BMJ Open

Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: the Echocardiographic Study of Latinos

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028729
Article Type:	Research
Date Submitted by the Author:	20-Dec-2018
Complete List of Authors:	Lopez, Lenny Swett, Katrina Rodriguez, Fatima Kizer, Jorge R.; Albert Einstein Coll Med Penedo, Frank Gallo, Linda; San Diego State University, Department of Psychology Allison, Matthew; 1University of California San Diego, Family Medicine and Public Health Arguelles, William; University of Miami, Department of Psychology Gonzalez, Franklyn Kaplan, Robert C.; Albert Einstein College of Medicine, Rodriguez, Carlos Rodriguez
Keywords:	Heart failure < CARDIOLOGY, SOCIAL MEDICINE, EPIDEMIOLOGY, Echocardiography < CARDIOLOGY

Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: the Echocardiographic Study of Latinos

Short Title: Acculturation and Cardiac Structure and Function

Address for correspondence
Lenny López, MD, MPH, MDiv. Division of Hospital Medicine, University of California San Francisco – San Francisco VA Medical Center. 4150 Clement St, San Francisco CA, 94121. (lenny.lopez@ucsf.edu). Phone: 617-270-6600.

Contributing authors:

1. Lenny López, MD, MPH, MDiv. Division of Hospital Medicine, University of California San Francisco – San Francisco VA Medical Center, San Francisco, CA. (lenny.lopez@ucsf.edu).
2. Katrina Swett, MS. Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC. (kswett@wakehealth.edu).
3. Fátima Rodríguez, MD, MPH. Division of Cardiovascular Medicine, Stanford University, Palo Alto, CA. (frodrigu@stanford.edu).
4. Jorge R. Kizer, MD. Division of Cardiology, Albert Einstein College of Medicine, Bronx, NY. (jorge.kizer@einstein.yu.edu).
5. Frank J. Penedo, PhD. Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois. (frank.penedo@northwestern.edu).
6. Linda C. Gallo, PhD. Department of Psychology, San Diego State University, San Diego, CA. (lgallo@mail.sdsu.edu).
7. Matthew A. Allison, MD, MPH, FAHA. Division of Preventive Medicine, University of California San Diego, San Diego, CA. (mallison@ucsd.edu).
8. William Arguelles, PhD. Center for Research and Grants, Baptist Health South Florida, Miami, FL. (warguelles@psy.miami.edu).
9. Franklyn Gonzalez, MS. Department of Biostatistics, University of North Carolina, Chapel Hill, NC. (fgonzale@email.unc.edu).
10. Robert Kaplan, PhD. Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY. (robert.kaplan@einstein.yu.edu).
11. Carlos J. Rodríguez, MD, MPH. Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC. (crodrigu@wakehealth.edu).

Manuscript Word Count: 2,632
Number of Tables: 3
Number of Figures: 1
Number of Supplemental Tables: 2

Strengths and limitations of this study

- A population-based cohort study among predominantly immigrant Hispanic/Latinos in the United States.
- A detailed comprehensive echocardiographic examination was used to determine cardiac structure and function in every participant.
- Determined whether sociocultural factors, such as acculturation contribute to the heart failure risk factor burden among an immigrant population.
- We are specifically referring to acculturation into the US culture which may not be generalizable to acculturation in other settings.

Abstract

Background: Hispanics/Latinos, the largest immigrant population in the US, have a large burden of heart failure risk. There is a paucity of research regarding the impact of acculturation on cardiac structure and function.

Methods: In the Echocardiographic Study of Latinos, 1,818 Hispanic adult participants underwent assessment of left atrial volume index (LAVI), left ventricular mass index (LVMI), early diastolic transmitral inflow and mitral annular velocities. Acculturation was measured by the Short Acculturation Scale, nativity, immigration age, length of US residence, generation status, and language.

Results: The study population was predominantly Spanish-speaking and foreign-born with mean US residence of 22.7 years, mean age of 56.4 years; 50% had hypertension, 28% had diabetes, and 44% had a BMI >30kg/m^2. Multivariable analyses demonstrated higher LAVI with increasing years of US residence. Foreign-born and first generation participants had higher E/e' but lower LAVI and e' velocities compared to the second generation. Higher acculturation and income >$20K were associated with higher LVMI, LAVI, and E/e', but lower e' velocities. Preferential Spanish-speakers with an income <$20K had a higher E/e'.

Conclusions: Acculturation was associated with abnormal cardiac structure and function, with some effect modification seen according to socioeconomic status.

Abstract Word Count: 193

Keywords: Acculturation, Echocardiogram, Hispanics/Latinos, Socioeconomic Status

Cardiovascular disease (CVD) and heart failure (HF) risk factor burden is high among Hispanic/Latinos in the United States (US) [1] leading to abnormalities of cardiac structure and function[2] which have been associated with incident clinical HF,[3] incident CVD and increased mortality.[4-7]

With respect to HF, Hispanics/Latinos have a higher incidence of HF compared to Non-Hispanic Whites and Hispanics/Latinos who present with HF are younger with more co-morbidities and a lower left ventricular ejection fraction.[8-10] Beyond traditional HF risk factors, unique sociocultural factors such as acculturation, may contribute to HF risk among Hispanic/Latinos **(Figure/Conceptual Model)**.[9] The fact that Hispanics/Latinos are the largest immigrant population in the US affords the ideal opportunity to study the impact of acculturation on cardiac parameters. Acculturation is a multidimensional process whereby an immigrant culture adopts the beliefs and practices of a host culture with both positive and negative effects that may differentially influence CVD development.[11] Higher acculturation has been associated with increased psychosocial stress, deleterious cardiovascular health behaviors and a higher CV risk factor burden.[12-14] To our knowledge, there is only one prior study[15] demonstrating that lower acculturation was associated with a greater risk of HF re-hospitalization.

We sought primarily to test whether acculturation, as an important bio-sociocultural variable, is associated with cardiac structure and function among Hispanics/Latinos. Studies often overlook socioeconomic status (SES) as an interconnected correlate with acculturation. Because SES is associated with cardiac parameters[16] and modifies the association between acculturation and

other health-related variables,[17] secondarily, we sought to test whether our primary associations are moderated by SES.

Methods

Cohort Description

The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is a population-based study of 16,415 Hispanic/Latinos from randomly selected households at four US field centers (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA).[18] Probability sampling was used to ensure broad representation of the target population and to minimize the sources of bias that may otherwise enter into the cohort selection and recruitment process. Participants were between 18 and 74 years of age, and self-identified as Cuban, Central American, Dominican, Mexican, Puerto Rican, or South American Hispanic/Latino heritage. The ECHO-SOL ancillary study was designed to provide echocardiographic parameters characterizing cardiac structure and function in a representative HCHS/SOL baseline subsample of 1,818 participants ≥45 years old.[2,19] The Institutional Review Board approval was obtained at each study site and oversight of all study all ECHO-SOL participants gave informed consent.

In-Person Examination

The examination protocol for the parent HCHS/SOL has been previously published.[12] Obesity was defined as a body mass index (BMI) ≥ 30.0 kg/m2. Seated resting blood pressures were measured in triplicate and the average of the 2nd and 3rd readings was used for analysis. Type 2 diabetes was defined based on American Diabetes Association definition using one or more of the following criteria: 1) fasting serum glucose ≥126 mg/dl, 2) oral glucose tolerance test ≥200

mg/dl, 3) self-reported diabetes, 4) Hb A1C ≥6.5%, or 5) taking anti-diabetic medication or insulin. Renal function was measured by estimated glomerular filtration rate (eGFR). Physical activity levels, categorized as low or medium/high, were assessed using the Global Physical Activity Questionnaire.[20] Self-report questionnaires assessed smoking status (no/ever/current), alcohol consumption (current/no), and insurance coverage (yes/no) and type (Private/Medicare/Medicaid). Socioeconomic status was defined as highest degree or level of school completed and household income level – dichotomized as <$20,000 and >$20,000, given the low number of participants with incomes >$40,000. Our secondary analysis focused on income rather than education because education was completed prior to migration for most immigrants in our study population and current income while living in the US may more relevantly impact on a participant's acculturative process, acting as a proxy for the participant's ability to integrate and be exposed to mainstream US contexts. Marital status categorized as (single/married/partnered/separated/divorced/widowed).

Primary Echocardiographic Measurements

Trained sonographers performed transthoracic echocardiography examinations, including 2D imaging, and spectral, color and tissue Doppler.[19] The following measured and derived cardiac variables utilized in this study were: left ventricular mass index (LVMI), relative wall thickness (RWT) and LV Ejection Fraction (LVEF) as per American Society of Echocardiography guidelines.[21] Per guidelines, diastolic function was defined using three echocardiographic parameters: 1) peak early (E) and late (A) diastolic transmitral inflow velocities; 2) early diastolic (e') annular velocities (the average of septal and lateral annular velocities were used); 3) left atrial volume indexed (LAVI) to body surface area.[22]

Acculturation Measures

Acculturation was measured by six variables. First, nativity was classified as either born or not outside the US mainland (50 states) and those born in Puerto Rico or other US territories were classified as born outside the US mainland to better reflect their migration and acculturation experiences. Second, foreign-born individuals were asked the number of years lived in the US and categorized as <5, 5-10, 11-20, >20 years. We used Marin's Short Acculturation Scale for Hispanics (SASH),[23] which has a two-factor structure and the two subscales (items related to language use [e.g., language they speak, think] as the SASH language subscale; items related to media preference and social affiliations [e.g., language of media programs watched; ethnicity of close friends] as the SASH social relations subscale) were analyzed separately in our models with higher scores representing higher acculturation. Fifth, language preference was categorized as English vs. Spanish based on language of interview. Finally, generational status (first vs. higher generation) was collected as well as age at the time of migration to the US.

Statistical Analyses

Sampling weights were used to obtain weighted frequencies of descriptive variables and population estimates in the ECHO-SOL target population. We used means ± standard errors (SEs) for continuous variables and proportions for categorical variables. LVMI, RWT, LVEF, e' annular velocities and LAVI were analyzed as continuous variables. LV diastolic dysfunction (LVDD) was analyzed as a binary variable (present vs. absent).[2] Acculturation variables were categorical (foreign- vs. US-born; 1st generation vs. 2nd; Spanish language preference vs. English), ordinal (<5, 5-10, 11-20, and >20 years in the US) and continuous measures (age at

immigration and SASH subscales). Means were compared across categorical acculturation variables using ANOVA for each measure of cardiac structure (LVMI, RWT, LAVI) and function (LVEF, e', E/e'). Only significant unadjusted associations for our measures of acculturation were explored in multivariable analysis. Unadjusted and multivariable separate linear and logistic regression analyses were used for our continuous and categorical acculturation variables respectively with each dependent variable measure of cardiac structure and function with sequential modeling for age and sex followed by models including clinical covariates (diabetes, hypertension, and obesity), and behavioral characteristics (physical activity, tobacco use, and alcohol use). For years in the US, we compared >20 years to <5 years as well as an overall comparison across each category of years in the US. We tested effect moderation with income through the use of interaction terms in models followed by stratified analyses by income for statistically significant interactions at the $p<0.01$ level. All other statistical tests were 2-sided at a significance level of 0.05. All reported values were weighted to account for the HCHS/SOL sampling probability design, stratification, clustering and nonresponse and to make the estimates applicable to the target population from which the HCHS/SOL sample was drawn. All analyses were performed with SAS 9.3 (SAS Institute, Cary, NC)

Patient and public involvement

No patients were involved in the development of the research question or design of this cohort study.

Results

Fifty-seven percent of the study population were women; almost half had a reported annual income under $20K; over half were married and most had some type of health insurance (mostly Medicaid and/or Medicare). Hypertension and diabetes were prevalent in half and almost one-

third of the study population respectively. Most of the study population was foreign-born, only 14% preferred English, almost half had been in the US >20 years with a mean age of migration of 34 years of age, signifying that the majority came to the US as adults **(Table 1).** Mean values of echocardiographic variables (LAVI, RWT, LVMI, LVEF) are all within normal limits for this study population. However, mean e' annular velocities and E/e' ratio are borderline abnormal. Some degree of diastolic dysfunction was seen in over half of the study population but this has been previously described.[2]

Table S1 shows unadjusted relationships between acculturation measures and echocardiographic characteristics. LAVI significantly increased with increasing years in the US whereas RWT appeared to have a bimodal distribution. A significantly lower annular relaxation velocity and higher E/e' ratio was seen among the foreign-born compared to US-born and among those 1st generation compared to 2nd generation. Increasing acculturation as measured by increasing SASH language scale was associated with increasing LAVI. Younger age of migration to US was associated with higher RWT and increased LAVI.

Adjusted analyses **(Table 2)** demonstrated significantly lower RWT and increased LAVI with increasing years in the US. A significantly higher E/e' ratio was seen among the foreign-born participants. Those 1st generation had lower LAVI, lower e' annular velocities and higher E/e' ratios compared to 2nd generation. Increasing SASH language scale was associated with increasing LAVI. Lower age of migration to US was associated with increased LAVI. These associations persisted in sequential models adjusted for clinical factors and behavioral factors both separately and together. Although greater odds of LVDD was seen in unadjusted

associations with nativity, generational status, SASH language, and age of immigration **(Table 3),** these associations did not persist on adjusted analysis.

Significant interactions ($p<0.01$) were found between our main exposure (acculturation) and income on the effect of cardiac structure and function. Among those whose annual income is >$20K, increasing years in the US was associated with increased LVMI, lower e' annular velocities, and higher E/e' ratio. Generational status was associated with increased LAVI among those making >$20K annually. However, being a preferential Spanish-speaker carried a significantly higher E/e' ratio among those making <$20K. **(Table S2).**

Discussion

Hispanics/Latinos in the US represent a relatively young demographic such that the future public health burden of HF as this population ages is potentially underestimated. Acculturation is complex, and HCHS-SOL has demonstrated significant heterogeneity in CVD risk factor burden among Hispanics/Latinos by country of origin and acculturation measures.[12] Despite the limited understanding of HF risk among Hispanics/Latinos,[9,24] our analysis of multidimensional validated acculturation scales provides several important contributions. First, increasing acculturation, an important phenomenon among immigrant populations, is associated with abnormal cardiac structure and function in a predominately foreign-born, Spanish-speaking adult study population despite long residence in the US. Second, different dimensions of acculturation had varying associations with echocardiographic measures of structure and function. Finally, income significantly moderated these associations. These findings suggest that exposure to the social and environmental sources of acculturative stress may promote unhealthy behaviors[25] or

act via currently undefined pathways to contribute to HF risk among Hispanics/Latinos. Further elucidating the acculturative factors influencing HF risk in Hispanics/Latinos is warranted.

Although to our knowledge, there is no existing literature on the association between acculturation and HF risk, our study found several measures of acculturation (increasing years of US residence, English preference, and younger age at immigration) were associated with abnormal cardiac structure and function (increased LAVI, increased LVMI, increased RWT, lower annular e' relaxation velocity and higher E/e' ratio). Our multivariable models did not fully account for the deleterious effects of acculturation. An increased E/e' ratio, LAVI, and LVMI are markers of chronically-elevated filling pressures associated with impaired cardiac relaxation and HF with preserved ejection fraction.[26,27] The presence of measures of abnormal cardiac structure and function have been associated with increased HF hospitalizations, cardiovascular death and improved CV risk prediction.[27-29] Importantly, these abnormalities are additive, with worse outcomes seen in individuals with more than one alteration.[27] In order to identify preclinical CV disease, abnormalities in cardiac structure and function determined by echocardiography are important intermediary measures, many of which have been associated with incident CVD, incident clinical HF and increased mortality.[4-6] Given the high burden of acculturation among Hispanics/Latinos, echocardiography might help to identify a particularly high risk subset of participants.

LVM is associated with CVD, sudden cardiac death, and all–cause mortality.[26] Among foreign-born Hispanics/Latinos, we found increased LVMI with increasing years in the US. Our study is consistent with prior studies showing a high prevalence of LVM among Hispanics/Latinos

especially among low income Hispanics/Latinos with increasing years of US residence.[30-32] Prior studies have demonstrated that adjustment for socioeconomic factors did not fully account for the presence of increased LVMI among Hispanics/Latinos[33] possibly due to the residual effect of acculturation. Changes in LVM can occur without overt clinical hypertension in adrenergic states, such as chronic stress[34] with psychosocial factors such as perceived discrimination and low social support.[35,36] Acculturative stress, an inability to navigate the immigrant process and make decisions on retaining one's native culture while adapting to a new culture, may negatively affect mental and physical health through unhealthy and risky behaviors[25] but also increase rates of anxiety, depression, perceived discrimination and lack of social support[14,25,37] which may all lead to cardiac structural and functional abnormalities and increased HF risk.

The interaction of acculturation with SES on cardiac measures may shed light on the "Hispanic paradox" which states that Hispanics/Latinos, a disproportionately low SES group, have lower overall mortality and cardiovascular mortality compared to non-Hispanic Whites.[9] Low SES is a composite chronic psychological stressor encompassing multiple factors (e.g., work, housing and material factors) as well as unmeasured behavioral and situational stress features. Longitudinal studies have shown an inverse association gradient between SES level and adverse outcomes.[35] Studies have shown that low SES and racial/ethnic minority status may combine synergistically to create high burdens of stress that accumulate over time, leading to deleterious health consequences.[38] However, our study provides additional information, that is those with higher SES (defined as annual incomes >$20K) exhibited more deleterious effects of increasing acculturation on cardiac structural and functional measures. There may be more acculturative

stress for higher-SES immigrants, perhaps through increased contact and interaction with the mainstream culture, which may contribute to our findings. *Familismo* is a culture-specific factor characterized by having strong bonds with nuclear and extended family members resulting in a high level of perceived family support and associated with some indicators of improved health.[39,40] Studies suggest that increasing acculturation may erode the protective nature of *familismo*.[40-42] Further, as Hispanics acculturate into a more individualistic society, dimensions of *familismo* such as familial obligations may increase psychosocial stress rather than alleviate it. For example, a participant may agree that an aging parent should live with relatives, but having a limited income to provide such living arrangements may impart a negative psychosocial stress.

Several limitations of this analysis should be noted. First, this study is cross-sectional and precludes mechanistic causal inference, so our findings warrant replication and longitudinal follow up. Secondly, participants resided in one of four US cities, precluding generalizability to all US Hispanic/Latinos. Our study demonstrates cardiac structure and function abnormalities in a relatively young cohort with a high burden of traditional CVD factors. While this study is one of the largest studies of acculturation with cardiac structure and function in any population, the sample size is modest; thus we are underpowered to perform stratified analyses by national origin in order to characterize the heterogeneity within Hispanic/Latinos. We are specifically referring to acculturation into the US culture which may not be generalizable to acculturation in other settings. Finally, although the ECHO- SOL cohort does not include a non-Hispanic White comparison group, our study focuses on unique intra-ethnic phenomena, as prior research confirms inter-racial/ethnic differences.

Conclusions

In addition to traditional CV risk factors, acculturation may explain the disproportionate burden of HF risk among Hispanics/Latinos. Our study found significant associations between acculturation measures and deleterious cardiac structural and functional changes among low-SES, foreign-born Hispanic/Latinos with increasing years of residence in the US. Abnormal cardiac structure and function is known to increase the risk of incident clinical HF. Further elucidation of how acculturation impacts risk is warranted in order to possibly risk stratify a high-risk subgroup of Hispanics/Latinos and also to inform the development of culturally-appropriate interventions for Hispanics/Latinos and other immigrants.

Acknowledgements: The authors thank the staff and participants of HCHS/SOL and ECHO-SOL for their important contributions. Investigators website - http://www.cscc.unc.edu/hchs/

Contributors: Research Conception and design: CJR, LL; **Collection and assembly of data:** CJR, MAA, RK, LCG; **Analysis and interpretation of the data:** CJR, LL, KS; **Drafting of the article:** CJR, LL, FR; **Critical revision of the article for important intellectual content:** CJR, LL, FR, JRK, FJP, LCG, WA, FG; **Obtaining of funding:** CJR, RK, MAA; **Statistical expertise:** KS, FG

CJR and LL are responsible for the overall content as guarantors.

Funding: This study supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI) to the University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), and San Diego State University (N01-HC65237). The following institutes contributed to HCHS/SOL: National Institute on Minority Health and Health Disparities, National Institute on Deafness and Other Communication Disorders, National Institute of Dental and Craniofacial Research, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Neurological Disorders and Stroke, NIH Institution-Office of Dietary Supplements.

ECHO-SOL was supported by the National Heart, Lung, and Blood Institute (R01 HL104199, Epidemiologic Determinants of Cardiac Structure and Function among Hispanics: Carlos J. Rodriguez, MD, MPH Principal Investigator). Dr. Lenny L. López acknowledges the support of the Robert Wood Johnson Foundation Harold Amos Medical Faculty Development Program and NIDDK 1K23DK098280-01. No relationships with industry supported this work.

Competing interests: None declared.

Patient consent for publication: Not required.

Ethics approval: The Institutional Review Board at the Wake Forest School of Medicine and at each study site provided approval and oversight of all study materials and activities.

Data sharing statement: Data is publically available on request.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart Disease and Stroke Statistics—2015 Update: A Report From the American Heart Association. Circulation 2015;131:e29-e322.

2. Mehta H, Armstrong A, Swett K, et al. Burden of Systolic and Diastolic Left Ventricular Dysfunction Among Hispanics in the United States: Insights From the Echocardiographic Study of Latinos. Circ Heart Fail 2016;9.

3. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147-239.

4. Hobbs FD, Roalfe AK, Davis RC, Davies MK, Hare R, Midlands Research Practices C. Prognosis of all-cause heart failure and borderline left ventricular systolic dysfunction: 5 year mortality follow-up of the Echocardiographic Heart of England Screening Study (ECHOES). Eur Heart J 2007;28:1128-34.

5. Armstrong AC, Jacobs DR, Jr., Gidding SS, et al. Framingham score and LV mass predict events in young adults: CARDIA study. Int J Cardiol 2014;172:350-5.

6. Bombelli M, Facchetti R, Cuspidi C, et al. Prognostic significance of left atrial enlargement in a general population: results of the PAMELA study. Hypertension 2014;64:1205-11.

7. Echouffo-Tcheugui JB, Erqou S, Butler J, Yancy CW, Fonarow GC. Assessing the Risk of Progression From Asymptomatic Left Ventricular Dysfunction to Overt Heart Failure: A Systematic Overview and Meta-Analysis. JACC Heart Fail 2016;4:237-48.

8. Vivo RP, Krim SR, Cevik C, Witteles RM. Heart failure in Hispanics. Journal of the American College of Cardiology 2009;53:1167-75.

9. Rodriguez CJ, Allison M, Daviglus ML, et al. Status of cardiovascular disease and stroke in Hispanics/Latinos in the United States: a science advisory from the American Heart Association. Circulation 2014;130:593-625.

10. Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. Archives of internal medicine 2008;168:2138-45.

11. Zambrana RE, Carter-Pokras O. Role of acculturation research in advancing science and practice in reducing health care disparities among Latinos. Am J Public Health 2010;100:18-23.

12. Daviglus ML, Talavera GA, Aviles-Santa ML, et al. Prevalence of major cardiovascular risk factors and cardiovascular diseases among Hispanic/Latino individuals of diverse backgrounds in the United States. Jama 2012;308:1775-84.

13. Ayala GX, Baquero B, Klinger S. A systematic review of the relationship between acculturation and diet among Latinos in the United States: implications for future research. J Am Diet Assoc 2008;108:1330-44.

14. Steptoe A, Kivimaki M. Stress and cardiovascular disease: an update on current knowledge. Annu Rev Public Health 2013;34:337-54.

15. Peterson PN, Campagna EJ, Maravi M, et al. Acculturation and outcomes among patients with heart failure. Circ Heart Fail 2012;5:160-6.

16. Rodriguez CJ, Sciacca RR, Diez-Roux AV, et al. Relation between socioeconomic status, race-ethnicity, and left ventricular mass: the Northern Manhattan study. Hypertension 2004;43:775-9.

17. Lee H, Cardinal BJ, Loprinzi PD. Effects of socioeconomic status and acculturation on accelerometer-measured moderate-to-vigorous physical activity among Mexican American adolescents: findings from NHANES 2003-2004. J Phys Act Health 2012;9:1155-62.

18. Lavange LM, Kalsbeek WD, Sorlie PD, et al. Sample design and cohort selection in the Hispanic Community Health Study/Study of Latinos. Ann Epidemiol 2010;20:642-9.

19. Rodriguez CJ, Dharod A, Allison MA, et al. Rationale and Design of the Echocardiographic Study of Hispanics/Latinos (ECHO-SOL). Ethnicity & disease 2015;25:180-6.

20. Cleland CL, Hunter RF, Kee F, Cupples ME, Sallis JF, Tully MA. Validity of the global physical activity questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health 2014;14:1255.

21. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography 2005;18:1440-63.

22. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. Circulation 2000;102:1788-94.

23. Marin G, Sabogal F, Marin BV, Otero-Sabogal F, and Perez-Stable E. Development of a short acculturation scale for Hispanics. Hispanic Journal of Behavioral Sciences 1987;9:183-205.

24. Vivo RP, Krim SR, Cevik C, Witteles RM. Heart failure in Hispanics. J Am Coll Cardiol 2009;53:1167-75.

25. Lara M, Gamboa C, Kahramanian MI, Morales LS, Bautista DE. Acculturation and Latino health in the United States: a review of the literature and its sociopolitical context. Annu Rev Public Health 2005;26:367-97.

26. Abbate A, Arena R, Abouzaki N, et al. Heart failure with preserved ejection fraction: refocusing on diastole. Int J Cardiol 2015;179:430-40.

27. Shah AM, Claggett B, Sweitzer NK, et al. Cardiac structure and function and prognosis in heart failure with preserved ejection fraction: findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) Trial. Circ Heart Fail 2014;7:740-51.

28. Zile MR, Gottdiener JS, Hetzel SJ, et al. Prevalence and significance of alterations in cardiac structure and function in patients with heart failure and a preserved ejection fraction. Circulation 2011;124:2491-501.

29. Burke MA, Katz DH, Beussink L, et al. Prognostic importance of pathophysiologic markers in patients with heart failure and preserved ejection fraction. Circ Heart Fail 2014;7:288-99.

30. Zabalgoitia M, Ur Rahman SN, Haley WE, et al. Impact of ethnicity on left ventricular mass and relative wall thickness in essential hypertension. Am J Cardiol 1998;81:412-7.

31. Rodriguez CJ, Diez-Roux AV, Moran A, et al. Left ventricular mass and ventricular remodeling among Hispanic subgroups compared with non-Hispanic blacks and whites: MESA (Multi-ethnic Study of Atherosclerosis). J Am Coll Cardiol 2010;55:234-42.

32. Effoe VS, Chen H, Moran A, et al. Acculturation is associated with left ventricular mass in a multiethnic sample: the Multi-Ethnic Study of Atherosclerosis. BMC Cardiovasc Disord 2015;15:161.

33. Rodriguez CJ, Lin F, Sacco RL, et al. Prognostic implications of left ventricular mass among Hispanics: the Northern Manhattan Study. Hypertension 2006;48:87-92.

34. Julius S, Li Y, Brant D, Krause L, Buda AJ. Neurogenic pressor episodes fail to cause hypertension, but do induce cardiac hypertrophy. Hypertension 1989;13:422-9.

35. Rozanski A, Blumenthal JA, Davidson KW, Saab PG, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. J Am Coll Cardiol 2005;45:637-51.

36. Rodriguez CJ, Elkind MS, Clemow L, et al. Association between social isolation and left ventricular mass. Am J Med 2011;124:164-70.

37. Gallo LC, Penedo FJ, Espinosa de los Monteros K, Arguelles W. Resiliency in the face of disadvantage: do Hispanic cultural characteristics protect health outcomes? J Pers 2009;77:1707-46.

38. Gallo LC, de Los Monteros KE, Allison M, et al. Do socioeconomic gradients in subclinical atherosclerosis vary according to acculturation level? Analyses of Mexican-Americans in the multi-ethnic study of atherosclerosis. Psychosom Med 2009;71:756-62.

39. Davila YR, Reifsnider E, Pecina I. Familismo: influence on Hispanic health behaviors. Appl Nurs Res 2011;24:e67-72.

40. Sabogal F, Marin G, Otero-Sabogal R, Marin B. Hispanic familism and acculturation: What changes and what doesn't? Hispanic Journal of Behavioral Sciences 1987;9:397-412.

41. Miranda A, Estrada D, Firpo-Jimenez M. Differences in family cohesion, adaptability, and environment among Latino families in dissimilar stages of acculturation. The Family Journal 2000;8:341-50.

42. Rodriguez N, Mira C, Paez N, Myers H. Exploring the complexities of familism and acculturation: central constructs for people of Mexican origin. Am J Community Psychol 2007;39:61-77.

Table 1. ECHO-SOL Demographic and Clinical Characteristics

Demographic Characteristics	Participants (N = 1,818)†
Women	1187 (57.4)
Age, mean (SE)	56.4 (0.37)
High School Graduate or Higher	726 (43.3)
Annual Family Income > $20,000	787 (45.5)
Marital Status	

Single	332 (18.8)
Married/Partner	961 (53.2)
Separated/Divorced/Widow	522 (28.0)
Insured	1042 (60.1)
Short Acculturation Scale for Hispanics (SASH) [mean (SE)]	
Language Use Subscale	1.7 (0.05)
Social Relations Subscale	2.1 (0.03)
Length of US residence [N (%)]	
<5 years	178 (13.6)
5-10 years	247 (15.2)
11-20	385 (22.1)
>20	842 (49.1)
Second generation or higher	185 (9.3)
English language preference	225 (14.0)
Age at migration [mean (SE)]	34.0 (1.0)
US born	163 (7.9)
Clinical Characteristics [N (%)]	
Hypertension	861 (50.0)
Type 2 Diabetes	523 (28.4)
Current Smoker	304 (17.6)
Physical activity level low	1227 (67.3)
BMI ≥30	822 (44.3)
Current Alcohol Use	770 (43.5)
Echocardiographic Variables [mean (SE)]	
Left Atrial Volume Index	23.0 (0.25)
Relative Wall Thickness	0.40 (0.004)
Left Ventricular Mass Index	82.7 (0.7)
Ejection Fraction	59.8 (0.2)
E prime (e')	8.1 (0.09)
E/e'	10.0 (0.12)
Diastolic Dysfunction [N (%)]	916 (51.9)

†N's presented are unweighted counts of total participants in the ECHO-SOL with each respective characteristic. Percentages are weighted row percentages.

Table 2. Adjusted Analyses of Acculturation Measures with Cardiac Structure and Function.*

	LVMI (g/m^2) β (p)	**RWT** β (p)	**LAVI** (mL/m^2) β (p)	**LVEF** (%) β (p)	**e'** (cm/s) β (p)	**E/e'** β (p)
Nativity						
Age, sex					-0.349 (0.12)	0.571 (0.02)
Model 1	—	—	—	—	-0.320 (0.10)	0.524 (0.02)
Model 2					-0.324 (0.14)	0.532 (0.02)
Model 3					-0.303 (0.12)	0.503 (0.02)
Foreign Born (Years in the US)						
Age, sex	—	0.020 (0.06); all (0.03)	-1.74 (0.01); all (0.04)	—	—	—
Model 1		0.022 (0.02); all (0.02)	-1.74 (0.01); all (0.05)			
Model 2		0.018 (0.06); all (0.02)	-1.70 (0.009); all (0.05)			
Model 3		0.021 (0.02); all (0.007)	-1.71 (0.008); all (0.05)			
Generation						
Age, sex			-0.468 (0.21)		-0.529 (0.01)	0.710 (0.002)
Model 1	—	—	-1.797 (0.004)	—	-0.447 (0.01)	0.594 (0.003)
Model 2			-1.444 (0.03)		-0.499 (0.01)	0.671 (0.003)
Model 3			-1.584 (0.01)		-0.425 (0.02)	0.575 (0.006)
SASH Language						
Age, sex			0.580 (0.01)		0.125 (0.10)	
Model 1	—	—	0.610 (0.008)	—	0.097 (0.11)	—
Model 2			0.546 (0.01)		0.123 (0.15)	
Model 3			0.590 (0.007)		0.095 (0.16)	
Age at Immigration						
Age, sex		0.0005 (0.15)	-0.040 (0.008)		-0.005 (0.27)	
Model 1	—	0.0005 (0.13)	-0.040 (0.008)	—	-0.006 (0.14)	—
Model 2		0.0004 (0.15)	-0.038 (<0.001)		-0.005 (0.37)	
Model 3		0.0004 (0.13)	-0.038 (0.01)		-0.005 (0.22)	

*Only acculturation measures that were significant in unadjusted analyses were analyzed in multivariable adjusted models.
For Years in the US, 1st p value reflects <5 years vs. >20 years comparison. 2nd p value is p value overall for all Years in the US categories
Model 1: Age, Sex, Diabetes, Hypertension, Obesity | Model 2: Age, Sex, Physical Activity, Tobacco, Alcohol Use | Model 3: Model 1 + Model 2
LVMI = Left ventricular mass index; RWT = Relative wall thickness; LAVI = Left atrial volume index; LVEF = Left ventricular ejection fraction
e'= Mitral annular early diastolic velocity; E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Table 3. Unadjusted and Adjusted‡ Analyses of Acculturation Measures with Diastolic Dysfunction.

		Adjusted Sequential Models			
	Unadjusted	Age, Sex	Model 1	Model 2	Model 3
Nativity					
Foreign born	1.67 (1.08-2.58)	0.98 (0.62-1.55)	0.94 (0.59-1.51)	0.98 (0.62-1.55)	0.95 (0.59-1.53)
US born	Ref				
Years in the US					
<5	0.86 (0.60-1.24)				
5-10	0.72 (0.49-1.04)				
11-20	0.91 (0.61-1.37)	—	—	—	—
>20	Ref				
Generation					
1	1.90 (1.24-2.92)	1.29 (0.77-2.14)	1.18 (0.74-1.91)	1.26(0.77-2.06)	1.18 (0.73-1.89)
2	Ref				
Language Preference					
English	0.67 (0.34-1.32)	—	—	—	—
Spanish	Ref				
SASH Language	0.81 (0.67-0.98)	—	—	—	—
SASH Social	0.88 (0.68-1.15)	—	—	—	—
Age at Immigration	1.02 (1.004-1.03)	1.00 (0.99-1.02)	1.01 (0.995-1.02)	1.01 (0.99-1.02)	1.01 (0.995-1.02)

‡Only acculturation measures that were significant in unadjusted analyses were analyzed in adjusted models.
ORs (95% CIs) are presented
Model 1: Age, Sex, Diabetes, Hypertension, Obesity
Model 2: Age, Sex, Physical Activity, Tobacco, Alcohol Use
Model 3: Model 1 + Model 2

Table S1. Unadjusted Acculturation Measures with Echocardiographic Measures of Cardiac Structure and Function.

	LVMI (g/m^2)		RWT		LAVI (mL/m^2)		LVEF (%)		e' (cm/s)		E/e'	
Categorical Measures												
	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p
Nativity												
Foreign Born	82.74	0.92	0.40	0.07	22.93	0.10	59.83	0.54	7.98	<0.001	10.1	<0.001
US Born	82.54		0.38		24.10		59.50		8.99		8.8	
Years in US												
<5 yrs	79.80	0.16	0.41	0.03	21.70	0.03	59.94	0.09	7.71	0.11	10.2	0.25
5-10 yrs	80.43		0.39		22.40		60.04		8.18		9.7	
11-20 yrs	83.60		0.41		22.82		58.94		8.27		9.8	
>20 yrs	83.96		0.39		23.50		60.14		7.86		10.2	
Generation												
First	82.69	0.88	0.40	0.08	22.89	0.02	59.84	0.45	7.97	<0.001	10.1	<0.001
Second or Greater	82.96		0.38		24.41		59.45		9.01		8.8	
Language												
English	81.51	0.59	0.38	0.08	24.00	0.06	60.13	0.48	8.52	0.15	9.7	0.64
Spanish	82.92		0.40		22.87		59.75		7.99		10.0	
Continuous Measures												
	β (se)	p	β (se)	p	β (se)	p	β (se)	p	β (se)	p	β (se)	p
Age at Immigration	-0.0003 (0.0632)	0.99	0.0006 (0.0003)	0.02	-0.030 (0.014)	0.03	-0.003 (0.012)	0.79	-0.023 (0.007)	0.001	0.012 (0.010)	0.23
SASH Subscales												
Language	0.087 (0.735)	0.91	-0.005 (0.003)	0.10	0.539 (0.237)	0.02	0.166 (0.180)	0.36	0.255 (0.098)	0.009	-0.205 (0.109)	0.06
Social Relations	0.086 (1.392)	0.95	-0.009 (0.006)	0.15	0.732 (0.373)	0.05	0.539 (0.295)	0.07	0.266 (0.155)	0.09	-0.156 (0.217)	0.47

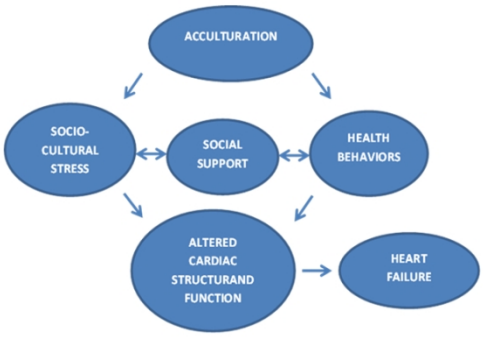
LVMI = Left ventricular mass index; RWT = Relative wall thickness; LAVI = Left atrial volume index
LVEF = Left ventricular ejection fraction; e'= Mitral annular early diastolic velocity
E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Table S2. Income Stratified Adjusted Analyses of Acculturation Measures with Cardiac Structure and Function.[¥]

	LVMI (g/m^2)				**LAVI** (mL/m^2)				**e'** (cm/s)				**E/e'**				**Diastolic Dysfunction**	
	<$20,000		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**	**>$20,000**
	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	ORs (95% CI)	ORs (95% CI)
Nativity																		
Foreign	—	—	—	—	—	—	—	—	7.90	0.0006	8.24	0.048	—	—	—	—	1.67 (0.89-3.14)	1.24 (0.70-2.19)
US born									8.83		8.99							
Years in the US																		
<5	80.02		73.35						7.70		9.03		10.20		9.17			
5-10	81.32	0.15	79.38	0.002	—	—	—	—	7.72	0.27	8.87	0.001	10.36	0.62	8.63	0.003	—	—
11-20	82.22		86.12						8.23		8.56		9.912		9.49			
>20	85.73		82.23						7.87		7.89		10.28		10.16			
Generation																		
1	—	—	—	—	23.04	0.45	22.85	0.02	—	—	—	—	—	—	—	—	1.82 (0.99-3.34)	1.50 (0.83-2.69)
2					23.91		24.67											
Language Preference																		
English	—	—	—	—	—	—	—	—	—	—	—	—	9.42	0.01	10.00	0.63	—	—
Spanish													10.21		9.55			
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	—	—
SASH Language	—	—	—	—	0.2686	0.32	0.7213	0.04	—	—	—	—	-0.3026	0.003	0.1065	0.60	—	—
SASH Social	—	—	—	—	—	—	—	—	—	—	—	—	-0.5410	0.008	0.4641	0.27	—	—

[¥]Only statistically significant interactions were analyzed in adjusted models; excludes cases where income is missing.
Multivariable models were adjusted for Age, Sex, Diabetes, Hypertension, Obesity, Physical Activity, Tobacco, and Alcohol Use.
LVMI = Left ventricular mass index; LAVI = Left atrial volume index
e'= Mitral annular early diastolic velocity; E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Figure Legend: Proposed Relationship Between Acculturation with Abnormal Cardiac Structure and Function.



338x190mm (96 x 96 DPI)

BMJ Open

Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: a cross-sectional analysis of the Echocardiographic Study of Latinos

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028729.R1
Article Type:	Original research
Date Submitted by the Author:	22-Jul-2019
Complete List of Authors:	Lopez, Lenny; San Francisco VA Medical Center, Hospital Medicine Swett, Katrina; Yeshiva University Albert Einstein College of Medicine, Medicine / Cardiology Rodriguez, Fatima ; Stanford University School of Medicine, Medicine / Cardiology Kizer, Jorge R.; San Francisco VA Medical Center, Medicine / Cardiology Penedo, Frank; Northwestern University, Medical Social Sciences. Gallo, Linda; San Diego State University Allison, Matthew; University of California San Diego, Medicine Arguelles, William; Baptist Health South Florida Gonzalez, Franklyn; University of North Carolina at Chapel Hill, Biostatistics Kaplan, Robert C.; Yeshiva University Albert Einstein College of Medicine, Epidemiology and Population Health Rodriguez, Carlos J.; Yeshiva University Albert Einstein College of Medicine, Medicine / Cardiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, SOCIAL MEDICINE, EPIDEMIOLOGY, Echocardiography < CARDIOLOGY

Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: a cross-sectional analysis of the Echocardiographic Study of Latinos

Short Title: Acculturation and Cardiac Structure and Function

Address for correspondence
Lenny López, MD, MPH, MDiv. Division of Hospital Medicine, University of California San Francisco – San Francisco VA Medical Center. 4150 Clement St, San Francisco CA, 94121. (lenny.lopez@ucsf.edu). Phone: 617-270-6600.

Contributing authors:

1. Lenny López, MD, MPH, MDiv. Division of Hospital Medicine, University of California San Francisco – San Francisco VA Medical Center, San Francisco, CA. (lenny.lopez@ucsf.edu).
2. Katrina Swett, MS. Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY. (katrina.swett@einstein.yu.edu).
3. Fátima Rodríguez, MD, MPH. Division of Cardiovascular Medicine, Stanford University, Palo Alto, CA. (frodrigu@stanford.edu).
4. Jorge R. Kizer, MD. Division of Cardiology, San Francisco VA Medical Center, San Francisco, CA. (jorge.kizer@ucsf.edu).
5. Frank J. Penedo, PhD. Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois. (frank.penedo@northwestern.edu).
6. Linda C. Gallo, PhD. Department of Psychology, San Diego State University, San Diego, CA. (lgallo@mail.sdsu.edu).
7. Matthew A. Allison, MD, MPH, FAHA. Division of Preventive Medicine, University of California San Diego, San Diego, CA. (mallison@ucsd.edu).
8. William Arguelles, PhD. Center for Research and Grants, Baptist Health South Florida, Miami, FL. (warguelles@psy.miami.edu).
9. Franklyn Gonzalez, MS. Department of Biostatistics, University of North Carolina, Chapel Hill, NC. (fgonzale@email.unc.edu).
10. Robert Kaplan, PhD. Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY. (robert.kaplan@einstein.yu.edu).
11. Carlos J. Rodríguez, MD, MPH. Departments of Cardiovascular Medicine, Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY. (carlos.rodriguez@einstein.yu.edu).

Manuscript Word Count: 3,425
Number of Tables: 3
Number of Figures: 2
Number of Supplemental Tables: 2

Abstract

Objective: Hispanics/Latinos, the largest immigrant population in the United States, undergo the process of acculturation and have a large burden of heart failure risk. Few studies have examined the association of acculturation on cardiac structure and function.

Design: cross-sectional

Setting: the Echocardiographic Study of Latinos

Participants: 1,818 Hispanic adult participants with baseline echocardiographic assessment and acculturation measured by the Short Acculturation Scale, nativity, immigration age, length of US residence, generational status and language.

Primary and secondary outcome measures: Echocardiographic assessment of left atrial volume index (LAVI), left ventricular mass index (LVMI), early diastolic transmitral inflow and mitral annular velocities.

Results: The study population was predominantly Spanish-speaking and foreign-born with mean US residence of 22.7 years, mean age of 56.4 years; 50% had hypertension, 28% had diabetes, and 44% had a BMI >30kg/m^2. Multivariable analyses demonstrated higher LAVI with increasing years of US residence. Foreign-born and first generation participants had higher E/e' but lower LAVI and e' velocities compared to the second generation. Higher acculturation and income >$20K were associated with higher LVMI, LAVI, and E/e', but lower e' velocities. Preferential Spanish-speakers with an income <$20K had a higher E/e'.

Conclusions: Acculturation was associated with abnormal cardiac structure and function, with some effect modification seen according to socioeconomic status.

Abstract Word Count: 207

Keywords: Acculturation, Echocardiogram, Hispanics/Latinos, Socioeconomic Status

Strengths and limitations of this study

- A population-based cohort study among predominantly immigrant Hispanic/Latinos in the United States.
- A detailed comprehensive echocardiographic examination was performed to determine cardiac structure and function in every participant.
- Determined whether acculturation, an important sociocultural factor, contributes to the heart failure risk factor burden among an immigrant population.
- We are specifically referring to acculturation into the US culture, which may not be generalizable to acculturation in other settings.

Cardiovascular disease (CVD) and heart failure (HF) risk factor burden is high among Hispanic/Latinos in the United States (US)[1,2] compared to non-Hispanic whites leading to abnormalities of cardiac structure and function[3] which have been associated with incident clinical HF,[4] incident CVD and increased mortality.[5-8]

With respect to HF, Hispanics/Latinos have a higher incidence compared to non-Hispanic whites and Hispanics/Latinos who present with HF are younger with more co-morbidities and a lower left ventricular (LV) ejection fraction (EF) compared to non-Hispanic whites.[2,9-11] Beyond traditional HF risk factors (hypertension, diabetes and obesity), sociocultural factors such as acculturation, may contribute to HF risk among Hispanic/Latinos **(Figure 1/Conceptual Model)**[2] but the impact of acculturation on cardiac structure and function has not been examined. The fact that Hispanics/Latinos are the largest immigrant population in the US accentuates the public health impact of studying the impact of acculturation on cardiac parameters.

Acculturation is a multidimensional process whereby immigrants adapt to the beliefs and practices of a host culture.[12] This can pose a chronic daily stressor for many immigrants that can affect physical health outcomes. Acculturation has been associated with increased psychosocial stress, deleterious CV health behaviors and a higher CV risk factor burden.[13-16] In our mechanistic framework, the acculturative process leads to increase stressors and worse health behaviors which separately or jointly alter cardiac structure and function to increase HF risk. Few studies[17,18] have examined acculturation in relation to HF risk specifically focusing on cardiac structure and function as key intermediary outcomes.

We primarily sought to test whether acculturation, an important sociocultural variable with biopsychosocial implications, is associated with cardiac structure and function among Hispanics/Latinos. Studies of acculturation and CVD often overlook socioeconomic status (SES) as an effect modifier. Because SES is associated with cardiac parameters[19] and modifies the association between acculturation and other health-related variables,[20] secondarily, we sought to test whether our primary associations are moderated by SES.

Methods

Cohort Description

The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is a population-based study of 16,415 Hispanic/Latinos from randomly selected households at four US field centers (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA).[21] Probability sampling was used to ensure broad representation of the target population and to minimize the sources of bias that may otherwise enter into the cohort selection and recruitment process. Participants were between 18 and 74 years of age, and self-identified as Cuban, Central American, Dominican, Mexican, Puerto Rican, or South American Hispanic/Latino heritage. The ECHO-SOL ancillary study was designed to provide echocardiographic parameters characterizing cardiac structure and function in a representative HCHS/SOL baseline subsample of 1,818 participants ≥45 years old.[3,22] Institutional Review Board approval was obtained at each study site and all ECHO-SOL participants gave informed consent prior to participating in the study.

Patient and public involvement

No patients were involved in the development of the research question, design, recruitment or implementation of this research cohort study. Results were disseminated to study participants in the form of a Data Book and periodic newsletters. See www.saludsol.net.

In-Person Examination

The examination protocol for the parent HCHS/SOL has been previously published.[13] Obesity was defined as a body mass index (BMI) ≥ 30.0 kg/m^2. Seated resting blood pressures were measured in triplicate and the average of the 2nd and 3rd readings was used for analysis. Type 2 diabetes was defined based on American Diabetes Association definition using one or more of the following criteria: 1) fasting serum glucose ≥126 mg/dl, 2) oral glucose tolerance test ≥200 mg/dl, 3) self-reported diabetes, 4) HbA1C ≥6.5%, or 5) taking anti-diabetic medication or insulin. Renal function was measured by estimated glomerular filtration rate (eGFR). Physical activity levels, categorized as low or medium/high, were assessed using the Global Physical Activity Questionnaire.[23] Self-report questionnaires assessed smoking status (no/ever/current), alcohol consumption (current/no), and insurance coverage (yes/no) and type (Private/Medicare/Medicaid). Socioeconomic status was defined as highest degree or level of school completed and household income level – dichotomized as <$20,000 and >$20,000, given the low number of participants with incomes >$40,000. Our secondary analysis focused on current income while living in the US as more relevantly influencing a participant's acculturative process, acting as a proxy for the ability to integrate and be exposed to mainstream US cultural contexts. Marital status categorized as (single/married/partnered/separated/divorced/widowed).

Echocardiographic Measurements

Trained sonographers performed transthoracic echocardiography examinations, including 2D imaging, and spectral, color and tissue Doppler.[22] Echocardiographic measures of left and right heart structure and function included:

1) LV mass index (LVMI) was determined according to guidelines,[24] by subtracting the LV endocardial cavity volume from the LV epicardial volume and multiplying the resultant myocardial volume by the myocardial density and indexing to body surface area.
2) LV systolic function and volumes. LVEF was derived from Volumetric Assessments using the method of discs from apical 4- and 2-chamber long-axis views to measure end-diastolic volume (EDV) and end-systolic volume (ESV). LVEF was calculated: (EDV - ESV)/EDV.
3) LV diastolic function was defined per guidelines,[25] using three echocardiographic parameters: 1) peak early (E) and late (A) diastolic transmitral inflow velocities; 2) early diastolic (e') annular velocities (the average of septal and lateral annular velocities were used); 3) left atrial volume indexed (LAVI) to body surface area.
4) Relative Wall Thickness (RWT) defined as: [(posterior wall thickness x 2) / LV diastolic diameter] predicates LV geometry. Higher RWT values are associated with a smaller LV cavity size and lower RWT values are associated with higher LV cavity sizes.

Acculturation Measures

Acculturation was characterized according to several measured variables. First, nativity was classified as either born in or outside the US mainland (50 states). Those born in Puerto Rico (PR) or other US territories were classified as born outside of the US mainland to reflect their migration and acculturation experiences. Second, foreign-born individuals were asked the number of years lived in the US and categorized as <5, 5-10, 11-20, >20 years. We used the

Short Acculturation Scale for Hispanics (SASH),[26] which has two subscales based on five-point Likert type questions: 1. the SASH language subscale (items related to language use [e.g., language they speak, think]); and 2. the SASH social relations subscale (items related to media preference and social affiliations [e.g., language of media programs watched; ethnicity of close friends]). The SASH has yielded reliabilities (α) of 0.92 (overall), 0.90 (language use), 0.86 (media preference), and 0.78 (ethnic and social relations). These subscales were analyzed separately with higher scores representing higher degrees of acculturation. Fifth, language preference was further characterized as English vs. Spanish based on language of interview. Finally, data on generational status (first- and second-generation Hispanics are US-born and distinct from their foreign-born immigrant parents) was collected as well as age at the time of migration to the US.

Statistical Analyses

Sampling weights were used to obtain weighted frequencies of descriptive variables and population estimates in the ECHO-SOL target population. We used means ± standard errors (SEs) for continuous variables and proportions for categorical variables. LVMI, RWT, LVEF, e' annular velocities and LAVI were analyzed as continuous variables. LV diastolic dysfunction (LVDD) was analyzed as a binary variable (present vs. absent).[3] Acculturation variables were categorical (foreign- vs. US-born; 1st generation vs. 2nd; Spanish language preference vs. English), ordinal (<5, 5-10, 11-20, and >20 years in the US) and continuous measures (age at immigration and SASH subscales). Weighted means and linear regression analysis was utilized for continuous variables whereas weighted frequencies and Rao-Scott Chi-Square was utilized for the categorical/ordinal variables. Means were compared across categorical acculturation

variables using ANOVA for each measure of cardiac structure (LVMI, RWT, LAVI) and function (LVEF, e', E/e'). Only significant unadjusted associations were further explored in multivariable analysis. Unadjusted and multivariable linear and logistic regression analyses were determined by our continuous and categorical dependent variable measures of cardiac structure and function, respectively utilizing sequential modeling for age and sex followed by models including clinical covariates (diabetes, hypertension, and obesity), and behavioral characteristics (physical activity, tobacco use, and alcohol use). For years in the US, we compared >20 years to <5 years as well as an overall comparison across each category of years in the US. We performed a couple of exploratory analyses (data not shown): 1. comparing acculturative characteristics of individuals born in the island of PR vs. other foreign-born Hispanics; 2. comparing acculturation and health care utilization using HCHS/SOL questions regarding primarily regarding difficulty obtaining health care in the past year and number of physician visits in the past year. We tested effect moderation with income through the use of interaction terms in models followed by stratified analyses by income for statistically significant interactions at the $p<0.01$ level. All other statistical tests were 2-sided at a significance level of 0.05. All reported values were weighted to account for HCHS/SOL sampling probability design, stratification, clustering and nonresponse and to make estimates applicable to the HCHS/SOL target population. All analyses were performed utilizing SAS 9.3 (SAS Institute, Cary, NC) survey statistics, which produce standard errors (SEs) not standard deviations.

Results

Fifty-seven percent of the study population were women; almost half (46%) had a reported annual income under $20K; over half were married and most had some type of health insurance

(mostly Medicaid and/or Medicare). Hypertension and diabetes were prevalent in half and almost one-third of the study population respectively. Most of the study population was foreign-born, only 14% preferred English, almost half (49%) had been in the US >20 years with a mean age of migration of 34 years of age, signifying that the majority came to the US as adults **(Table 1).** Mean values of echocardiographic variables (LAVI, RWT, LVMI, LVEF) were all within normal limits for this study population. However, mean e' annular velocities and E/e' ratio were borderline abnormal. Some degree of diastolic dysfunction was seen in over half (52%) of the study population but this has been previously described.[3]

Table S1 shows unadjusted relationships between acculturation measures and echocardiographic characteristics. LAVI was positively associated with increasing years in the US whereas RWT appeared to have a U-shaped association. A statistically significantly lower annular relaxation velocity and higher E/e' ratio was seen among the foreign-born compared to US-born and among those 1st generation compared to 2nd generation. Higher acculturation as measured by increasing SASH language scale was associated with increasing LAVI. Younger age of migration to US was associated with higher RWT and increased LAVI.

Adjusted analyses **(Table 2)** demonstrated statistically significantly greater RWT and higher LAVI with more years in the US. A statistically significantly higher E/e' ratio was seen among the foreign-born participants. Those 1st generation had lower LAVI, lower e' annular velocities and higher E/e' ratios compared to 2nd generation. Increasing SASH language scale was associated with higher LAVI whereas younger age of migration to US was associated with higher LAVI and RWT. These associations persisted in sequential models adjusted for clinical

factors and behavioral factors both separately and together. Although greater odds of LVDD was seen in unadjusted associations with nativity, generational status, SASH language, and age of immigration **(Table 3),** these associations did not persist on adjusted analysis.

Significant interactions ($p<0.01$) were found between our main exposure (acculturation) and income on the effect of cardiac structure and function. Among those whose annual income is >$20K, a greater number of years in the US was associated with higher LVMI, lower e' annular velocities, and a higher E/e' ratio compared to those making <$20K annually. Generational status was associated with increased LAVI only among those making >$20K annually. However, being a preferential Spanish-speaker carried a statistically significant higher E/e' ratio only among those making <$20K annually. **(Table S2).**

Of foreign-born Hispanics, 24% were born in the US Commonwealth of PR, none in the US Virgin Islands. Spanish language preference was less among Hispanics born in PR compared to other foreign-born Hispanics. PR-born Hispanics scored higher on the SASH language scale and social interaction scale indicating higher acculturation levels compared to other foreign-born Hispanics. However, the level of Spanish language preference and SASH scores was still lower among PR-born Hispanics compared to US born Hispanics. With regard to acculturation and health care utilization, being foreign-born, less years in the US and not having health insurance were all significantly associated with difficulty obtaining health care in the past year. Foreign-born individuals had less physician visits over the past year compared to US born. The relation between years in the US and physician visits was complex, non-linear and mirrored an opposite

pattern with income. **(Figure 2)** Having health insurance coverage was significantly associated with more physician visits over the past year.

Discussion

Hispanics/Latinos in the US represent a relatively young demographic such that the future public health burden of HF as this population ages is potentially underestimated.[27] The Hispanic population >65 years of age is expected to grow 328% between 2000 and 2030, making Hispanics the fastest growing aging population in the US.[28] As the Hispanic population ages, and HF risk factors and cardiac abnormalities progress, it is likely that an epidemic of HF in Hispanics will emerge.

Acculturation is complex and has four domains: (1) integration - maintaining attitudes and behaviors of the original parent culture while adopting the host culture; (2) assimilation - rejecting the ways of the parent culture and entirely adopting the host culture; (3) separation - rejecting the host culture and keeping the practices and behaviors of the parent culture; and (4) marginalization - not identifying with the original culture or the host culture. Prior studies show strong negative effects of greater acculturation on worsening CV risk factors but positive effects on use of preventive health services.[29-31] HCHS/SOL has demonstrated significant heterogeneity in CVD risk factor burden among Hispanics/Latinos by country of origin and acculturation measures.[13] Despite the current understanding of HF risk among Hispanics/Latinos,[2,9] our analysis of validated acculturation scales provides several important contributions. First,. Spanish language preference and SASH scores were higher among Hispanics born in PR compared to other foreign-born Hispanics but this proportion was still significantly less than US-born Hispanics. Suggesting that for many, living in the island of PR still allows for maintenance

of a culture that is distinct from the US culture. Second, higher levels of acculturation, an important phenomenon among immigrant populations, was associated with abnormal cardiac structure and function in our predominately foreign-born, Spanish-speaking adult population despite long residence in the US. Third, different measures of acculturation (each capturing different aspects of the acculturative process) had varying associations with echocardiographic measures of structure and function. Finally, income significantly moderated these associations. Our findings support the premise that exposure to the social and environmental stress of acculturation may promote unhealthy behaviors[32] and/or act via currently undefined pathways to contribute to HF risk among Hispanics/Latinos. **(Figure 2)** Further elucidating the acculturative factors influencing HF risk in Hispanics/Latinos is warranted.

Although to our knowledge, there is no existing literature on the association between acculturation and HF risk, our study found several measures of acculturation (increasing years of US residence, English preference, and younger age at immigration) were associated with abnormal cardiac structure and function (increased LAVI, increased LVMI, increased RWT, lower annular e' relaxation velocity and higher E/e' ratio). Although the magnitudes of our observed associations are modest, limiting the short-term clinical relevance of these findings, the long-term public health importance is likely high, given the potential for progression of cardiac damage with the accumulation of acculturative stress during the life course. This is particularly salient given the fact that abnormal cardiac structure and function is an independent risk factor for the future development of clinical HF. An increased E/e' ratio, LAVI, and LVMI are markers of chronically-elevated filling pressures associated with impaired cardiac relaxation and HF with preserved ejection fraction.[33,34] The presence of abnormal cardiac structure and function has been

associated with increased HF hospitalizations, cardiovascular death and improved CV risk prediction.[34-36] Importantly, these cardiac abnormalities are additive, with worse outcomes seen in individuals with more than one alteration.[34] In order to identify preclinical CV disease, abnormalities in cardiac structure and function determined by echocardiography are important intermediary measures, many of which have been associated with incident CVD, incident clinical HF and increased mortality.[5-7] Given the size of the US Hispanic/Latino population and high burden of acculturation (82% were foreign-born), echocardiography might help to identify a particularly high risk subset of participants.

LVM is associated with CVD, sudden cardiac death, and all–cause mortality.[33] Among foreign-born Hispanics/Latinos, we found increased LVMI with increasing years in the US. Our study is consistent with prior studies showing a high prevalence of LVM among Hispanics/Latinos especially among low income Hispanics/Latinos with increasing years of US residence.[18,37,38] Prior studies have demonstrated that adjustment for socioeconomic factors did not fully account for the presence of increased LVMI among Hispanics/Latinos[39] possibly due to the residual effect of acculturation. Changes in LVM can occur without overt clinical hypertension in adrenergic states, such as chronic stress[40] with psychosocial factors such as perceived discrimination and low social support.[41,42] Acculturative stress is the psychological impact or stress reaction of navigating the acculturation process and making decisions on retaining one's native culture while adapting to a new cultural context. Acculturation may act as a chronic stressor, negatively affecting mental and physical health through unhealthy behaviors,[30,32] increased anxiety, depression, perceived discrimination and lack of social support[15,32,43] which

may impact adrenergic biomarkers leadings to cardiac structural and functional abnormalities and increased HF risk. This is another area of research to further explore in future studies.

The interaction of acculturation with SES on cardiac measures may shed light on the "Hispanic paradox" which states that Hispanics/Latinos, a disproportionately low SES group, have lower overall mortality and cardiovascular mortality compared to non-Hispanic Whites.[2] Low SES is a composite chronic stressor encompassing multiple factors (e.g., work, housing and financial strain). Longitudinal studies have shown an inverse association between SES level and adverse outcomes.[41,44] We hypothesized that less acculturation (more retention of host culture) may be protective of the adverse health consequences of low SES. In our study, those with higher SES (defined as annual incomes >$20K) exhibited more deleterious effects of increasing acculturation on cardiac structural and functional measures. A prior study found the relationship between acculturation and health care utilization to be complex and moderated by SES.[45] Our exploratory analysis found that being foreign-born and having a higher income may make one less likely to utilize health care. A more extensive analysis on the complex nature of acculturation and health care utilization is beyond the scope of our paper but this area deserves further consideration in future studies. There may be more acculturative stress for higher-SES immigrants, perhaps through increased contact and interaction with the mainstream culture,[46] which may contribute to our findings. *Familismo* is a culture-specific factor characterized by having strong bonds with nuclear and extended family resulting in a high level of perceived family support and is associated with indicators of improved health.[47,48] Studies suggest that with increasing acculturation, *familismo* is eroded and dimensions of *familismo* begin to increase psychosocial stress rather than alleviate it.[48-50]

Several limitations should be noted. Our study is cross-sectional and precludes the ability to assess the temporal sequence of the relationships and causal inference. However, our findings warrant replication and longitudinal follow up. Participants resided in one of four US cities, precluding generalizability to all Hispanic/Latinos in the US. While this study is one of the largest studies of acculturation with cardiac structure and function in any population, the sample size is relatively modest; thus, we were underpowered to perform stratified analyses by national origin in order to characterize the heterogeneity within Hispanic/Latinos. We are specifically referring to acculturation into the US culture, which may not be generalizable to acculturation in other settings. Finally, our study focuses on acculturation as a unique intra-ethnic phenomenon. By including several measures (nativity, years of US residence/age at migration, SASH subscales, language preference and generational status) our goal was to be comprehensive and to capture several aspects of acculturation. We believe acculturation cannot be captured by just one measure, as has been done in much of the prior literature; however, we agree that even our multivariable approach may not fully capture the complexities of all aspects and dimensions of the acculturative process.

Conclusions

In addition to traditional CV risk factors, acculturation may explain the disproportionate burden of HF risk among Hispanics/Latinos. Our study found significant associations between several acculturation measures with deleterious cardiac structural and functional parameters among a predominantly low-SES, foreign-born Hispanic/Latino population with increasing years of residence in the US. The acculturation experience is not unique to Hispanics/Latinos. Our study

may help generate further research in other immigrant populations. Further elucidation of how acculturation impacts HF risk is warranted in order to possibly risk stratify a high-risk subgroup of Hispanics/Latinos and to inform the development of culturally appropriate interventions to amplify protective factors and to make the acculturative process less deleterious for Hispanics/Latinos and other immigrants.

Acknowledgements: The authors thank the staff and participants of HCHS/SOL and ECHO-SOL for their important contributions. Investigators website - http://www.cscc.unc.edu/hchs/

Contributors: Research Conception and design: CJR, LL; **Collection and assembly of data:** CJR, MAA, RK, LCG; **Analysis and interpretation of the data:** CJR, LL, KS; **Drafting of the article:** CJR, LL, FR; **Critical revision of the article for important intellectual content:** CJR, LL, FR, JRK, FJP, LCG, WA, FG; **Obtaining of funding:** CJR, RK, MAA; **Statistical expertise:** KS, FG

CJR and LL are responsible for the overall content as guarantors.

Funding: This study supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI) to the University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), and San Diego State University (N01-HC65237). The following institutes contributed to HCHS/SOL: National Institute on Minority Health and Health Disparities, National Institute on Deafness and Other Communication Disorders, National Institute of Dental and Craniofacial Research, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Neurological Disorders and Stroke, NIH Institution-Office of Dietary Supplements.

ECHO-SOL was supported by the National Heart, Lung, and Blood Institute (R01 HL104199, Epidemiologic Determinants of Cardiac Structure and Function among Hispanics: Carlos J. Rodriguez, MD, MPH Principal Investigator). Dr. Lenny L. López acknowledges the support of the Robert Wood Johnson Foundation Harold Amos Medical Faculty Development Program and NIDDK 1K23DK098280-01. No relationships with industry supported this work.

Competing interests: None declared.

Patient consent for publication: Not required.

Ethics approval: The Institutional Review Board at the Wake Forest School of Medicine and at each study site provided approval and oversight of all study materials and activities.

Data sharing statement: Data is publically available on request.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart Disease and Stroke Statistics—2015 Update: A Report From the American Heart Association. Circulation 2015;131:e29-e322.
2. Rodriguez CJ, Allison M, Daviglus ML, et al. Status of cardiovascular disease and stroke in Hispanics/Latinos in the United States: a science advisory from the American Heart Association. Circulation 2014;130:593-625.
3. Mehta H, Armstrong A, Swett K, et al. Burden of Systolic and Diastolic Left Ventricular Dysfunction Among Hispanics in the United States: Insights From the Echocardiographic Study of Latinos. Circ Heart Fail 2016;9.
4. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147-239.
5. Hobbs FD, Roalfe AK, Davis RC, Davies MK, Hare R, Midlands Research Practices C. Prognosis of all-cause heart failure and borderline left ventricular systolic dysfunction: 5 year mortality follow-up of the Echocardiographic Heart of England Screening Study (ECHOES). Eur Heart J 2007;28:1128-34.
6. Armstrong AC, Jacobs DR, Jr., Gidding SS, et al. Framingham score and LV mass predict events in young adults: CARDIA study. Int J Cardiol 2014;172:350-5.
7. Bombelli M, Facchetti R, Cuspidi C, et al. Prognostic significance of left atrial enlargement in a general population: results of the PAMELA study. Hypertension 2014;64:1205-11.
8. Echouffo-Tcheugui JB, Erqou S, Butler J, Yancy CW, Fonarow GC. Assessing the Risk of Progression From Asymptomatic Left Ventricular Dysfunction to Overt Heart Failure: A Systematic Overview and Meta-Analysis. JACC Heart Fail 2016;4:237-48.
9. Vivo RP, Krim SR, Cevik C, Witteles RM. Heart failure in Hispanics. J Am Coll Cardiol 2009;53:1167-75.
10. Vivo RP, Krim SR, Krim NR, et al. Care and outcomes of Hispanic patients admitted with heart failure with preserved or reduced ejection fraction: findings from get with the guidelines-heart failure. Circ Heart Fail 2012;5:167-75.

11. Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. Archives of internal medicine 2008;168:2138-45.
12. Zambrana RE, Carter-Pokras O. Role of acculturation research in advancing science and practice in reducing health care disparities among Latinos. Am J Public Health 2010;100:18-23.
13. Daviglus ML, Talavera GA, Aviles-Santa ML, et al. Prevalence of major cardiovascular risk factors and cardiovascular diseases among Hispanic/Latino individuals of diverse backgrounds in the United States. Jama 2012;308:1775-84.
14. Ayala GX, Baquero B, Klinger S. A systematic review of the relationship between acculturation and diet among Latinos in the United States: implications for future research. J Am Diet Assoc 2008;108:1330-44.
15. Steptoe A, Kivimaki M. Stress and cardiovascular disease: an update on current knowledge. Annu Rev Public Health 2013;34:337-54.
16. Suh M, Barksdale DJ, Logan J. Relationships among acculturative stress, sleep, and nondipping blood pressure in Korean American women. Clin Nurs Res 2013;22:112-29.
17. Peterson PN, Campagna EJ, Maravi M, et al. Acculturation and outcomes among patients with heart failure. Circ Heart Fail 2012;5:160-6.
18. Effoe VS, Chen H, Moran A, et al. Acculturation is associated with left ventricular mass in a multiethnic sample: the Multi-Ethnic Study of Atherosclerosis. BMC Cardiovasc Disord 2015;15:161.
19. Rodriguez CJ, Sciacca RR, Diez-Roux AV, et al. Relation between socioeconomic status, race-ethnicity, and left ventricular mass: the Northern Manhattan study. Hypertension 2004;43:775-9.
20. Lee H, Cardinal BJ, Loprinzi PD. Effects of socioeconomic status and acculturation on accelerometer-measured moderate-to-vigorous physical activity among Mexican American adolescents: findings from NHANES 2003-2004. J Phys Act Health 2012;9:1155-62.
21. Lavange LM, Kalsbeek WD, Sorlie PD, et al. Sample design and cohort selection in the Hispanic Community Health Study/Study of Latinos. Ann Epidemiol 2010;20:642-9.
22. Rodriguez CJ, Dharod A, Allison MA, et al. Rationale and Design of the Echocardiographic Study of Hispanics/Latinos (ECHO-SOL). Ethnicity & disease 2015;25:180-6.

23. Cleland CL, Hunter RF, Kee F, Cupples ME, Sallis JF, Tully MA. Validity of the global physical activity questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health 2014;14:1255.

24. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography 2005;18:1440-63.

25. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures - A comparative simultaneous Doppler-Catheterization study. Circulation 2000;102:1788-94.

26. Marin G, Sabogal F, Marin BV, Otero-Sabogal F, and Perez-Stable E. Development of a short acculturation scale for Hispanics. Hispanic Journal of Behavioral Sciences 1987;9:183-205.

27. Rangel MO, Kaplan R, Daviglus M, et al. Estimation of Incident Heart Failure Risk among US Hispanics/Latinos Using a Validated Echocardiographic Risk-Stratification Index: the Echocardiographic Study of Latinos. J Card Fail 2018;24:622-4.

28. US Census Bureau. 65+ in the United States:2005. Current Population Reports December 2005.

29. Moran A, Diez Roux AV, Jackson SA, et al. Acculturation is associated with hypertension in a multiethnic sample. Am J Hypertens 2007;20:354-63.

30. Abraido-Lanza AF, Chao MT, Florez KR. Do healthy behaviors decline with greater acculturation? Implications for the Latino mortality paradox. Soc Sci Med 2005;61:1243-55.

31. DuBard CA, Gizlice Z. Language spoken and differences in health status, access to care, and receipt of preventive services among US Hispanics. Am J Public Health 2008;98:2021-8.

32. Lara M, Gamboa C, Kahramanian MI, Morales LS, Bautista DE. Acculturation and Latino health in the United States: a review of the literature and its sociopolitical context. Annu Rev Public Health 2005;26:367-97.

33. Abbate A, Arena R, Abouzaki N, et al. Heart failure with preserved ejection fraction: refocusing on diastole. Int J Cardiol 2015;179:430-40.

34. Shah AM, Claggett B, Sweitzer NK, et al. Cardiac structure and function and prognosis in heart failure with preserved ejection fraction: findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) Trial. Circ Heart Fail 2014;7:740-51.

35. Zile MR, Gottdiener JS, Hetzel SJ, et al. Prevalence and significance of alterations in cardiac structure and function in patients with heart failure and a preserved ejection fraction. Circulation 2011;124:2491-501.

36. Burke MA, Katz DH, Beussink L, et al. Prognostic importance of pathophysiologic markers in patients with heart failure and preserved ejection fraction. Circ Heart Fail 2014;7:288-99.

37. Zabalgoitia M, Ur Rahman SN, Haley WE, et al. Impact of ethnicity on left ventricular mass and relative wall thickness in essential hypertension. Am J Cardiol 1998;81:412-7.

38. Rodriguez CJ, Diez-Roux AV, Moran A, et al. Left ventricular mass and ventricular remodeling among Hispanic subgroups compared with non-Hispanic blacks and whites: MESA (Multi-ethnic Study of Atherosclerosis). J Am Coll Cardiol 2010;55:234-42.

39. Rodriguez CJ, Lin F, Sacco RL, et al. Prognostic implications of left ventricular mass among Hispanics: the Northern Manhattan Study. Hypertension 2006;48:87-92.

40. Julius S, Li Y, Brant D, Krause L, Buda AJ. Neurogenic pressor episodes fail to cause hypertension, but do induce cardiac hypertrophy. Hypertension 1989;13:422-9.

41. Rozanski A, Blumenthal JA, Davidson KW, Saab PG, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. J Am Coll Cardiol 2005;45:637-51.

42. Rodriguez CJ, Elkind MS, Clemow L, et al. Association between social isolation and left ventricular mass. Am J Med 2011;124:164-70.

43. Gallo LC, Penedo FJ, Espinosa de los Monteros K, Arguelles W. Resiliency in the face of disadvantage: do Hispanic cultural characteristics protect health outcomes? J Pers 2009;77:1707-46.

44. Gallo LC, de Los Monteros KE, Allison M, et al. Do socioeconomic gradients in subclinical atherosclerosis vary according to acculturation level? Analyses of Mexican-Americans in the multi-ethnic study of atherosclerosis. Psychosom Med 2009;71:756-62.

45. Peng BL, Zou GY, Chen W, Lin YW, Ling L. Association between health service utilisation of internal migrant children and parents' acculturation in Guangdong, China: a cross-sectional study. BMJ Open 2018;8:e018844.

46. McClure LA, Zheng DD, Lam BL, et al. Factors Associated With Ocular Health Care Utilization Among Hispanics/Latinos: Results From an Ancillary Study to the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). JAMA Ophthalmol 2016;134:320-9.

47. Davila YR, Reifsnider E, Pecina I. Familismo: influence on Hispanic health behaviors. Appl Nurs Res 2011;24:e67-72.

48. Sabogal F, Marin G, Otero-Sabogal R, Marin B. Hispanic familism and acculturation: What changes and what doesn't? Hispanic Journal of Behavioral Sciences 1987;9:397-412.

49. Miranda A, Estrada D, Firpo-Jimenez M. Differences in family cohesion, adaptability, and environment among Latino families in dissimilar stages of acculturation. The Family Journal 2000;8:341-50.

50. Rodriguez N, Mira C, Paez N, Myers H. Exploring the complexities of familism and acculturation: central constructs for people of Mexican origin. Am J Community Psychol 2007;39:61-77.

Table 1. ECHO-SOL Demographic and Clinical Characteristics (N = 1,818)†

Demographic Characteristics	**[N (%)]**
Women	1187 (57.4)
Age, [mean (SE)]	56.4 (0.37)
High School Graduate or Higher	726 (43.3)
Annual Family Income > $20,000	787 (45.5)
Marital Status	
Single	332 (18.8)
Married/Partner	961 (53.2)
Separated/Divorced/Widow	522 (28.0)
Health Insurance	1042 (60.1)
Short Acculturation Scale for Hispanics (SASH)	**[mean (SE)]**
Language Use Subscale	1.7 (0.05)
Social Relations Subscale	2.1 (0.03)
Length of US residence	[N (%)]
<5 years	178 (13.6)
5-10 years	247 (15.2)
11-20	385 (22.1)
>20	842 (49.1)
Second generation or higher	185 (9.3)
English language preference	225 (14.0)
Age at migration [mean (SE)]	34.0 (1.0)
US born	163 (7.9)
Clinical Characteristics	**[N (%)]**
Hypertension	861 (50.0)
Type 2 Diabetes	523 (28.4)
Current Smoker	304 (17.6)
Physical activity level low	1227 (67.3)
BMI ≥30	822 (44.3)
Current Alcohol Use	770 (43.5)
Echocardiographic Variables	**[mean (SE)]**
Left Atrial Volume Index (≤33 mL/m^2)	23.0 (0.25)
Relative Wall Thickness (0.22-0.42)	0.40 (0.004)
Left Ventricular Mass Index (45-105 g/m^2)	82.7 (0.7)
Ejection Fraction (≥55 %)	59.8 (0.2)
E prime (e') (8-16 cm/s)	8.1 (0.09)
E/e' (≤12)	10.0 (0.12)
Diastolic Dysfunction [N (%)]	916 (51.9)

†N's presented are unweighted counts of total participants in the ECHO-SOL with each respective characteristic.
Percentages are weighted row percentages.
Normal values are provided for cardiac structure and function variables.

Table 2. Adjusted Analyses of Acculturation Measures with Cardiac Structure and Function.*

	LVMI (g/m^2) β (p)	**RWT** β (p)	**LAVI** (mL/m^2) β (p)	**LVEF** (%) β (p)	**e'** (cm/s) β (p)	**E/e'** β (p)
Nativity						
Age, sex					-0.349 (0.12)	0.571 (0.02)
Model 1	—	—	—	—	-0.320 (0.10)	0.524 (0.02)
Model 2					-0.324 (0.14)	0.532 (0.02)
Model 3					-0.303 (0.12)	0.503 (0.02)
Foreign Born (Years in the US)						
Age, sex	—	0.020 (0.06); all (0.03)	1.57 (0.02); all (<0.05)	—	—	—
Model 1		0.022 (0.02); all (0.02)	1.63 (0.02); all (<0.05)			
Model 2		0.018 (0.06); all (0.02)	1.55 (0.02); all (0.05)			
Model 3		0.021 (0.02); all (0.007)	1.71 (0.01); all (0.04)			
Generation						
Age, sex			-0.468 (0.21)		-0.529 (0.01)	0.710 (0.002)
Model 1	—	—	-1.797 (0.004)	—	-0.447 (0.01)	0.594 (0.003)
Model 2			-1.444 (0.03)		-0.499 (0.01)	0.671 (0.003)
Model 3			-1.584 (0.01)		-0.425 (0.02)	0.575 (0.006)
SASH Language						
Age, sex			0.580 (0.01)		0.125 (0.10)	
Model 1	—	—	0.610 (0.008)	—	0.097 (0.11)	—
Model 2			0.546 (0.01)		0.123 (0.15)	
Model 3			0.590 (0.007)		0.095 (0.16)	
Age at Immigration						
Age, sex		0.0005 (0.15)	-0.040 (0.008)		-0.005 (0.27)	
Model 1	—	0.0005 (0.13)	-0.040 (0.008)	—	-0.006 (0.14)	—
Model 2		0.0004 (0.15)	-0.038 (<0.001)		-0.005 (0.37)	
Model 3		0.0004 (0.13)	-0.038 (0.01)		-0.005 (0.22)	

*Only acculturation measures that were significant in unadjusted analyses were analyzed in multivariable adjusted models.
For Years in the US, the 1st p-value reflects <5 years vs. >20 years comparison; whereas the 2nd p-value is for overall comparison across all the Years in the US categories (<5; 5-10; 11-20; >20)
Model 1: Age, Sex, Diabetes, Hypertension, Obesity | Model 2: Age, Sex, Physical Activity, Tobacco, Alcohol Use | Model 3: Model 1 + Model 2
LVMI = Left ventricular mass index; RWT = Relative wall thickness; LAVI = Left atrial volume index; LVEF = Left ventricular ejection fraction
e'= Mitral annular early diastolic velocity; E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Table 3. Unadjusted and Adjusted‡ Analyses of Acculturation Measures with Diastolic Dysfunction.

		Adjusted Sequential Models			
	Unadjusted	Age, Sex	Model 1	Model 2	Model 3
Nativity					
Foreign born	1.67 (1.08-2.58)	0.98 (0.62-1.55)	0.94 (0.59-1.51)	0.98 (0.62-1.55)	0.95 (0.59-1.53)
US born	Ref				
Years in the US					
<5	0.86 (0.60-1.24)				
5-10	0.72 (0.49-1.04)				
11-20	0.91 (0.61-1.37)	—	—	—	—
>20	Ref				
Generation					
1	1.90 (1.24-2.92)	1.29 (0.77-2.14)	1.18 (0.74-1.91)	1.26(0.77-2.06)	1.18 (0.73-1.89)
2	Ref				
Language Preference					
English	0.67 (0.34-1.32)	—	—	—	—
Spanish	Ref				
SASH Language	0.81 (0.67-0.98)	—	—	—	—
SASH Social	0.88 (0.68-1.15)	—	—	—	—
Age at Immigration	1.02 (1.004-1.03)	1.00 (0.99-1.02)	1.01 (0.995-1.02)	1.01 (0.99-1.02)	1.01 (0.995-1.02)

‡Only acculturation measures that were significant in unadjusted analyses were analyzed in adjusted models.
ORs (95% CIs) are presented
Model 1: Age, Sex, Diabetes, Hypertension, Obesity
Model 2: Age, Sex, Physical Activity, Tobacco, Alcohol Use
Model 3: Model 1 + Model 2

Figure Legend:

Figure 1. Proposed Relationships Between Acculturation with Cardiac Structure and Function.

Figure 2. Relation of Years Residing in the US or Income Level with Number of Physician Visits

Figure 1.

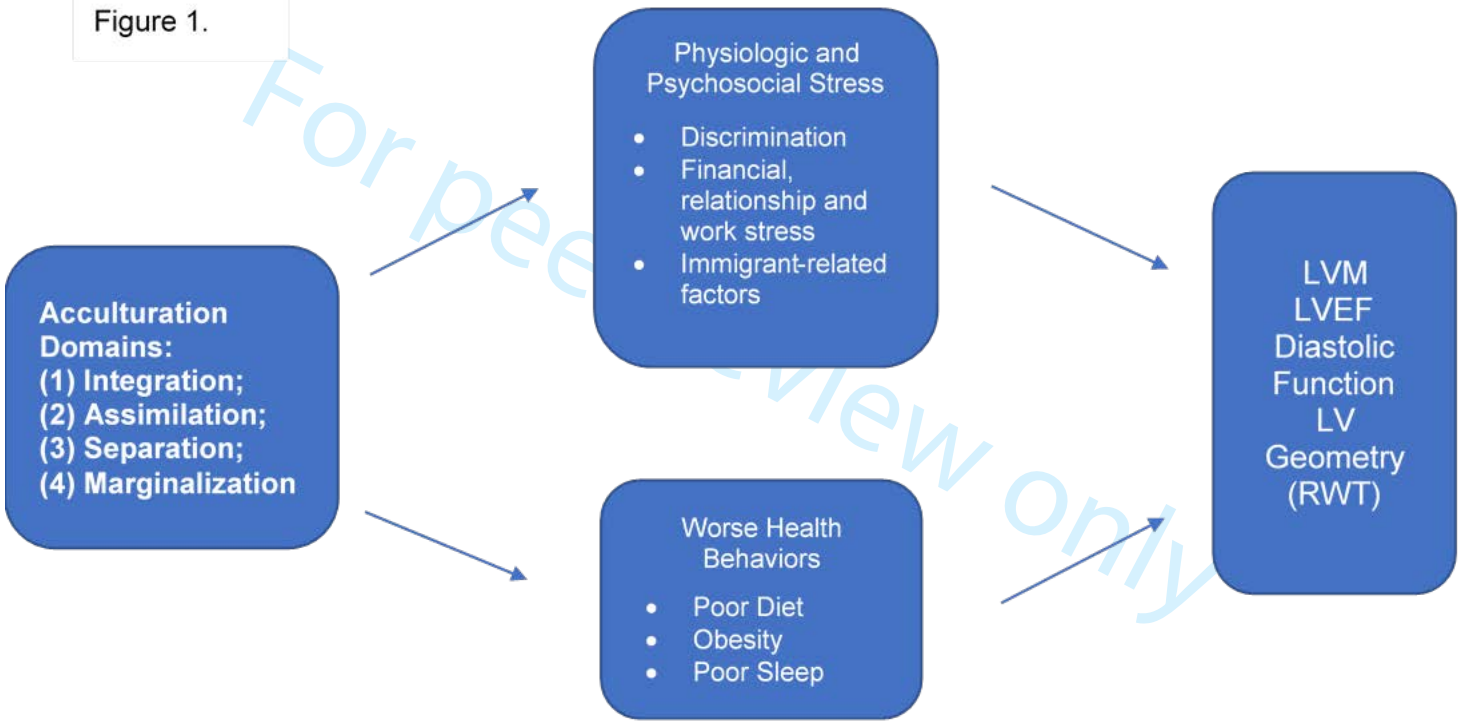


Figure 2.

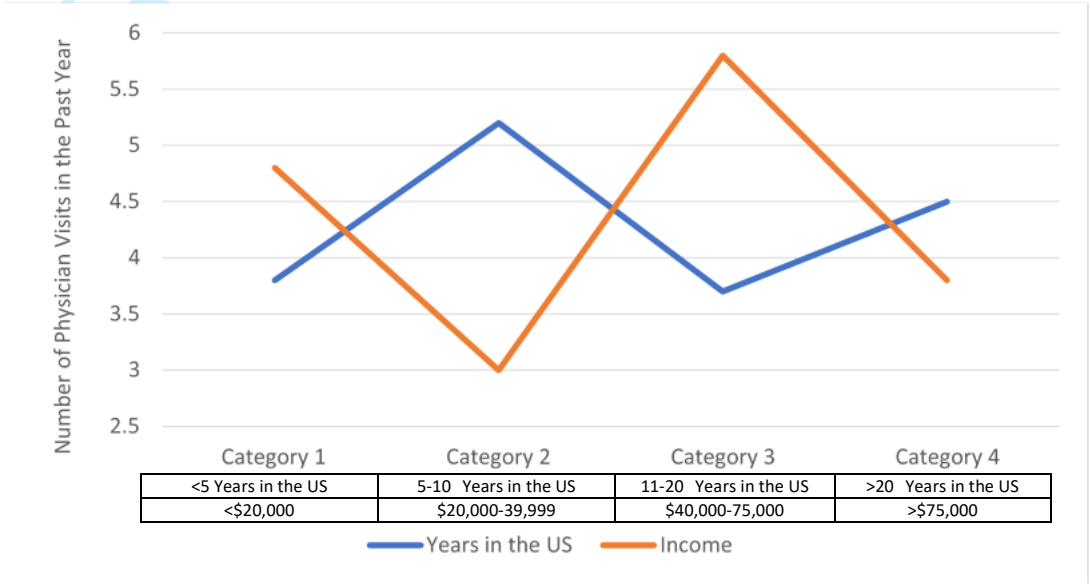

Number of Physician Visits in the Past Year
6
5.5
5
4.5
4
3.5
3
2.5
Category 1
Category 2
Category 3
Category 4
<5 Years in the US
5-10 Years in the US
11-20 Years in the US
>20 Years in the US
<$20,000
$20,000-39,999
$40,000-75,000
>$75,000
Years in the US
Income

Table S1. Unadjusted Acculturation Measures with Echocardiographic Measures of Cardiac Structure and Function.

	LVMI (g/m^2)		RWT		LAVI (mL/m^2)		LVEF (%)		e' (cm/s)		E/e'	
Categorical Measures												
	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p
Nativity												
Foreign Born	82.74	0.92	0.40	0.07	22.93	0.10	59.83	0.54	7.98	<0.001	10.1	<0.001
US Born	82.54		0.38		24.10		59.50		8.99		8.8	
Years in US												
<5 years	79.80	0.16	0.41	0.03	21.70	0.03	59.94	0.09	7.71	0.11	10.2	0.25
5-10 years	80.43		0.39		22.40		60.04		8.18		9.7	
11-20 years	83.60		0.41		22.82		58.94		8.27		9.8	
>20 years	83.96		0.39		23.50		60.14		7.86		10.2	
Generation												
First	82.69	0.88	0.40	0.08	22.89	0.02	59.84	0.45	7.97	<0.001	10.1	<0.001
Second or Greater	82.96		0.38		24.41		59.45		9.01		8.8	
Language												
English	81.51	0.59	0.38	0.08	24.00	0.06	60.13	0.48	8.52	0.15	9.7	0.64
Spanish	82.92		0.40		22.87		59.75		7.99		10.0	
Continuous Measures												
	β (se)	p	β (se)	p	β (se)	p	β (se)	p	β (se)	p	β (se)	p
Age at Immigration	-0.0003 (0.0632)	0.99	0.0006 (0.0003)	0.02	-0.030 (0.014)	0.03	-0.003 (0.012)	0.79	-0.023 (0.007)	0.001	0.012 (0.010)	0.23
SASH Subscales												
Language	0.087 (0.735)	0.91	-0.005 (0.003)	0.10	0.539 (0.237)	0.02	0.166 (0.180)	0.36	0.255 (0.098)	0.009	-0.205 (0.109)	0.06
Social Relations	0.086 (1.392)	0.95	-0.009 (0.006)	0.15	0.732 (0.373)	0.05	0.539 (0.295)	0.07	0.266 (0.155)	0.09	-0.156 (0.217)	0.47

LVMI = Left ventricular mass index; RWT = Relative wall thickness; LAVI = Left atrial volume index
LVEF = Left ventricular ejection fraction; e'= Mitral annular early diastolic velocity
E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Table S2. Income Stratified Adjusted Analyses of Acculturation Measures with Cardiac Structure and Function.[¥]

	LVMI (g/m^2)				**LAVI** (mL/m^2)				**e'** (cm/s)				**E/e'**				**Diastolic Dysfunction**	
	<$20,000		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**	**>$20,000**
	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	ORs (95% CI)	ORs (95% CI)
Nativity																		
Foreign	—	—	—	—	—	—	—	—	7.90	0.0006	8.24	0.048	—	—	—	—	1.67 (0.89-3.14)	1.24 (0.70-2.19)
US born									8.83		8.99							
Years in the US																		
<5	80.02		73.35						7.70		9.03		10.20		9.17			
5-10	81.32	0.15	79.38	0.002	—	—	—	—	7.72	0.27	8.87	0.001	10.36	0.62	8.63	0.003	—	—
11-20	82.22		86.12						8.23		8.56		9.912		9.49			
>20	85.73		82.23						7.87		7.89		10.28		10.16			
Generation																		
1	—	—	—	—	23.04	0.45	22.85	0.02	—	—	—	—	—	—	—	—	1.82 (0.99-3.34)	1.50 (0.83-2.69)
2					23.91		24.67											
Language Preference																		
English	—	—	—	—	—	—	—	—	—	—	—	—	9.42	0.01	10.00	0.63	—	—
Spanish													10.21		9.55			
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	—	—
SASH Language	—	—	—	—	0.2686	0.32	0.7213	0.04	—	—	—	—	-0.3026	0.003	0.1065	0.60	—	—
SASH Social	—	—	—	—	—	—	—	—	—	—	—	—	-0.5410	0.008	0.4641	0.27	—	—

[¥]Only statistically significant interactions were analyzed in adjusted models; excludes cases where income is missing.
Multivariable models were adjusted for Age, Sex, Diabetes, Hypertension, Obesity, Physical Activity, Tobacco, and Alcohol Use.
LVMI = Left ventricular mass index; LAVI = Left atrial volume index
e'= Mitral annular early diastolic velocity; E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

STROBE Statement—Checklist of items that should be included in reports of ***Observational studies in epidemiology***

	Item No	Recommendation	Page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1&
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3&4
		Introduction	
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4&5
		Methods	
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6&7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6&7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5&9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6&7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8&9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
		Results	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	10&11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10&11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a	

		meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
		Discussion	
Key results	18	Summarise key results with reference to study objectives	12&13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14&15
Generalizability	21	Discuss the generalizability (external validity) of the study results	16
		Other information	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: a cross-sectional analysis of the Echocardiographic Study of Latinos

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028729.R2
Article Type:	Original research
Date Submitted by the Author:	07-Oct-2019
Complete List of Authors:	Lopez, Lenny; San Francisco VA Medical Center, Hospital Medicine Swett, Katrina; Yeshiva University Albert Einstein College of Medicine, Medicine / Cardiology Rodriguez, Fatima ; Stanford University School of Medicine, Medicine / Cardiology Kizer, Jorge R.; San Francisco VA Medical Center, Medicine / Cardiology Penedo, Frank; Northwestern University, Medical Social Sciences. Gallo, Linda; San Diego State University Allison, Matthew; University of California San Diego, Medicine Arguelles, William; Baptist Health South Florida Gonzalez, Franklyn; University of North Carolina at Chapel Hill, Biostatistics Kaplan, Robert C.; Yeshiva University Albert Einstein College of Medicine, Epidemiology and Population Health Rodriguez, Carlos J.; Yeshiva University Albert Einstein College of Medicine, Medicine / Cardiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, SOCIAL MEDICINE, EPIDEMIOLOGY, Echocardiography < CARDIOLOGY

Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: a cross-sectional analysis of the Echocardiographic Study of Latinos

Short Title: Acculturation and Cardiac Structure and Function

Address for correspondence
Lenny López, MD, MPH, MDiv. Division of Hospital Medicine, University of California San Francisco – San Francisco VA Medical Center. 4150 Clement St, San Francisco CA, 94121. (lenny.lopez@ucsf.edu). Phone: 617-270-6600.

Contributing authors:

1. Lenny López, MD, MPH, MDiv. Division of Hospital Medicine, University of California San Francisco – San Francisco VA Medical Center, San Francisco, CA. (lenny.lopez@ucsf.edu).
2. Katrina Swett, MS. Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY. (katrina.swett@einstein.yu.edu).
3. Fátima Rodríguez, MD, MPH. Division of Cardiovascular Medicine, Stanford University, Palo Alto, CA. (frodrigu@stanford.edu).
4. Jorge R. Kizer, MD. Division of Cardiology, San Francisco VA Medical Center, San Francisco, CA. (jorge.kizer@ucsf.edu).
5. Frank J. Penedo, PhD. Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois. (frank.penedo@northwestern.edu).
6. Linda C. Gallo, PhD. Department of Psychology, San Diego State University, San Diego, CA. (lgallo@mail.sdsu.edu).
7. Matthew A. Allison, MD, MPH, FAHA. Division of Preventive Medicine, University of California San Diego, San Diego, CA. (mallison@ucsd.edu).
8. William Arguelles, PhD. Center for Research and Grants, Baptist Health South Florida, Miami, FL. (warguelles@psy.miami.edu).
9. Franklyn Gonzalez, MS. Department of Biostatistics, University of North Carolina, Chapel Hill, NC. (fgonzale@email.unc.edu).
10. Robert Kaplan, PhD. Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY. (robert.kaplan@einstein.yu.edu).
11. Carlos J. Rodríguez, MD, MPH. Departments of Cardiovascular Medicine, Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY. (carlos.rodriguez@einstein.yu.edu).

Manuscript Word Count: 3,483
Number of Tables: 3
Number of Figures: 2
Number of Supplemental Tables: 2

Abstract

Objective: Hispanics/Latinos, the largest immigrant population in the United States, undergo the process of acculturation and have a large burden of heart failure risk. Few studies have examined the association of acculturation on cardiac structure and function. **Design**: cross-sectional

Setting: the Echocardiographic Study of Latinos

Participants: 1,818 Hispanic adult participants with baseline echocardiographic assessment and acculturation measured by the Short Acculturation Scale, nativity, immigration age, length of US residence, generational status and language.

Primary and secondary outcome measures: Echocardiographic assessment of left atrial volume index (LAVI), left ventricular mass index (LVMI), early diastolic transmitral inflow and mitral annular velocities.

Results: The study population was predominantly Spanish-speaking and foreign-born with mean US residence of 22.7 years, mean age of 56.4 years; 50% had hypertension, 28% had diabetes, and 44% had a BMI >30kg/m^2. Multivariable analyses demonstrated higher LAVI with increasing years of US residence. Foreign-born and first generation participants had higher E/e' but lower LAVI and e' velocities compared to the second generation. Higher acculturation and income >$20K were associated with higher LVMI, LAVI, and E/e', but lower e' velocities. Preferential Spanish-speakers with an income <$20K had a higher E/e'.

Conclusions: Acculturation was associated with abnormal cardiac structure and function, with some effect modification seen according to socioeconomic status.

Abstract Word Count: 207

Keywords: Acculturation, Echocardiogram, Hispanics/Latinos, Socioeconomic Status

Strengths and limitations of this study

- A population-based cohort study design focusing on the predominantly immigrant Hispanic/Latino population in the United States (US).
- A detailed comprehensive echocardiographic examination was performed to determine cardiac structure and function in every participant.
- By including several acculturation measures (nativity, years of US residence/age at migration, SASH subscales, language preference and generational status) our goal was to be comprehensive and to capture several aspects of acculturation.
- We are specifically referring to acculturation into the US culture, which may not be generalizable to acculturation in other settings.

Cardiovascular disease (CVD) and heart failure (HF) risk factor burden is higher among Hispanic/Latinos in the United States (US)[1,2] compared to non-Hispanic whites leading to abnormalities of cardiac structure and function[3] which have been associated with incident clinical HF,[4] incident CVD and increased mortality.[5-8]

With respect to HF, Hispanics/Latinos have a higher incidence compared to non-Hispanic whites and Hispanics/Latinos who present with HF are younger with more co-morbidities and a lower left ventricular (LV) ejection fraction (EF) compared to non-Hispanic whites.[2,9-11] Beyond traditional HF risk factors (hypertension, diabetes and obesity), sociocultural factors such as acculturation, may contribute to HF risk among Hispanic/Latinos **(Figure 1/Conceptual Model)**[2] but the impact of acculturation on cardiac structure and function has not been examined. The fact that Hispanics/Latinos are the largest immigrant population in the US accentuates the public health impact of studying the influence of acculturation on cardiac parameters.

Acculturation is a multidimensional process whereby immigrants adapt to the beliefs and practices of a host culture.[12] This can pose a chronic daily stressor for many immigrants that can affect physical health outcomes. Higher acculturation levels have been associated with increased psychosocial stress, deleterious CV health behaviors and a higher CV risk factor burden.[13-16] In our mechanistic framework, the acculturative process leads to increase stress and worse health behaviors which separately or jointly alter cardiac structure and function to increase HF risk. Few studies[17,18] have examined acculturation in relation to HF risk specifically focusing on cardiac structure and function as key intermediary outcomes.

We primarily sought to test whether acculturation, an important sociocultural variable with biopsychosocial implications, is associated with cardiac structure and function among Hispanics/Latinos. Studies of acculturation and CVD often overlook socioeconomic status (SES) as an effect modifier. Because SES is associated with cardiac parameters[19] and modifies the association between acculturation and other health-related variables,[20] secondarily, we sought to test whether our primary associations are moderated by SES.

Methods

Cohort Description

The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is a population-based study of 16,415 Hispanic/Latinos from randomly selected households at four US field centers (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA).[21] Probability sampling was used to ensure broad representation of the target population and to minimize the sources of bias that may otherwise enter into the cohort selection and recruitment process. Participants were between 18 and 74 years of age, and self-identified as Cuban, Central American, Dominican, Mexican, Puerto Rican, or South American Hispanic/Latino heritage. The ECHO-SOL ancillary study was designed to provide echocardiographic parameters characterizing cardiac structure and function in a representative HCHS/SOL baseline subsample of 1,818 participants ≥45 years old.[3,22] Institutional Review Board approval was obtained at each study site (Albert Einstein College of Medicine, Bronx, NY; Northwestern University, Chicago, Illinois; University of Miami, Miami, FL; University of California, San Diego, San Diego, CA; Wake Forest School of Medicine, Winston-Salem, NC) and all ECHO-SOL participants gave informed consent prior to participating in the study.

Patient and public involvement

No patients were involved in the development of the research question, design, recruitment or implementation of this research cohort study. Results were disseminated to study participants in the form of a Data Book and periodic newsletters. See www.saludsol.net.

In-Person Examination

The examination protocol for the parent HCHS/SOL has been previously published.[13] Obesity was defined as a body mass index (BMI) ≥ 30.0 kg/m^2. Seated resting blood pressures were measured in triplicate and the average of the 2nd and 3rd readings was used for analysis. Type 2 diabetes was defined based on American Diabetes Association definition using one or more of the following criteria: 1) fasting serum glucose ≥126 mg/dl, 2) oral glucose tolerance test ≥200 mg/dl, 3) self-reported diabetes, 4) HbA1C ≥6.5%, or 5) taking anti-diabetic medication or insulin. Renal function was measured by estimated glomerular filtration rate (eGFR). Physical activity levels, categorized as low or medium/high, were assessed using the Global Physical Activity Questionnaire.[23] Self-report questionnaires assessed smoking status (no/ever/current), alcohol consumption (current/no), and insurance coverage (yes/no) and type (Private/Medicare/Medicaid). Educational level was defined as highest degree or level of school completed. Current household income while living in the US was dichotomized as <$20,000 and >$20,000, given the low number of participants with incomes >$40,000. Our secondary analysis focused on current income as a more relevant influencer of a participant's acculturative process, acting as a proxy for the ability to integrate and be exposed to mainstream US cultural contexts.

Marital status was categorized as either single, married, partnered, separated, divorced or widowed.

Echocardiographic Measurements

Trained sonographers performed transthoracic echocardiography examinations, including 2D imaging, and spectral, color and tissue Doppler.[22] Echocardiographic measures of left and right heart structure and function included:

1) LV mass index (LVMI) was determined according to guidelines,[24] by subtracting the LV endocardial cavity volume from the LV epicardial volume and multiplying the resultant myocardial volume by the myocardial density and indexing to body surface area.
2) LV systolic function and volumes. LVEF was derived from Volumetric Assessments using the method of discs from apical 4- and 2-chamber long-axis views to measure end-diastolic volume (EDV) and end-systolic volume (ESV). LVEF was calculated: (EDV - ESV)/EDV.
3) LV diastolic function was defined per guidelines,[25] using three echocardiographic parameters: 1) peak early (E) and late (A) diastolic transmitral inflow velocities; 2) early diastolic (e') annular velocities (the average of septal and lateral annular velocities were used); 3) left atrial volume indexed (LAVI) to body surface area.
4) Relative Wall Thickness (RWT) predicates LV geometry and was defined as: [(posterior LV wall thickness x 2) / LV diastolic diameter]. Higher RWT values are associated with a smaller LV cavity size and lower RWT values are associated with higher LV cavity sizes.

Acculturation Measures

Acculturation was defined using several validated measures. First, nativity was classified as either born in or outside the US mainland (50 states). Those born in Puerto Rico (PR) or other US territories were classified as born outside of the US mainland to reflect their migration and acculturation experiences. Second, foreign-born individuals were asked the number of years lived in the US and categorized as <5, 5-10, 11-20, >20 years. We used the Short Acculturation Scale for Hispanics (SASH),[26] which has two subscales based on five-point Likert type questions: 1. the SASH language subscale (items related to language use [e.g., language they speak, think]); and 2. the SASH social relations subscale (items related to media preference and social affiliations [e.g., language of media programs watched; ethnicity of close friends]). The SASH has yielded reliabilities (α) of 0.92 (overall), 0.90 (language use), 0.86 (media preference), and 0.78 (ethnic and social relations). These subscales were analyzed separately with higher scores representing higher degrees of acculturation. Fifth, language preference was further characterized as English vs. Spanish based on language of interview. Finally, data on generational status (first- and second-generation Hispanics are US-born and distinct from their foreign-born immigrant parents) was collected as well as age at the time of migration to the US.

Statistical Analyses

Sampling weights were used to obtain weighted frequencies of descriptive variables and population estimates in the ECHO-SOL target population. We used means ± standard errors (SEs) for continuous variables and proportions for categorical variables. LVMI, RWT, LVEF, e' annular velocities and LAVI were analyzed as continuous variables. LV diastolic dysfunction (LVDD) was analyzed as a binary variable (present vs. absent).[3] Acculturation variables were categorical (foreign- vs. US-born; 1st generation vs. 2nd; Spanish language preference vs.

English), ordinal (<5, 5-10, 11-20, and >20 years in the US) and continuous measures (age at immigration and SASH subscales). Weighted means and linear regression analysis was utilized for continuous variables whereas weighted frequencies and Rao-Scott Chi-Square was utilized for the categorical/ordinal variables. Means were compared across categorical acculturation variables using regression analysis for each dependent variable measure of cardiac structure (LVMI, RWT, LAVI) and function (LVEF, e', E/e'). Only associations that were statistically significant in unadjusted analyses were further explored in multivariable analysis. Unadjusted and multivariable linear and logistic regression analyses were determined by our continuous and categorical dependent variable, respectively, utilizing sequential modeling for age and sex followed by models including clinical covariates (diabetes, hypertension, and obesity), and behavioral characteristics (physical activity, tobacco use, and alcohol use). For years in the US, we compared >20 years to <5 years as well as an overall comparison across each category of years in the US. We performed a couple of sensitivity analyses (data not shown): 1. comparing acculturative characteristics of individuals born in the island of PR vs. other foreign-born Hispanics; 2. comparing acculturation and health care utilization using HCHS/SOL questions regarding difficulty obtaining health care in the past year and number of physician visits in the past year. We tested effect moderation with income through the use of interaction terms in models followed by stratified analyses by income for statistically significant interactions at the $p<0.01$ level. All other statistical tests were 2-sided at a significance level of 0.05. All reported values were weighted to account for HCHS/SOL sampling probability design, stratification, clustering and nonresponse and to make estimates applicable to the HCHS/SOL target population. All analyses were performed utilizing SAS 9.3 (SAS Institute, Cary, NC) PROC SURVEY procedures.

Results

Fifty-seven percent of the study population were women; almost half (46%) had a reported annual income under $20K; over half were married and most had some type of health insurance (mostly Medicaid and/or Medicare). Hypertension and diabetes were prevalent in half and almost one-third of the study population respectively. Most of the study population was foreign-born, only 14% preferred English, almost half (49%) had been in the US >20 years with a mean age of migration of 34 years of age, signifying that the majority came to the US as adults **(Table 1).** Mean values of echocardiographic variables (LAVI, RWT, LVMI, LVEF) were all within normal limits for this study population. However, mean e' annular velocities and E/e' ratio were borderline abnormal. Some degree of diastolic dysfunction was seen in over half (52%) of the study population but this has been previously described.[3]

Table S1 shows unadjusted relationships between acculturation measures and echocardiographic characteristics. There were statistically significantly higher mean LAVI values across categories of length of time spent in the US whereas RWT appeared to have a U-shaped association. A statistically significantly lower annular relaxation velocity and higher E/e' ratio was seen among the foreign-born compared to US-born and among those 1st generation compared to 2nd generation. Greater acculturation, as measured by higher SASH language scale scores, was associated with greater LAVI. Younger age of migration to US was associated with increased RWT and LAVI.

Adjusted analyses **(Table 2)** demonstrated greater time spent in the US is significantly associated with increased RWT and LAVI. A statistically significantly higher E/e' ratio was seen among the foreign-born participants. Those 1st generation had lower LAVI, lower e' annular velocities and higher E/e' ratios compared to 2nd generation. Higher SASH language scale scores and younger age of migration to US were both associated with increased LAVI. These associations persisted in sequential models adjusted for clinical factors and behavioral factors both separately and together. Although greater odds of LVDD was seen in unadjusted associations with nativity, generational status, SASH language, and age of immigration **(Table 3),** these associations did not persist on adjusted analysis.

Significant interactions ($p<0.01$) were found between our main exposure (acculturation) and income on the effect of cardiac structure and function. Among those whose annual income is >$20K, a greater number of years in the US was associated with higher LVMI, lower e' annular velocities, and a higher E/e' ratio compared to those making <$20K annually. Generational status was associated with increased LAVI only among those making >$20K annually. However, being a preferential Spanish-speaker carried a statistically significant higher E/e' ratio only among those making <$20K annually. **(Table S2).**

Of foreign-born Hispanics, 24% were born in the US Commonwealth of PR, none in the US Virgin Islands. Spanish language preference was less among Hispanics born in PR compared to other foreign-born Hispanics. PR-born Hispanics scored higher on the SASH language scale and social interaction scale indicating higher acculturation levels compared to other foreign-born Hispanics. However, the level of Spanish language preference and SASH scores was still lower

among PR-born Hispanics compared to US born Hispanics. With regard to acculturation and health care utilization, being foreign-born, having less years in the US and not having health insurance were all significantly associated with difficulty obtaining health care in the past year. Foreign-born individuals had less physician visits over the past year compared to US born. The relation between years in the US and physician visits was complex, non-linear and mirrored an opposite pattern with income. **(Figure 2)** Having health insurance coverage was significantly associated with more physician visits over the past year.

Discussion

Hispanics/Latinos in the US represent a relatively young demographic such that the future public health burden of HF as this population ages is potentially underestimated.[27] The Hispanic population >65 years of age is expected to grow 328% between 2000 and 2030, making Hispanics the fastest growing aging population in the US.[28] As the Hispanic population ages, and HF risk factors and cardiac abnormalities progress, it is likely that an epidemic of HF will emerge in this population.

Acculturation is a complex but important phenomenon among immigrant populations that encompasses multiple domains: (1) integration - maintaining the original parent culture while adopting the host culture; (2) assimilation - rejecting the parent culture and entirely adopting the host culture; (3) separation - rejecting the host culture and keeping the parent culture; and (4) marginalization - not identifying with either the original culture or the host culture.[29] The acculturation process can be positive, improved life opportunities in the host culture compared to the parent culture, and/or it could be negative due to the challenging nature of change and adaptation to new cultural and social expectations. Prior studies show strong negative effects of

greater acculturation on worsening CV risk factors but positive effects on use of preventive health services.[30-32] HCHS/SOL has demonstrated significant heterogeneity in CVD risk factor burden among Hispanics/Latinos by country of origin and acculturation measures.[13] Our analysis of validated acculturation measures provides several important contributions. First, higher levels of acculturation were associated with abnormal cardiac structure and function in our predominately foreign-born, Spanish-speaking adult population. Second, different measures of acculturation (each capturing different aspects of the acculturative process) had varying associations with different measures of cardiac structure and function (each considered its own specific outcome). Finally, income significantly moderated these associations. Our findings support the premise that exposure to the social and environmental stress of acculturation may promote unhealthy behaviors[33] and/or act via undefined pathways of physiologic/psychosocial stress to contribute to the increased HF risk seen among Hispanics/Latinos.[27] **(Figure 1)** Additionally, our sensitivity analysis suggests that living in the island of PR still allows for maintenance of a culture that is distinct from the US culture. Further elucidating the complexities of acculturative factors influencing HF risk in immigrant populations is warranted.

Although to our knowledge, there is no existing literature on the association between acculturation and HF risk, our study found several measures of acculturation (increasing years of US residence, English preference, and younger age at immigration) were associated with abnormal cardiac structure and function (increased LAVI, increased LVMI, increased RWT, lower annular e' relaxation velocity and higher E/e' ratio). Although the magnitudes of our observed associations are modest, limiting the short-term clinical relevance of these findings, the long-term public health importance is likely high, given the potential for progression of cardiac

damage with the accumulation of acculturative stress during the life course. This is particularly salient given the fact that abnormal cardiac structure and function is an independent risk factor for the future development of clinical HF. An increased E/e' ratio, LAVI, and LVMI are markers of chronically-elevated filling pressures associated with impaired cardiac relaxation and HF with preserved ejection fraction.[34,35] The presence of abnormal cardiac structure and function has been associated with increased HF hospitalizations, cardiovascular death and improved CV risk prediction.[35-37] Importantly, these cardiac abnormalities are additive, with worse outcomes seen in individuals with more than one alteration.[35] In order to identify preclinical CV disease, abnormalities in cardiac structure and function determined by echocardiography are important intermediary measures, many of which have been associated with incident CVD, incident clinical HF and increased mortality.[5-7] Given the size of the US Hispanic/Latino population and high burden of acculturation (82% were foreign-born), echocardiography might help to identify a particularly high risk subset of participants.

LVM is associated with CVD, sudden cardiac death, and all–cause mortality.[34] Among foreign-born Hispanics/Latinos, we found increased LVMI with increasing years in the US. Our study is consistent with prior studies showing a high prevalence of LVM among Hispanics/Latinos especially among low income Hispanics/Latinos with increasing years of US residence.[18,38,39] Prior studies have demonstrated that adjustment for socioeconomic factors did not fully account for the presence of increased LVMI among Hispanics/Latinos[40] possibly due to the residual effect of acculturation. Changes in LVM can occur without overt clinical hypertension in adrenergic states, such as chronic stress[41] with psychosocial factors such as perceived discrimination and low social support.[42,43] Acculturative stress is the psychological impact of

navigating the acculturation process and making decisions on retaining one's native culture while adapting to a new cultural context. Acculturation as a chronic stressor may negatively affect mental and physical health through unhealthy behaviors,[31,33] increased anxiety, depression, perceived discrimination and lack of social support[15,33,44] all of which may impact adrenergic biomarkers leading to cardiac structural and functional abnormalities and increased HF risk observed in our study. This is an area of research to further explore in future studies.

The statistically significant interaction between acculturation and SES on cardiac measures may shed light on the "Hispanic paradox" which states that Hispanics/Latinos, a disproportionately low SES group, have lower overall mortality and cardiovascular mortality compared to non-Hispanic Whites.[2] Low SES is a composite chronic stressor encompassing multiple factors (e.g., work, housing and financial strain). Longitudinal studies have shown an inverse association between SES level and adverse outcomes.[42,45] We hypothesized that less acculturation (more retention of the parent culture) may be protective of the adverse health consequences of low SES. In our study, those with higher SES (defined as annual incomes >$20K) exhibited more deleterious effects of increasing acculturation on cardiac structural and functional measures. A prior study found the relationship between acculturation and health care utilization to be complex and moderated by SES.[46] Our exploratory analysis found that being foreign-born and having a higher income may make one less likely to utilize health care. A more extensive analysis on the complex nature of acculturation and health care utilization is beyond the scope of our paper but this area deserves further consideration in future studies. There may be more acculturative stress for higher-SES immigrants, perhaps through increased contact and interaction with the mainstream culture,[47] which may contribute to our findings. *Familismo* is a culture-specific

factor characterized by having strong bonds with nuclear and extended family resulting in a high level of perceived family support and is associated with indicators of improved health.[48,49] Studies suggest that with increasing acculturation, *familismo* is eroded and dimensions of *familismo* begin to increase psychosocial stress rather than alleviate it.[49-51]

Several limitations should be noted. Our study is cross-sectional and precludes the ability to assess the temporal sequence of the relationships and causal inference. However, our findings warrant replication and longitudinal follow up. Participants resided in one of four US cities, precluding generalizability to all Hispanic/Latinos in the US. While this study is one of the largest studies of acculturation with cardiac structure and function in any population, the sample size is relatively modest; thus, we were underpowered to perform stratified analyses by national origin in order to characterize the heterogeneity within Hispanic/Latinos. We are specifically referring to acculturation into the US culture, which may not be generalizable to acculturation in other settings. Finally, our study focuses on acculturation as a unique intra-ethnic phenomenon. By including several measures (nativity, years of US residence/age at migration, SASH subscales, language preference and generational status) our goal was to be comprehensive and to capture several aspects of acculturation. We believe acculturation cannot be captured by just one measure, as has been done in much of the prior literature; however, we agree that even our multivariable approach may not fully capture the complexities of all aspects and dimensions of the acculturative process.

Conclusions

In addition to traditional CV risk factors, acculturation may explain the disproportionate burden of HF risk among Hispanics/Latinos. Our study found significant deleterious associations between several acculturation measures with cardiac structural and functional parameters among a predominantly low-SES, foreign-born Hispanic/Latino population with increasing years of residence in the US. The acculturation experience is not unique to Hispanics/Latinos. Our study may help generate further research in other immigrant populations. Further elucidation of how acculturation impacts HF risk is warranted in order to possibly risk stratify a high-risk subgroup of Hispanics/Latinos and to inform the development of culturally appropriate interventions to amplify protective factors and to make the acculturative process less deleterious for Hispanics/Latinos and other immigrants.

Acknowledgements: The authors thank the staff and participants of HCHS/SOL and ECHO-SOL for their important contributions. Investigators website - http://www.cscc.unc.edu/hchs/

Contributors: Research Conception and design: CJR, LL; **Collection and assembly of data:** CJR, MAA, RK, LCG; **Analysis and interpretation of the data:** CJR, LL, KS; **Drafting of the article:** CJR, LL, FR; **Critical revision of the article for important intellectual content:** CJR, LL, FR, JRK, FJP, LCG, WA, FG; **Obtaining of funding:** CJR, RK, MAA; **Statistical expertise:** KS, FG

CJR and LL are responsible for the overall content as guarantors.

Funding: This study supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI) to the University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), and San Diego State University (N01-HC65237). The following institutes contributed to HCHS/SOL: National Institute on Minority Health and Health Disparities, National Institute on Deafness and Other Communication Disorders, National Institute of Dental and Craniofacial Research, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Neurological Disorders and Stroke, NIH Institution-Office of Dietary Supplements.

ECHO-SOL was supported by the National Heart, Lung, and Blood Institute (R01 HL104199, Epidemiologic Determinants of Cardiac Structure and Function among Hispanics: Carlos J. Rodriguez, MD, MPH Principal Investigator). Dr. Lenny L. López acknowledges the support of the Robert Wood Johnson Foundation Harold Amos Medical Faculty Development Program and NIDDK 1K23DK098280-01. No relationships with industry supported this work.

Competing interests: None declared.

Patient consent for publication: Not required.

Ethics approval: The Institutional Review Board at the Wake Forest School of Medicine and at each study site provided approval and oversight of all study materials and activities.

Data sharing statement: The data are available according to NIH/HLBI data sharing policies through the NHLBI BioLINCC repository or through the HCHS/SOL Data Coordinating Center on request.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart Disease and Stroke Statistics—2015 Update: A Report From the American Heart Association. Circulation 2015;131:e29-e322.

2. Rodriguez CJ, Allison M, Daviglus ML, et al. Status of cardiovascular disease and stroke in Hispanics/Latinos in the United States: a science advisory from the American Heart Association. Circulation 2014;130:593-625.

3. Mehta H, Armstrong A, Swett K, et al. Burden of Systolic and Diastolic Left Ventricular Dysfunction Among Hispanics in the United States: Insights From the Echocardiographic Study of Latinos. Circ Heart Fail 2016;9.

4. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147-239.

5. Hobbs FD, Roalfe AK, Davis RC, Davies MK, Hare R, Midlands Research Practices C. Prognosis of all-cause heart failure and borderline left ventricular systolic dysfunction: 5 year mortality follow-up of the Echocardiographic Heart of England Screening Study (ECHOES). Eur Heart J 2007;28:1128-34.

6. Armstrong AC, Jacobs DR, Jr., Gidding SS, et al. Framingham score and LV mass predict events in young adults: CARDIA study. Int J Cardiol 2014;172:350-5.

7. Bombelli M, Facchetti R, Cuspidi C, et al. Prognostic significance of left atrial enlargement in a general population: results of the PAMELA study. Hypertension 2014;64:1205-11.

8. Echouffo-Tcheugui JB, Erqou S, Butler J, Yancy CW, Fonarow GC. Assessing the Risk of Progression From Asymptomatic Left Ventricular Dysfunction to Overt Heart Failure: A Systematic Overview and Meta-Analysis. JACC Heart Fail 2016;4:237-48.

9. Vivo RP, Krim SR, Cevik C, Witteles RM. Heart failure in Hispanics. J Am Coll Cardiol 2009;53:1167-75.

10. Vivo RP, Krim SR, Krim NR, et al. Care and outcomes of Hispanic patients admitted with heart failure with preserved or reduced ejection fraction: findings from get with the guidelines-heart failure. Circ Heart Fail 2012;5:167-75.

11. Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. Archives of internal medicine 2008;168:2138-45.
12. Zambrana RE, Carter-Pokras O. Role of acculturation research in advancing science and practice in reducing health care disparities among Latinos. Am J Public Health 2010;100:18-23.
13. Daviglus ML, Talavera GA, Aviles-Santa ML, et al. Prevalence of major cardiovascular risk factors and cardiovascular diseases among Hispanic/Latino individuals of diverse backgrounds in the United States. Jama 2012;308:1775-84.
14. Ayala GX, Baquero B, Klinger S. A systematic review of the relationship between acculturation and diet among Latinos in the United States: implications for future research. J Am Diet Assoc 2008;108:1330-44.
15. Steptoe A, Kivimaki M. Stress and cardiovascular disease: an update on current knowledge. Annu Rev Public Health 2013;34:337-54.
16. Suh M, Barksdale DJ, Logan J. Relationships among acculturative stress, sleep, and nondipping blood pressure in Korean American women. Clin Nurs Res 2013;22:112-29.
17. Peterson PN, Campagna EJ, Maravi M, et al. Acculturation and outcomes among patients with heart failure. Circ Heart Fail 2012;5:160-6.
18. Effoe VS, Chen H, Moran A, et al. Acculturation is associated with left ventricular mass in a multiethnic sample: the Multi-Ethnic Study of Atherosclerosis. BMC Cardiovasc Disord 2015;15:161.
19. Rodriguez CJ, Sciacca RR, Diez-Roux AV, et al. Relation between socioeconomic status, race-ethnicity, and left ventricular mass: the Northern Manhattan study. Hypertension 2004;43:775-9.
20. Lee H, Cardinal BJ, Loprinzi PD. Effects of socioeconomic status and acculturation on accelerometer-measured moderate-to-vigorous physical activity among Mexican American adolescents: findings from NHANES 2003-2004. J Phys Act Health 2012;9:1155-62.
21. Lavange LM, Kalsbeek WD, Sorlie PD, et al. Sample design and cohort selection in the Hispanic Community Health Study/Study of Latinos. Ann Epidemiol 2010;20:642-9.
22. Rodriguez CJ, Dharod A, Allison MA, et al. Rationale and Design of the Echocardiographic Study of Hispanics/Latinos (ECHO-SOL). Ethnicity & disease 2015;25:180-6.

23. Cleland CL, Hunter RF, Kee F, Cupples ME, Sallis JF, Tully MA. Validity of the global physical activity questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health 2014;14:1255.

24. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography 2005;18:1440-63.

25. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures - A comparative simultaneous Doppler-Catheterization study. Circulation 2000;102:1788-94.

26. Marin G, Sabogal F, Marin BV, Otero-Sabogal F, and Perez-Stable E. Development of a short acculturation scale for Hispanics. Hispanic Journal of Behavioral Sciences 1987;9:183-205.

27. Rangel MO, Kaplan R, Daviglus M, et al. Estimation of Incident Heart Failure Risk among US Hispanics/Latinos Using a Validated Echocardiographic Risk-Stratification Index: the Echocardiographic Study of Latinos. J Card Fail 2018;24:622-4.

28. US Census Bureau. 65+ in the United States:2005. Current Population Reports December 2005.

29. Schwartz SJ, Unger JB, Zamboanga BL, Szapocznik J. Rethinking the concept of acculturation: implications for theory and research. Am Psychol 2010;65:237-51.

30. Moran A, Diez Roux AV, Jackson SA, et al. Acculturation is associated with hypertension in a multiethnic sample. Am J Hypertens 2007;20:354-63.

31. Abraido-Lanza AF, Chao MT, Florez KR. Do healthy behaviors decline with greater acculturation? Implications for the Latino mortality paradox. Soc Sci Med 2005;61:1243-55.

32. DuBard CA, Gizlice Z. Language spoken and differences in health status, access to care, and receipt of preventive services among US Hispanics. Am J Public Health 2008;98:2021-8.

33. Lara M, Gamboa C, Kahramanian MI, Morales LS, Bautista DE. Acculturation and Latino health in the United States: a review of the literature and its sociopolitical context. Annu Rev Public Health 2005;26:367-97.

34. Abbate A, Arena R, Abouzaki N, et al. Heart failure with preserved ejection fraction: refocusing on diastole. Int J Cardiol 2015;179:430-40.

35. Shah AM, Claggett B, Sweitzer NK, et al. Cardiac structure and function and prognosis in heart failure with preserved ejection fraction: findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) Trial. Circ Heart Fail 2014;7:740-51.

36. Zile MR, Gottdiener JS, Hetzel SJ, et al. Prevalence and significance of alterations in cardiac structure and function in patients with heart failure and a preserved ejection fraction. Circulation 2011;124:2491-501.

37. Burke MA, Katz DH, Beussink L, et al. Prognostic importance of pathophysiologic markers in patients with heart failure and preserved ejection fraction. Circ Heart Fail 2014;7:288-99.

38. Zabalgoitia M, Ur Rahman SN, Haley WE, et al. Impact of ethnicity on left ventricular mass and relative wall thickness in essential hypertension. Am J Cardiol 1998;81:412-7.

39. Rodriguez CJ, Diez-Roux AV, Moran A, et al. Left ventricular mass and ventricular remodeling among Hispanic subgroups compared with non-Hispanic blacks and whites: MESA (Multi-ethnic Study of Atherosclerosis). J Am Coll Cardiol 2010;55:234-42.

40. Rodriguez CJ, Lin F, Sacco RL, et al. Prognostic implications of left ventricular mass among Hispanics: the Northern Manhattan Study. Hypertension 2006;48:87-92.

41. Julius S, Li Y, Brant D, Krause L, Buda AJ. Neurogenic pressor episodes fail to cause hypertension, but do induce cardiac hypertrophy. Hypertension 1989;13:422-9.

42. Rozanski A, Blumenthal JA, Davidson KW, Saab PG, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. J Am Coll Cardiol 2005;45:637-51.

43. Rodriguez CJ, Elkind MS, Clemow L, et al. Association between social isolation and left ventricular mass. Am J Med 2011;124:164-70.

44. Gallo LC, Penedo FJ, Espinosa de los Monteros K, Arguelles W. Resiliency in the face of disadvantage: do Hispanic cultural characteristics protect health outcomes? J Pers 2009;77:1707-46.

45. Gallo LC, de Los Monteros KE, Allison M, et al. Do socioeconomic gradients in subclinical atherosclerosis vary according to acculturation level? Analyses of Mexican-Americans in the multi-ethnic study of atherosclerosis. Psychosom Med 2009;71:756-62.

46. Peng BL, Zou GY, Chen W, Lin YW, Ling L. Association between health service utilisation of internal migrant children and parents' acculturation in Guangdong, China: a cross-sectional study. BMJ Open 2018;8:e018844.

47. McClure LA, Zheng DD, Lam BL, et al. Factors Associated With Ocular Health Care Utilization Among Hispanics/Latinos: Results From an Ancillary Study to the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). JAMA Ophthalmol 2016;134:320-9.

48. Davila YR, Reifsnider E, Pecina I. Familismo: influence on Hispanic health behaviors. Appl Nurs Res 2011;24:e67-72.

49. Sabogal F, Marin G, Otero-Sabogal R, Marin B. Hispanic familism and acculturation: What changes and what doesn't? Hispanic Journal of Behavioral Sciences 1987;9:397-412.

50. Miranda A, Estrada D, Firpo-Jimenez M. Differences in family cohesion, adaptability, and environment among Latino families in dissimilar stages of acculturation. The Family Journal 2000;8:341-50.

51. Rodriguez N, Mira C, Paez N, Myers H. Exploring the complexities of familism and acculturation: central constructs for people of Mexican origin. Am J Community Psychol 2007;39:61-77.

Table 1. ECHO-SOL Demographic and Clinical Characteristics (N = 1,818)†

Demographic Characteristics	**[N (%)]**
Women	1187 (57.4)
Age, [mean (SE)]	56.4 (0.37)
High School Graduate or Higher	726 (43.3)
Annual Family Income > $20,000	787 (45.5)
Marital Status	
Single	332 (18.8)
Married/Partner	961 (53.2)
Separated/Divorced/Widow	522 (28.0)
Health Insurance	1042 (60.1)
Short Acculturation Scale for Hispanics (SASH)	**[mean (SE)]**
Language Use Subscale	1.7 (0.05)
Social Relations Subscale	2.1 (0.03)
Length of US residence	[N (%)]
<5 years	178 (13.6)
5-10 years	247 (15.2)
11-20	385 (22.1)
>20	842 (49.1)
Second generation or higher	185 (9.3)
English language preference	225 (14.0)
Age at migration [mean (SE)]	34.0 (1.0)
US born	163 (7.9)
Clinical Characteristics	**[N (%)]**
Hypertension	861 (50.0)
Type 2 Diabetes	523 (28.4)
Current Smoker	304 (17.6)
Physical activity level low	1227 (67.3)
BMI ≥30	822 (44.3)
Current Alcohol Use	770 (43.5)
Echocardiographic Variables	**[mean (SE)]**
Left Atrial Volume Index (<33 mL/m^2)	23.0 (0.25)
Relative Wall Thickness (0.22-0.42)	0.40 (0.004)
Left Ventricular Mass Index (45-105 g/m^2)	82.7 (0.7)
Ejection Fraction (≥55 %)	59.8 (0.2)
E prime (e') (8-16 cm/s)	8.1 (0.09)
E/e' (≤12)	10.0 (0.12)
Diastolic Dysfunction [N (%)]	916 (51.9)

†N's presented are unweighted counts of total participants in the ECHO-SOL with each respective characteristic.
Percentages are weighted row percentages.
Normal values are provided for cardiac structure and function variables.

Table 2. Adjusted Analyses of Acculturation Measures with Cardiac Structure and Function.*

	LVMI (g/m^2) β (p)	**RWT** β (p)	**LAVI** (mL/m^2) β (p)	**LVEF** (%) β (p)	**e'** (cm/s) β (p)	**E/e'** β (p)
Nativity						
Age, sex					-0.349 (0.12)	0.571 (0.02)
Model 1	—	—	—	—	-0.320 (0.10)	0.524 (0.02)
Model 2					-0.324 (0.14)	0.532 (0.02)
Model 3					-0.303 (0.12)	0.503 (0.02)
Foreign Born (Years in the US)						
Age, sex	—	0.020 (0.06); all (0.03)	1.57 (0.02); all (<0.05)	—	—	—
Model 1		0.022 (0.02); all (0.02)	1.63 (0.02); all (<0.05)			
Model 2		0.018 (0.06); all (0.02)	1.55 (0.02); all (0.05)			
Model 3		0.021 (0.02); all (0.007)	1.71 (0.01); all (0.04)			
Generation						
Age, sex			-0.468 (0.21)		-0.529 (0.01)	0.710 (0.002)
Model 1	—	—	-1.797 (0.004)	—	-0.447 (0.01)	0.594 (0.003)
Model 2			-1.444 (0.03)		-0.499 (0.01)	0.671 (0.003)
Model 3			-1.584 (0.01)		-0.425 (0.02)	0.575 (0.006)
SASH Language						
Age, sex			0.580 (0.01)		0.125 (0.10)	
Model 1	—	—	0.610 (0.008)	—	0.097 (0.11)	—
Model 2			0.546 (0.01)		0.123 (0.15)	
Model 3			0.590 (0.007)		0.095 (0.16)	
Age at Immigration						
Age, sex		0.0005 (0.15)	-0.040 (0.008)		-0.005 (0.27)	
Model 1	—	0.0005 (0.13)	-0.040 (0.008)	—	-0.006 (0.14)	—
Model 2		0.0004 (0.15)	-0.038 (<0.001)		-0.005 (0.37)	
Model 3		0.0004 (0.13)	-0.038 (0.01)		-0.005 (0.22)	

*Only acculturation measures that were significant in unadjusted analyses were analyzed in multivariable adjusted models.

For Years in the US, the 1st p-value reflects <5 years vs. >20 years comparison; whereas the 2nd p-value is for overall comparison across all the Years in the US categories (<5; 5-10; 11-20; >20) Model 1: Age, Sex, Diabetes, Hypertension, Obesity | Model 2: Age, Sex, Physical Activity, Tobacco, Alcohol Use | Model 3: Model 1 + Model 2

LVMI = Left ventricular mass index; RWT = Relative wall thickness; LAVI = Left atrial volume index; LVEF = Left ventricular ejection fraction

e'= Mitral annular early diastolic velocity; E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Table 3. Unadjusted and Adjusted‡ Analyses of Acculturation Measures with Diastolic Dysfunction.

		Adjusted Sequential Models			
	Unadjusted	Age, Sex	Model 1	Model 2	Model 3
Nativity					
Foreign born	1.67 (1.08-2.58)	0.98 (0.62-1.55)	0.94 (0.59-1.51)	0.98 (0.62-1.55)	0.95 (0.59-1.53)
US born	Ref				
Years in the US					
<5	0.86 (0.60-1.24)				
5-10	0.72 (0.49-1.04)				
11-20	0.91 (0.61-1.37)	—	—	—	—
>20	Ref				
Generation					
1	1.90 (1.24-2.92)	1.29 (0.77-2.14)	1.18 (0.74-1.91)	1.26(0.77-2.06)	1.18 (0.73-1.89)
2	Ref				
Language Preference					
English	0.67 (0.34-1.32)	—	—	—	—
Spanish	Ref				
SASH Language	0.81 (0.67-0.98)	—	—	—	—
SASH Social	0.88 (0.68-1.15)	—	—	—	—
Age at Immigration	1.02 (1.004-1.03)	1.00 (0.99-1.02)	1.01 (0.995-1.02)	1.01 (0.99-1.02)	1.01 (0.995-1.02)

‡Only acculturation measures that were significant in unadjusted analyses were analyzed in adjusted models.

ORs (95% CIs) are presented

Model 1: Age, Sex, Diabetes, Hypertension, Obesity

Model 2: Age, Sex, Physical Activity, Tobacco, Alcohol Use

Model 3: Model 1 + Model 2

Figure Legend:

Figure 1. Proposed Relationships Between Acculturation with Cardiac Structure and Function.

Figure 2. Relation of Years Residing in the US or Income Level with Number of Physician Visits

Figure 1.

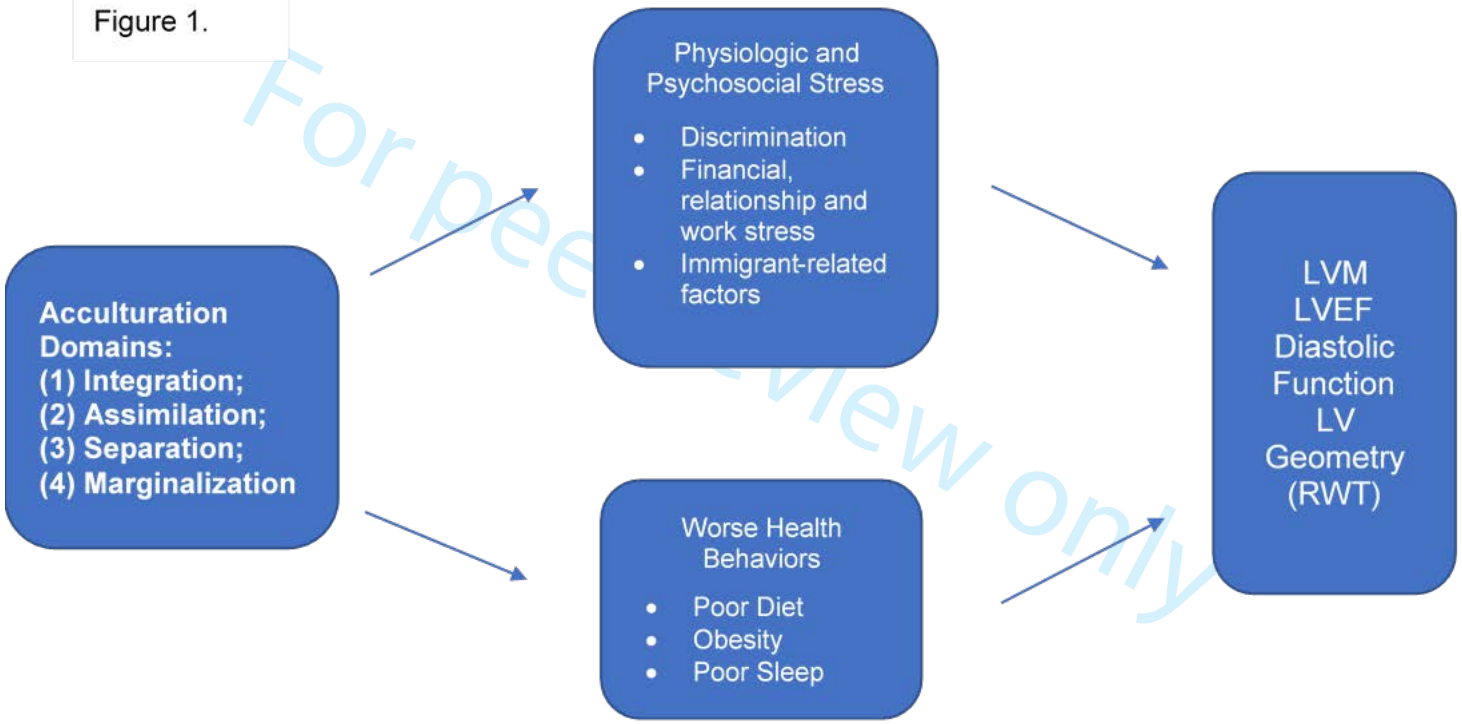


Figure 2.

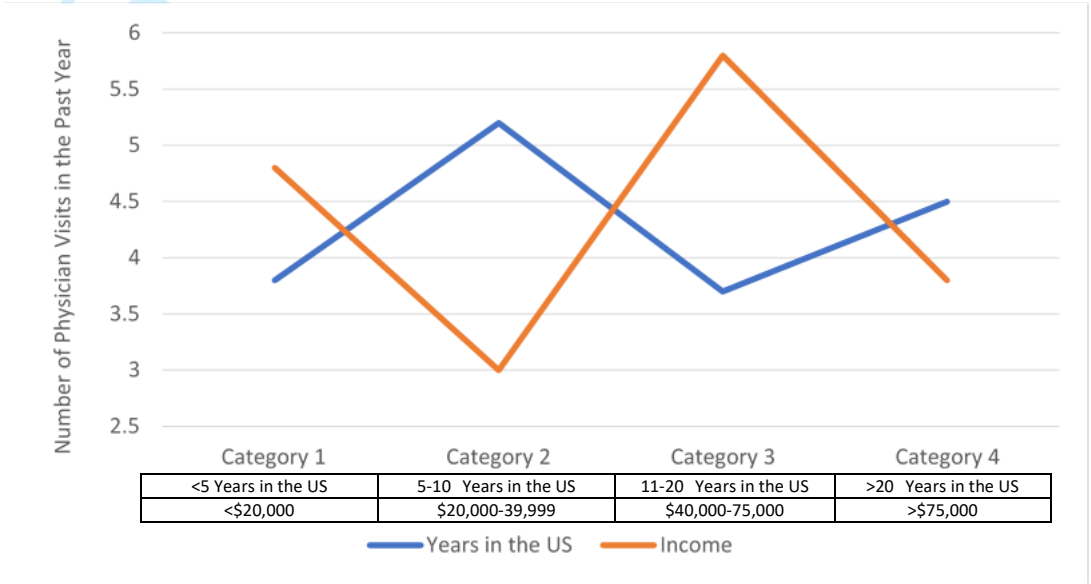

Number of Physician Visits in the Past Year
6
5.5
5
4.5
4
3.5
3
2.5
Category 1
Category 2
Category 3
Category 4
<5 Years in the US
5-10 Years in the US
11-20 Years in the US
>20 Years in the US
<$20,000
$20,000-39,999
$40,000-75,000
>$75,000
Years in the US
Income

Table S1. Unadjusted Acculturation Measures with Echocardiographic Measures of Cardiac Structure and Function.

	LVMI (g/m^2)		RWT		LAVI (mL/m^2)		LVEF (%)		e' (cm/s)		E/e'	
Categorical Measures												
	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p
Nativity												
Foreign Born	82.74	0.92	0.40	0.07	22.93	0.10	59.83	0.54	7.98	<0.001	10.1	<0.001
US Born	82.54		0.38		24.10		59.50		8.99		8.8	
Years in US												
<5 years	79.80	0.16	0.41	0.03	21.70	0.03	59.94	0.09	7.71	0.11	10.2	0.25
5-10 years	80.43		0.39		22.40		60.04		8.18		9.7	
11-20 years	83.60		0.41		22.82		58.94		8.27		9.8	
>20 years	83.96		0.39		23.50		60.14		7.86		10.2	
Generation												
First	82.69	0.88	0.40	0.08	22.89	0.02	59.84	0.45	7.97	<0.001	10.1	<0.001
Second or Greater	82.96		0.38		24.41		59.45		9.01		8.8	
Language												
English	81.51	0.59	0.38	0.08	24.00	0.06	60.13	0.48	8.52	0.15	9.7	0.64
Spanish	82.92		0.40		22.87		59.75		7.99		10.0	
Continuous Measures												
	β (se)	p	β (se)	p	β (se)	p	β (se)	p	β (se)	p	β (se)	p
Age at Immigration	-0.0003 (0.0632)	0.99	0.0006 (0.0003)	0.02	-0.030 (0.014)	0.03	-0.003 (0.012)	0.79	-0.023 (0.007)	0.001	0.012 (0.010)	0.23
SASH Subscales												
Language	0.087 (0.735)	0.91	-0.005 (0.003)	0.10	0.539 (0.237)	0.02	0.166 (0.180)	0.36	0.255 (0.098)	0.009	-0.205 (0.109)	0.06
Social Relations	0.086 (1.392)	0.95	-0.009 (0.006)	0.15	0.732 (0.373)	0.05	0.539 (0.295)	0.07	0.266 (0.155)	0.09	-0.156 (0.217)	0.47

LVMI = Left ventricular mass index; RWT = Relative wall thickness; LAVI = Left atrial volume index
LVEF = Left ventricular ejection fraction; e'= Mitral annular early diastolic velocity
E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

Table S2. Income Stratified Adjusted Analyses of Acculturation Measures with Cardiac Structure and Function.[¥]

	LVMI (g/m^2)				**LAVI** (mL/m^2)				**e'** (cm/s)				**E/e'**				**Diastolic Dysfunction**	
	<$20,000		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**		**>$20,000**		**<$20,000**	**>$20,000**
	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	Mean	p	ORs (95% CI)	ORs (95% CI)
Nativity																		
Foreign	—	—	—	—	—	—	—	—	7.90	0.0006	8.24	0.048	—	—	—	—	1.67 (0.89-3.14)	1.24 (0.70-2.19)
US born									8.83		8.99							
Years in the US																		
<5	80.02		73.35						7.70		9.03		10.20		9.17			
5-10	81.32	0.15	79.38	0.002	—	—	—	—	7.72	0.27	8.87	0.001	10.36	0.62	8.63	0.003	—	—
11-20	82.22		86.12						8.23		8.56		9.912		9.49			
>20	85.73		82.23						7.87		7.89		10.28		10.16			
Generation																		
1	—	—	—	—	23.04	0.45	22.85	0.02	—	—	—	—	—	—	—	—	1.82 (0.99-3.34)	1.50 (0.83-2.69)
2					23.91		24.67											
Language Preference																		
English	—	—	—	—	—	—	—	—	—	—	—	—	9.42	0.01	10.00	0.63	—	—
Spanish													10.21		9.55			
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	—	—
SASH Language	—	—	—	—	0.2686	0.32	0.7213	0.04	—	—	—	—	-0.3026	0.003	0.1065	0.60	—	—
SASH Social	—	—	—	—	—	—	—	—	—	—	—	—	-0.5410	0.008	0.4641	0.27	—	—

[¥]Only statistically significant interactions were analyzed in adjusted models; excludes cases where income is missing.
Multivariable models were adjusted for Age, Sex, Diabetes, Hypertension, Obesity, Physical Activity, Tobacco, and Alcohol Use.
LVMI = Left ventricular mass index; LAVI = Left atrial volume index
e'= Mitral annular early diastolic velocity; E/e' = Ratio between early mitral inflow velocity and mitral annular early diastolic velocity

STROBE Statement—Checklist of items that should be included in reports of ***Observational studies in epidemiology***

	Item No	Recommendation	Page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1&
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3&4
		Introduction	
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4&5
		Methods	
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6&7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6&7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5&9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6&7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8&9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
		Results	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	10&11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10&11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a	

		meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
		Discussion	
Key results	18	Summarise key results with reference to study objectives	12&13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14&15
Generalizability	21	Discuss the generalizability (external validity) of the study results	16
		Other information	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.