and noise, and gaps filled in by interpolated linear splines. In the time domain, we assessed the standard deviation of each normal-to-normal beat, or SDNN (i.e., each normal R-R interval). The power spectrum was computed using a fast Fourier transform with a Parzen window and corrected for attenuation due to windowing and sampling. The power spectrum was

integrated over three frequency bands (19)- very low frequency (VLF) 0.0033 to < 0.04 Hz; low frequency (LF) 0.04 to <0.15 Hz; and high frequency (HF) 0.15 to 0.40 Hz. As expected, HRV values in the frequency domain were non-normal, so were natural log transformed (20).

Covariates

Age and gender were per self-report. A1c was assayed from venous blood samples in the University of Connecticut clinical laboratory using high pressure liquid chromatography. To isolate the effect of FI from other sources of economic hardship, we controlled for socioeconomic indicators including educational attainment (high school graduate/GED or less than high school graduate/GED), and total monthly household income including government assistance. We also controlled for self-reported financial strain over the past 12 months, on a scale from 1= “We have enough and can save” to 4= “We don’t have enough and we have great difficulties” (21).

Data Analysis

Data were analyzed using SPSSv21. ANOVA was used to detect unadjusted differences in HRV indices between FI groups, and ANCOVA was used for the same analyses adjusted for covariates. Partial eta squared values were calculated for each ANOVA as an indicator of effect size. Multiple linear regression was performed to examine the relationship between continuous FI scores and HRV indices. Alpha was set at 0.05.

Results

One hundred and twenty one individuals participated in baseline assessments for the Community Health Educators Assisting Latinos Manage Stress and Diabetes (CALMS-D) trial. Of those, n=11 did not have HRV data, data from n=15 required >20%

interpolation so were excluded from analysis and one individual did not provide food security data. This yielded a final n=94 for analysis. See table 1 for participant characteristics.

Using our diabetes-specific food security item, 48 reported diabetes-specific food security and 46 reported diabetes-specific FI. Using the USDA 6-item food security module, 31 participants were food secure and 63 were food insecure. HRV values were substantially lower than reported for a healthy, middle-aged sample (SDNN=96 vs 141) (19).

In ANOVA, participants who reported diabetes-specific FI had lower SDNN, lnVLF, lnLF, and lnHF than participants who reported diabetes-specific food security. In ANCOVA, when covariates were added to the model, results for SDNN, lnVLF, and lnLF remained significant, all $p<.05$. Results for lnHF remained significant with all demographic and socioeconomic covariates, but were reduced to $p=.06$ with the inclusion of A1c, although A1c was not a significant predictor of lnHF. A1c was a significant predictor of lnVLF and lnLF. Results indicated partial eta squared values ranging from .05 for SDNN and VLF to .06 for LF and HF, each of which indicates a small-to-medium effect size for the association between diabetes-related FI and HRV.

In ANOVA, using the USDA 6-item food insecurity module to classify participants as having high or marginal food security vs low food security vs very low food security, food security status was not associated with any HRV index, all $p>.20$. Using the USDA 6-item food insecurity module to dichotomize participants as food secure or food insecure, food security status was not associated with any HRV index, all $p>.30$. In

146 regression, using the total sum score on the USDA 6-item scale, food security score
147 was not associated with any HRV index, all p's>.44.

148 ## Discussion

149 The main finding from this exploratory study is that among low-income Latinos
150 with T2DM, individuals who report diabetes-specific FI have lower HRV than individuals
151 who report diabetes-specific food security. Specifically, individuals who cannot afford to
152 buy the foods that they believe are necessary for diabetes self-management have lower
153 HRV. Our findings also suggest that diabetes-specific FI is associated with HRV through
154 mechanisms other than, or in addition to, glycemic control. Whereas FI worsens
155 glycemic control, and glycemic control worsens HRV, the link between FI and HRV is
156 not solely due to glycemic control. Further, diabetes-specific FI was related to HRV
157 independent of common socioeconomic indicators. This implies that diabetes-specific FI
158 uniquely exerts deleterious effects on the autonomic system above and beyond
159 commonly accepted poverty proxies. To our knowledge, these are the first data linking
160 FI with HRV.

161 Previous work has demonstrated that social adversity is related to lower HRV.
162 This includes racial minority status, social class, cumulative life stress (22), and poverty
163 (23). Yet, here we demonstrate that even among minorities of low socioeconomic
164 status, diabetes-specific FI exerts a unique effect on HRV above and beyond other
165 socioeconomic stressors.

166 Several studies have shown that low HRV is predictive of early mortality, even
167 after controlling for other risk factors. In the Framingham Heart Study, a one standard
168 deviation difference in the lnLF power nearly doubled the risk of all-cause mortality (24).

Similar findings have been reported in other studies and appear to be especially strong among persons with diabetes (10). Thus our findings have important implications for diabetes-related health outcomes. Whereas we are limited by a cross-sectional design and we were unable to follow the sample for mortality, our findings might suggest that HRV is one mechanism through which FI increases risk for early mortality.Limitations include secondary data analysis, cross-sectional design, small sample, and a subjective measure of diabetes-specific FI. Putative mediators such as nutritional composition, energy intake, and psychological distress should be tested to understand the various potential mechanisms through which diabetes-specific FI may impair autonomic function. These limitations are generally outweighed by the study's strengths including a hard-to-reach clinical sample, state of the art HRV assessment, and a novel, simple and clinically relevant research question.

Conclusions

Participants who reported diabetes-specific FI had lower HRV than those who reported diabetes-specific food security. If these exploratory findings are replicated, efforts to end, decrease, or mitigate the effects of FI could have beneficial effects on diabetes outcomes.

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Statement of authors' contributions to manuscript: JW and RPE designed the study; RL analyzed the HRV data; JW performed statistical analysis; JW, RL, and ABM wrote the manuscript; SSP and GD supervised data collection; JC supervised recruitment; all authors contributed to the review and editing of the manuscript. All authors read and approved the final version of this paper.

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Table 1. Participant characteristics by diabetes-specific food security status.

Characteristic	Total (n=94)	Diabetes-Specific Food Secure (n=48)	Diabetes-Specific Food Insecure (n=46)	P-Value
Age in years	59.70 ± 10.90	61.98 ± 10.59	57.37 ± 10.81	.041*
Gender				.026*
Female	69 (73%)	40 (83%)	29 (63%)	
Marital Status				.659
Single	64 (68%)	34 (71%)	30 (65%)	
Language Speak				.541
English & Spanish	52 (55%)	25 (52%)	27 (59%)	
Spanish only	42 (45%)	23 (48%)	19 (41%)	
Years in U.S.	35.80 ± 14.39	36.72 ± 15.27	34.85 ± 13.54	.533
Employment Status				.325
Employed	0 (0%)	0 (0%)	0 (0%)	
Unemployed looking for work	15 (16%)	5 (10%)	10 (22%)	
Unemployed not looking	26 (28%)	14 (29%)	12 (26%)	
Disabled	53 (56%)	29 (60%)	24 (52%)	

Educational Attainment				.359
Less than high school	68 (72%)	37 (77%)	31 (67%)	
Monthly Household Income				.176
$0 - 1000	63 (67%)	37 (77%)	26 (57%)	
$1001 - 1500	26 (28%)	8 (17%)	18 (39%)	
$1501 -2000	2 (2%)	1 (2%)	1 (2%)	
$2001 – 3000	3 (3%)	2 (4%)	1 (2%)	
>$3000	0 (0%)	0 (0)	0 (0%)	
Financial Strain	2.53 ± 0.84	2.21 ± 0.74	2.87 ± 0.81	.000*
A1c mmol/mol IFCC	70.06 ± 18.49	66.73 ± 18.20	73.47 ± 18.35	.079
A1c % NGSP	8.56 ± 1.69	8.26 ± 1.67	8.87 ± 1.68	.079
SDNN	95.80 ± 28.16	102.12 ± 24.15	89.35 ± 30.67	.028*
lnVLF	6.44 ± 0.84	6.64 ± 0.77	6.24 ± 0.86	.022*
lnLF	5.31 ± 1.02	5.56 ± 1.00	5.05 ± 1.03	.014*
lnHF	4.53 ± 1.11	4.78 ± 1.11	4.28 ± 1.06	.028*

Values are n (%) or mean ± SD. Chi square tests were performed to examine differences in FI status on categorical variables and t-tests were performed for continuous variables.

All HRV values are unadjusted.

IFCC=International Federation of Clinical Chemistry; NGSP=National Glycohemoglobin Standardization Program; SDNN= standard deviation of the R- R interval; lnVLF=

natural log transformed very low frequency; lnLF= natural log transformed low frequency; lnHF= natural log transformed high frequency

Financial strain was measured on a 4-point Likert scale from 1= “We have enough and can save”, to 4= “We don’t have enough and we have great difficulties”.