PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Association of Acculturation with Cardiac Structure and Function among Hispanic/Latinos: a cross-sectional analysis of the Echocardiographic Study of Latinos
AUTHORS	Lopez, Lenny; Swett, Katrina; Rodriguez, Fatima; Kizer, Jorge R.; Penedo, Frank; Gallo, Linda; Allison, Matthew; Arguelles, William; Gonzalez, Franklyn; Kaplan, Robert C.; Rodriguez, Carlos J.

VERSION 1 – REVIEW

REVIEWER	Cha-Nam Shin, PhD, RN Assistant Professor College of Nursing and Health Innovation Arizona State University USA
REVIEW RETURNED	02-Feb-2019

GENERAL COMMENTS	This paper examined the impact of acculturation on cardiac structure and function in Latinos. The topic falls within the journal aims and scope (relevant to patients and clinicians) and is of great significance given that Latinos have a large burden of heart failure risk and are the largest immigrants in the U.S. **The article title** clearly describes the article although it does not include the research question and the study design. **Abstract** is structured and concise, but some elements (objectives, design, setting, eligibility criteria, statistical significance) are missing. It would be worth adding them. p. 4 • lines 3-10: the word “high” is very vague. How high is significant to get attention? Provide a supporting evidence with statistics (%). • line 14: “of HF” is redundant so please delete it. • lines 14-20: this sentence is confusing. Please add a comma before “and Hispanics/Latinos who…” Also, provide a supporting evidence with statistics (%). • line 17: “younger” than whom and “lower” than what? Please clarify whom you compare with. • line 19: what are those traditional HF risk factors?

	• lines 20-24: this statement alone is not a strong argument. Is it a unique phenomenon happening to only Hispanic or any immigrants? Please articulate and add more evidence (literature). • line 22: what do you mean by "unique" sociocultural factors? unique to immigrants, not only to Hispanic/Latinos because acculturation occurs in any immigrants? • lines 24-29: this sentence is another very weak argument. 'The fact that this specific ethnic group is the largest immigrants in the U.S.' is not a good reason for conducting this study. Please find what is out there in literature and what is a gap you need to fill. Please add a clear and reasonable justification for conducting this study. • lines 38-40: I wonder why the authors separate this specific reference from others and make it distinct in a new sentence. Is this a justification for conducting this study? • line 44: acculturation is described as a "bio-sociocultural variable" here, while you described "sociocultural factor" on line 22. Be consistent. In literature, acculturation is described as a "cultural" or "sociocultural" factor, not "bio-sociocultural variable." • lines 47-49: what are those "studies often overlook SES…?" please add some literature here. • Overall, a little more in-depth explanation in the Background/Introduction section would be helpful. **Research question:** it is not clearly explicated, and there is no clear justification. **Review of literature** is not comprehensive. Probably the authors need to do more literature review and add them in the Intro section: what is unknown or any conflicting information about the association between acculturation and CS & CF in Latinos and other immigrants (foreign-born; first-generation). A comprehensive literature review helps you to determine the topic is worth studying, and more importantly the readers would see it as well. A comprehensive literature review also leads you to have a more extensive discussion. **Method:** • Study design (cohort study) is appropriate for the purpose of the study and described in depth. • The study sample and setting are clearly described and appropriate for the study purpose: selection criteria of participants are adequately described. • Ethical consideration: IRB approval and informed consent from participants were acknowledged. • p. 5 line 42 – p. 6 line 6: presenting a specific definition for each biomarkers is appropriate. However, too detail information on the SES (p. 6 lines 15-31) is not necessary because they are presented in Table 1. p. 7

	• lines 6-34: probably a brief description about how acculturation is measured would be sufficient; too much detail is presented here. All those details are presented in Table 1. Regarding the SASH, it would be helpful to present information on reliability and validity in previous studies. Is it a 5-point Likert scale? add this information, too. • lines 38-42: in general, mean age is reported with SD, not SE. A brief explanation why reporting SE (instead of SD) would be helpful for clinicians who are not familiar with the reason of reporting SE. Also, add a reference for that explanation. • line 52: "foreign-born" is considered as "1st generation," while "US-born" is equivalent to "2nd generation." It is not clear why differentiating them? • p. 7 lines 47-49: the authors say, "LV diastolic dysfunction was analyzed as a binary variable." There is no description about which statistical method used to examine the association of LVDD with acculturation variables. Please specify. • p. 8 lines 3-8: ANOVA is the right statistical technique to compare mean scores of continuous variables (e.g., LVMI, RWT, LAVI, LVEF, e', E/e') across ordinal level acculturation variable (i.e., years of US residency), but not for dichotomous acculturation variables (i.e., nativity, generational status, and preferred language). Specify which statistic was used for these variables. • What statistics are used to examine the association between cardiac structure and function (e.g., LVMI, RWT, LAVI, LVEF, e', E/e') and continuous level acculturation variables (i.e., age at immigration and SASH subscales)? Specify. • Data analysis was not clearly described or appropriate in some parts. **Results:** • p. 8 line 50 – p. 9 line 18: specify %, rather than saying "almost half" "over half" "most" or "some degree of diastolic." p. 9 • lines 8-12: if "values of echocardiographic variables were all within normal limits," what is the clinical significance of this study? Justify and acknowledge in the Discussion section as needed. • lines 26-31: "foreign-born" is considered as "1st generation," whereas "US-born" is equivalent to "2nd generation." What is the point of differentiating them? • lines 31-34: the authors report the association between SASH language subscale and LAVI, but no description on the association between SASH social relations subscale and LAVI. Two subscales (language and social relations) of the SASH were analyzed separately in their models (p. 7 lines 17-29). However, no report on the SASH social relations subscale associated with outcome variables in the Results section and further documentation. Please specify. • lines 31-36: the wording of this sentence is a bit odd. The following would be better: "Acculturation measured by SASH language scale was positively associated with LAVI, whereas age at migration to US was negatively associated with LAVI and RWT." • line 42: "higher" than whom? Specify. • lines 42-47: each word should be used consistently throughout the documentation; choose either "foreign-born" or "1st

	generation" (the same rule applies to either "US born" or "2nd generation") if they refer the same thing. • line 49: "younger age" would be more appropriate than "lower age." **Discussion** p. 10 • lines 30-32: it is difficult to follow this argument without seeing some statistical evidence; population characteristics of this ethnic group in terms of age. Please add evidence with references. • lines 32-36: by all acculturation measures or some of them? Be specify. • lines 39-41: it is hard to agree with this argument because the authors used a few proxy measures of acculturation (nativity, generational status, age at immigration, preferred language) in addition to the short version of a multidimensional acculturation scale. Also, the results were not consistent (not all of cardiac structure and function variables were significantly associated with all of these acculturation measures). • lines 48-50: what do you mean by "different dimensions of acculturation?" Be specific. • lines 53-55: this sounds like jumping to conclusion. You did neither have any literature review about the association between acculturation, acculturative stress, and unhealthy behaviors, nor examine the associations among those variables in your study. p. 11 • lines 10-13: if there is no existing literature in Latinos, how about in other immigrant populations? • lines 40-45: what do you mean by "high burden of acculturation?" Please specify and provide references. p. 12 • lines 15-27: this is too much extension of the primary study variables and literature provided in the Intro section. This is another area of research to further explore in the future. • lines 49 -54: your finding is contradictory of other findings but very interesting. • p. 12 line 54 – p. 13 line 6: please add a reference for this statement. p. 13 lines 6-22: these sentences do not support your findings. It is rather illustrating conflict between 2 cultural values. Maybe delete? **Conclusions** • p. 14 lines 7-12: there has been a great deal of research on acculturation, including acculturation measures. Significant associations of acculturation with HF risk found in this study depended on some proxy measure of acculturation, not multidimensional measures. Therefore, it would be more appropriate to state "significant associations between some proxy measures of acculturation (and add those proxy measures here) and… " rather than saying "…acculturation

	measures…" Also, you may acknowledge it as one of the limitations. • line 22: it is not appropriate to include "other immigrants" because your study focus, literature review, and collected data were not related to other immigrants at all. Conclusion should be based on data presented and liked with current literature. • Acculturation is not bidirectional (on either side of opposing ends of a single continuum; being assimilated to the main culture or retaining the original culture); rather it is multidirectional. If we consider acculturation as bidirectional and apply the results of your study (the more acculturated, the worse HF risk), we (clinicians and society) should keep Latinos from being acculturated. This is not what we want, though. For that reason, it would be appropriate to say that your findings should be interpreted with caution when translating to clinical care of the Hispanic population. You have to consider what you found in your study sample data: "Our multivariable models did not fully account for the deleterious effects of acculturation." (p. 11 lines 19-21) **Conclusions** References are appropriate. However, only 29% (12/42) of the references are up-to-date; published within last 5 years.

REVIEWER	Carol Oladele Yale University, USA
REVIEW RETURNED	19-Mar-2019

GENERAL COMMENTS	**Introduction:** The conceptual model presented is overly simplistic. The pathway through which acculturation influences cardiac function should be further elucidated. This would serve to strengthen the justification for investigating the relationship between acculturation and measures of cardiac function. A summary of literature that supports the study premise is needed. A brief explanation of the cardiac and structure variables would be helpful at some point in the manuscript. **Methods:** I recommend the authors conduct sensitivity analyses to determine if persons born in US territories are different from foreign born individuals. Acculturative experiences of persons living in territories may differ from foreign-born individuals who do not have added psychosocial stressors associated with true foreign-born status. Lines 10-13 state "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…." The statement suggests that the type of models used were determined

	by the acculturation variables and not your dependent cardiac structure variables. This statement should be clarified. **Results:** The results statement regarding income appears incorrect. Table 1 shows that 45.5 percent of individuals had an annual family income >20 K. However, the text states that almost half reported an income < 20 K. The inclusion of normal range values for cardiac structure and function variables are needed either in the text or tables. It is hard to evaluate values with no information about normal ranges. The study is cross-sectional and language such as “significantly increased with increasing years in the US” suggests that individuals were assessed prospectively. Though an association was observed, the cross-sectional nature of the study precludes the ability to assess the temporal sequence of the relationships. The language used to describe results should reflect the type of study design used. Alternate phrasing could include: “LAVI was positively associated with years spent in the US.” Line 24: bimodal distribution should be corrected to read “bimodal association” or “U-shaped association.” “Increasing acculturation” is incorrect. Acculturation was not measured over time. Language like “higher acculturation” or “greater acculturation” or “higher level of acculturation” should be used throughout the manuscript. The same applies to explanations including cardiac function and structure variables. (e.g. increasing LAVI) The statement that younger age of migration is associated with increased LAVI is inconsistent with the Beta estimate provided in Table S1. Findings presented in line 40 regarding associations between years in the US, RWT and LAVI are inconsistent with the results presented in table 2. Data in the table shows that RWT is positively associated with years spent in the US or increased time spent in the US is associated with greater RWT. Table 2 also shows that LAVI is inversely associated with years spent in the US. The authors statement that “lower RWT and increased LAVI are associated increasing years in the US “do not match the data. Table 2. The footnote regarding the second p-value is unclear. Is this the p-value for years in the US as a continuous variable? Language describing statistically significant associations should explicitly state that associations are “statistically significant” instead of describing statistical significance of associations as “significantly higher.” This should be corrected throughout the manuscript.

	Line 47: Increasing SASH language scales and increasing LAVI should be revised to reflect the cross-sectional nature of this study. Language such as “higher SASH score and “higher LAVI” is appropriate. **Discussion:** The first line of the discussion section is unclear. The authors should address the exclusion of information on healthcare utilization and usual source of care in models. Evidence shows that foreign-born persons are less likely to have a usual source of care, which could explain the observed associations. In the absence of these and other potential explanatory factors, caution should be taken in drawing strong conclusions. The section could be strengthened by unpacking aspects of acculturative experiences that may explain the associations observed in the study. The authors highlight the Hispanic Paradox but do not fully explain how the study findings support this phenomenon. Limitations associated with measures of acculturation used should be discussed.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

1. The conceptual model presented is overly simplistic. The pathway through which acculturation influences cardiac function should be further elucidated….A summary of literature that supports the study premise is needed.
   Response: We have revised the Introduction section and updated our Figure 1 to provide a better conceptual model and to elucidate our study premise.
2. A brief explanation of the cardiac and structure variables would be helpful at some point in the manuscript.
   Response: We now provide in the Methods better detailing and explanation of our cardiac structure and function variables.
3. I recommend the authors conduct sensitivity analyses to determine if persons born in US territories are different from foreign-born individuals. Acculturative experiences of persons living in territories may differ from foreign-born individuals….
   Response: We agree with the reviewer regarding this distinction.
   We performed a sensitivity analysis comparing individuals born in the island of PR vs. other foreign-born Hispanics. Interestingly, 24% of foreign-born Hispanics were born in the US Commonwealth of Puerto Rico (PR) (none in the US Virgin Islands). Spanish language preference was less among foreign-born Hispanics born in PR compared to other foreign-born Hispanics. PR born Hispanics also scored higher on the SASH language scale and the SASH social interaction scale indicating higher acculturation levels compared to other foreign-born Hispanics. However, the levels of Spanish language preference and SASH scores were still lower among foreign-born Hispanics born in PR compared to US born Hispanics.

Spanish language preference and SASH language scores were higher among Hispanics born in PR compared to other foreign-born Hispanics but this proportion was still significantly less than Hispanics born in the US. Suggesting that to many, living in the island of PR still allows for maintaining of a culture that is distinct and different from the US culture. We now include this in the Results and Discussion sections of the manuscript.

4. Lines 10-13 state “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….” The statement suggests that the models used were determined by the acculturation variables and not your dependent cardiac structure variables. This statement should be clarified.
   Response: This statement has been revised according to the reviewer suggestion.
5. The results statement regarding income appears incorrect. Table 1 shows that 45.5 percent of individuals had an annual family income >20 K. However, the text states that almost half reported an income < 20 K.
   Response: We rounded out 46% to reflect almost half of the population. We have added the actual rounded percentages to the text to better clarify.
6. The inclusion of normal range values for cardiac structure and function variables are needed in either the text or tables.
   Response: Normal values have been added to Table 1.
7. The study is cross-sectional and language such as “significantly increased with increasing years in the US” suggests that individuals were assessed prospectively. Though an association was observed, the cross-sectional nature of the study precludes the ability to assess the temporal sequence of the relationships.
   Response: We have expanded mention of the limitations of the cross-sectional nature of our study and have revised the text throughout the manuscript accordingly to reflect this phrasing as suggested by the reviewer.
8. Line 24: bimodal distribution should be corrected to read “bimodal association” or “U-shaped association.”
   Response: This has been corrected.
9. “Increasing acculturation” is incorrect. Acculturation was not measured over time. Language like “higher acculturation” or “greater acculturation” or “higher level of acculturation” should be used throughout the manuscript.
   Response: (please see comment #7)
10. The statement that younger age of migration is associated with increased LAVI is inconsistent with the Beta estimate provided in Table S1.
    Response: The negative beta estimates in Table 2 and Table S1 reflect an inverse (negative) association of age at immigration with LAVI. This is interpreted as a younger (lower) age of migration associated with higher LAVI. This observation is also consistent with the converse observation in Table 2 where LAVI was positively associated with years spent in the US.
11. Findings presented in line 40 regarding associations between years in the US, RWT and LAVI are inconsistent with the results presented in table 2.
    Response: We thank the reviewer for pointing this out. This has been corrected in the manuscript. Table 2 now demonstrate positive beta estimates for Years in the US with RWT and LAVI, respectively, signifying greater RWT and lower LAVI with more years in the US.
12. Table 2. The footnote regarding the second p-value is unclear. Is this the p-value for years in the US as a continuous variable?
    Response: We apologize for the confusion. Categories of Years in the US (<5; 5-10; 11-20; >20) are being utilized for the analysis in Table 2. For Years in the US, the 1st p-value reflects <5 years vs. >20 years comparison; whereas the 2nd p-value is p value overall across all the Years in the US categories. This is now better clarified in the footnote wording.
13. Language describing statistically significant associations should explicitly state that associations are “statistically significant” instead of describing statistical significance of associations as “significantly higher.”
    Response: This has been corrected.

14. Line 47: Increasing SASH language scales and increasing LAVI should be revised to reflect the cross- sectional nature of this study. Language such as “higher SASH score and “higher LAVI” is appropriate.
    Response: please see comment #7.
15. The first line of the discussion section is unclear.
    Response: We apologize for the confusion. The Hispanic population >65 years of age is expected to grow 328% between 2000 and 2030. As the Hispanic population ages, and HF risk factors and cardiac abnormalities progress, it is likely that an epidemic of clinical HF in Hispanics will emerge. We have added further language and references to reflect this.
16. The authors should address the exclusion of information on healthcare utilization and usual source of care in models.
    Response: We thank the reviewer for this comment.
    HCHS/SOL has a few questions regarding health care utilization, primarily regarding difficulty obtaining health care in the past year and number of physician visits in the past year. We performed an additional exploratory analysis:
    The relationship between acculturation and health care utilization was complex. Being foreign-born, having less years in the US and not having health insurance were all significantly associated with having difficulty obtaining health care in the past year.
    Foreign-born individuals had less physician visits over the past year compared to US born but the absolute difference was only 0.1 visit. The relation between years in the US and MD visits was complex and non-linear (bimodal) and mirrored an opposite pattern with income. (Figure 2)
    Having health insurance coverage was significantly associated with HC utilization. This highlights the complex nature of acculturation where being foreign-born may make one less likely to utilize health care. A more extensive analysis on HC utilization is beyond the scope of our paper. This area deserves further consideration in a future study. We now added this information to our Results and Discussion.
17. The section could be strengthened by unpacking aspects of acculturative experiences that may explain the associations observed in the study. The authors highlight the Hispanic Paradox but do not fully explain how the study findings support this phenomenon. Limitations associated with measures of acculturation used should be discussed.
    Response: We thank the reviewer for these comments and feedback.
    We have expanded our Discussion on the acculturative experience and added further rationale supporting our scientific premise.
    We have revised our mention of the Hispanic Paradox to better explain our rationale and hypothesis. We now mention in the Limitations that our several acculturation measures (nativity, years of US residence/age at migration, SASH subscales, language preference and generational status) may not fully capture the acculturative experience. However, we do believe acculturation cannot be captured by just one measure, as has been done in much of the prior literature.

Reviewer #2:

1. Abstract/Background/Introduction
    a. lines 3-10: the word “high” is very vague.
       Response: We now clarify and provide further reference that this high compared to non-Hispanic whites.

    b. line 14: “of HF” is redundant so please delete it.
       Response: This has been corrected.

    c. lines 14-20: this sentence is confusing. Please add a comma before “and Hispanics/Latinos who…” Also, provide a supporting evidence with statistics (%).
       Response: This has been corrected.

Our text provides the supporting references which include the supporting statistics. For the sake of space, we provide further elaboration here:

- 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: During a median follow-up of 4.0 years, 79 participants developed CHF (incidence rate: 3.1 per 1000 person-years). African Americans had the highest incidence rate of CHF, followed by Hispanic, white, and Chinese American participants (incidence rates: 4.6, 3.5, 2.4, and 1.0 per 1000 person-years, respectively).
- 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: Over one-third of Hispanics with HF were younger than 66 years compared to ~20% of non-Hispanic whites. Hispanics with HF and were more likely to have non-ischemic etiologies compared to non-Hispanic whites.
- Vivo RP, Krim SR, Cevik C, Witteles RM. Heart failure in Hispanics. Journal of the American College of Cardiology 2009;53:1167-75: Retrospective and observational studies have largely documented that compared with non-Hispanic whites, Hispanics with HF are more likely to be younger (12–14), underinsured (12), and to have higher rates of diabetes, dyslipidemia, and kidney disease (12–15). In addition, Hispanics have a relatively higher prevalence of abnormal LV ejection fraction (13,14,16)—usually implying worse prognosis in HF.

d. line 17: “younger” than whom and “lower” than what? Please clarify whom you compare with.
Response: This has been clarified as compared to non-Hispanic whites.

e. line 19: what are those traditional HF risk factors?
Response: We now list those specifically as hypertension, diabetes and obesity.

f. line 22: what do you mean by “unique” sociocultural factors? unique to immigrants, not only to Hispanic/Latinos because acculturation occurs in any immigrants?
Response: By ‘unique’ we meant that acculturation was a unique (special type of) sociocultural factor given its complexity and impact. We have removed the word ‘unique’ from this sentence to avoid the confusion.

g. lines 24-29: this sentence is another very weak argument. ‘The fact that this specific ethnic group is the largest immigrants in the U.S.’ is not a good reason for conducting this study. Please find what is out there in literature and what is a gap you need to fill. Please add a clear and reasonable justification for conducting this study.
Response: The fact that Hispanics/Latinos are the largest US immigrant group provides added significance to the public health impact of our study. It was not meant to be interpreted as the reason for conducting the study. This has been corrected in the text.

We now include mention of specific gaps in the literature regarding acculturation, cardiac structure/function and HF; gaps regarding the mechanistic pathways linking acculturation with CVD with cardiac structure and function as intermediary variables.

h. lines 38-40: I wonder why the authors separate this specific reference from others and make it distinct in a new sentence. Is this a justification for conducting this study?
Response: This reference was not justification for our study but was highlighted to demonstrate the paucity of studies with regards to acculturation and HF. In fact, ours is the largest study of acculturation with cardiac structure and function.

i.line 44: acculturation is described as a “bio-sociocultural variable” here, while you described “sociocultural factor” on line 22. Be consistent. In literature, acculturation is described as a “cultural” or “sociocultural” factor, not “bio-sociocultural variable.”
Response: We have revised the text to use consistent language. We define acculturation as an important sociocultural variable with biological implications that have not been well-studied.

j.lines 47-49: what are those “studies often overlook SES…?” please add some literature here.
Response: We were specifically referring to studies of acculturation and CVD, which we cited. These studies have not examined SES as a modifier between acculturation and health-variables, which is what we sought to do with our secondary analysis.

2. Research question: it is not clearly explicated, and there is no clear justification. Review of literature is not comprehensive. Probably the authors need to do more literature review and add them in the Intro section.
Response: please see Reviewer 1, comment #7.
An extensive and comprehensive re-review of the literature was performed for this paper and several more up to date references were added. The fact is, not a lot has been published about the association between acculturation and cardiac structure and function in Latinos and other immigrants. Ours will be one of the first studies to describe this.

3. p. 5 line 42 – p. 6 line 6: presenting a specific definition for each biomarkers is appropriate. However, too detail information on the SES (p. 6 lines 15-31)… p. 7 lines 6-34: probably a brief description about how acculturation is measured would be sufficient… All those details are presented in Table 1.
Response: We have abbreviated our information on SES. However, we chose not to abbreviate this information since 1. acculturation is the focus of this study and our primary exposure variable; and 2. we expanded the information on our primary outcome variables at the request of Reviewer 1.

4. Regarding the SASH, it would be helpful to present information on reliability and validity in previous studies. Is it a 5-point Likert scale?
Response: We added further details regarding the SASH including a recent reference that describes the SASH reliability and validity.

5. p. 7 lines 38-42: in general, mean age is reported with SD, not SE. A brief explanation why reporting SE (instead of SD) would be helpful for clinicians who are not familiar with the reason of reporting SE.
Response: With regards to the use of SEs (standard errors), we are following the recommendations of the HCHS/SOL Statistical Analysis Center. HCHS/SOL utilized a random sampling process as described in our Methods section. Due to the sampling weights that were used in Echo-SOL analyses to account for the complex survey design of HCHS/SOL, SEs are reported. Survey statistics data analysis using SAS produces SEs not standard deviations. This is now mentioned in the Methods section.

6. line 52: “foreign-born” is considered as “1st generation,” while “US-born” is equivalent to “2nd generation.” It is not clear why differentiating them?
Response: We thank the reviewer for pointing this out because we did not define first generation as foreign-born. First- and second-generation are both US-born Hispanics and distinct from their foreign-born immigrant parents. This distinction is important because both First- and second-generation Hispanics complete all of their education in the United States and are generally the first in their families to graduate high school or attend college. This has been clarified in the text.

7. p. 7 lines 47-49: the authors say, “LV diastolic dysfunction was analyzed as a binary variable.” There is no description about which statistical method used to examine the association of LVDD with acculturation variables.
Response: We have now added details regarding this analysis, which used frequencies and Rao-Scott Chi-Square for the categorical LVDD variables.

8. p. 8 lines 3-8: ANOVA is the right statistical technique to compare mean scores of continuous variables (e.g., LVMI, RWT, LAVI, LVEF, e’, E/e’) across ordinal level acculturation variable (i.e., years of US residency), but not for dichotomous acculturation variables (i.e., nativity, generational status, and preferred language). Specify which statistic was used for these variables.

Response: We have now added details regarding this analysis, which used frequencies and Rao-Scott Chi-Square for the dichotomous variables.

9. What statistics are used to examine the association between cardiac structure and function (e.g., LVMI, RWT, LAVI, LVEF, e', E/e') and continuous level acculturation variables (i.e., age at immigration and SASH subscales)?
   Response: We used weighted means and linear regression for continuous variables. This is now clarified in the text.

10. p. 8 line 50 – p. 9 line 18: specify %, rather than saying "almost half" "over half" "most" or "some degree of diastolic."
    Response: we respectfully disagree with the reviewer but in an effort to not be redundant with the tables we did not want to repeat the same percent values already listed.

11. p. 9 lines 8-12: if "values of echocardiographic variables were all within normal limits," what is the clinical significance of this study?
    Response: We describe the significance in Discussion. Briefly, this is a relatively young cohort (mean age 56) so it is not surprising that mean values of echocardiographic variables were all within normal limits. 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 size of the Hispanic population and 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.

12. p. 9 lines 31-34: the authors report the association between SASH language subscale and LAVI, but no description on the association between SASH social relations subscale and LAVI. Two subscales (language and social relations) of the SASH were analyzed separately in their models (p. 7 lines 17-29). However, no report on the SASH social relations subscale associated with outcome variables in the Results section….
    Response: Only acculturation measures that were significant in unadjusted analyses were analyzed in multivariable adjusted models. SASH social relations subscale was not significant on unadjusted analysis as shown in Table S1.

13. lines 31-36: the wording of this sentence is a bit odd. The following would be better: "Acculturation measured by SASH language scale was positively associated with LAVI, whereas age at migration to US was negatively associated with LAVI and RWT."
    Response: We have revised the text according to the reviewer suggestions.

14. line 42: "higher" than whom?
    Response: We now specify compared to those making <$20K.

15. lines 42-47: each word should be used consistently throughout the documentation; choose either "foreign-born" or "1st generation" (the same rule applies to either "US born" or "2nd generation") if they refer the same thing.
    Response: please see comment #6

16. line 49: "younger age" would be more appropriate than "lower age."
    Response: This has been corrected.

Discussion

17. p. 10
    a. lines 30-32: it is difficult to follow this argument without seeing some statistical evidence; population characteristics of this ethnic group in terms of age.
       Response: We have added evidence with references.

b. lines 32-36: by all acculturation measures or some of them?
Response: This general statement was in reference to all acculturation measures.
c. lines 39-41: it is hard to agree with this argument because the authors used a few proxy measures of acculturation (nativity, generational status, age at immigration, preferred language) in addition to the short version of a multidimensional acculturation scale. Also, the results were not consistent (not all of cardiac structure and function variables were significantly associated with all of these acculturation measures).
Response: The measurement of acculturation in research is challenging and has been criticized for being too linear and relying heavily on English language use. We used several measures of acculturation (nativity, years of US residence/age at migration, SASH subscales, language preference and generational status), each captures different dimensions of acculturation and each variable of cardiac structure and function is also a distinct outcome to its own, capturing a different dimension of cardiac structure and function. It is not surprising that not every variable of cardiac will be associated with all of the acculturation measures.

d. lines 48-50: what do you mean by "different dimensions of acculturation?"
Response: We have removed the word 'dimensions' to avoid confusion and but what we meant is that different measures of acculturation capture different aspects. For example, nativity alone captures one aspect but years in the US tell another story whereas age at migration (an immigrant may have spent 30 years in the US but migration at age 10 vs age 40) tells a different story.

e. lines 53-55: this sounds like jumping to conclusion. You did neither have any literature review about the association between acculturation, acculturative stress, and unhealthy behaviors, nor examine the associations among those variables in your study.
Response: We base our conclusions based on our updated conceptual Figure and mechanistic framework. We now provide specific text and cite references highlighting our re-review regarding the association of acculturation, acculturative stress, and unhealthy behaviors.

18. p. 11
a. lines 10-13: if there is no existing literature in Latinos, how about in other immigrant populations?
Response: To the best of our knowledge, there is no existing literature between acculturation and HF risk, specifically with regard to cardiac structure and function, in other immigrant populations.

b. lines 40-45: what do you mean by "high burden of acculturation?"
Response: By sheer numbers, because of the size of the US Hispanic population and its large predominant immigrant component, the Hispanic population has a high burden of acculturation.

19. p. 12 lines 15-27: this is too much extension of the primary study variables and literature provided...This is another area of research to further explore in the future.
Response: We now state this as the reviewer suggested.

20. p. 12 line 54 – p. 13 line 6: please add a reference for this statement.
Response: We have added a reference for this statement.

21. p. 13 lines 6-22: these sentences do not support your findings. It is rather illustrating conflict between two cultural values. Maybe delete?
Response: This paragraph has been modified and the alignment with our findings is clarified. Our purpose was to further illustrate the complexities of the acculturative process, which is being impacted upon by SES and traditional values such as familismo.

22. p. 14 lines 7-12: there has been a great deal of research on acculturation, including acculturation measures. Significant associations of acculturation with HF risk found in this study depended on

some proxy measure of acculturation, not multidimensional measures. Therefore, it would be more appropriate to state “significant associations between some proxy measures of acculturation (and add those proxy measures here) and… “rather than saying “…acculturation measures…” Also, you may acknowledge it as one of the limitations.
Response: Thank you for your feedback and comments. We have removed the word ‘multidimensional’ to avoid confusion (see comment #17). All measures of acculturation in the literature are proxy by definition. By including several measures (nativity, years of US residence/age at migration, SASH subscales, language preference and generational status) our goal was to be as comprehensive as possible and to capture several aspects of acculturation. We respectfully see this as a strength not a limitation since we believe acculturation cannot be captured by just one measure, as has been done in much of the prior literature. We agree that even our multivariable approach may not still fully capture all aspects of acculturation.

23. line 22: it is not appropriate to include “other immigrants” because your study focus, literature review, and collected data were not related to other immigrants at all.
Response: We agree with the reviewer; however, as reviewer #1 has pointed out, the acculturation experience is not unique to Hispanics and it is our hope that our study can help shed some light and generate further study in other immigrant populations. We have revised this statement.

24. If we consider acculturation as bidirectional and apply the results of your study (the more acculturated, the worse HF risk), we (clinicians and society) should keep Latinos from being acculturated. This is not what we want, though. For that reason, it would be appropriate to say that your findings should be interpreted with caution when translating to clinical care of the Hispanic population. You have to consider what you found in your study sample data: “Our multivariable models did not fully account for the deleterious effects of acculturation.” (p. 11 lines 19-21)
Response: We thank the reviewer for the feedback. Your comments raise some interesting and important issues. Our study intent was to highlight the hypothesis that the acculturative process can affect HF risk. Our intent was to bring to the forefront the notion that what immigrants go through is not necessarily a benign and inert experience and that we (as clinicians and society) should lend more thought and further study as to how can we make the acculturative process easier to navigate and less deleterious. In order to start thinking about potential future interventions, one must first acknowledge the impact of acculturation on health variables such as HF risk. We have revised the language of our Conclusion to better reflect our intent.

25. References are appropriate. However, only 29% (12/42) of the references are up-to-date; published within last 5 years.
Response: We have increased the number references (from 42 to now 50) including adding several more up-to-date references.

Figure 1.

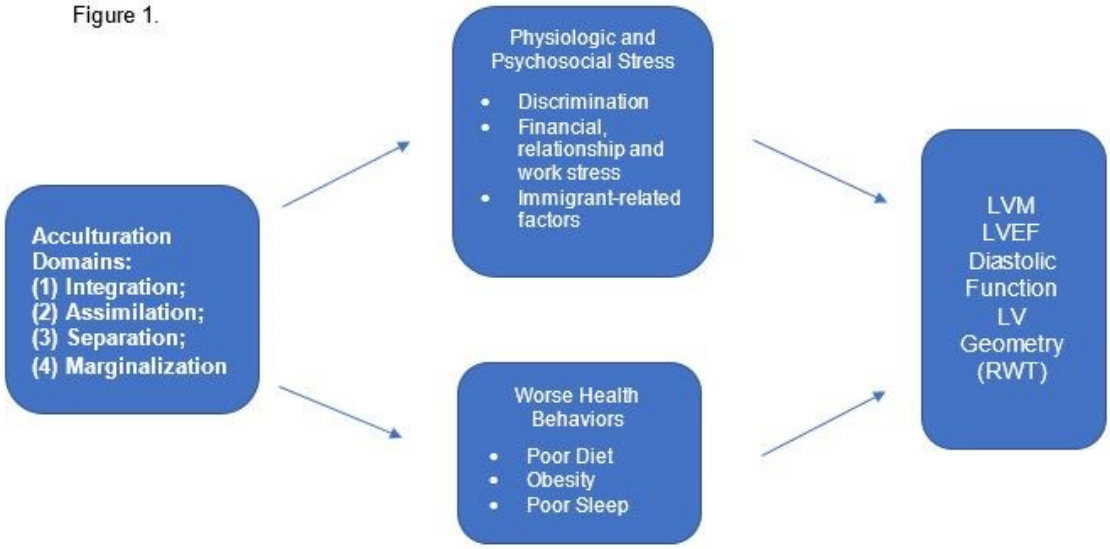
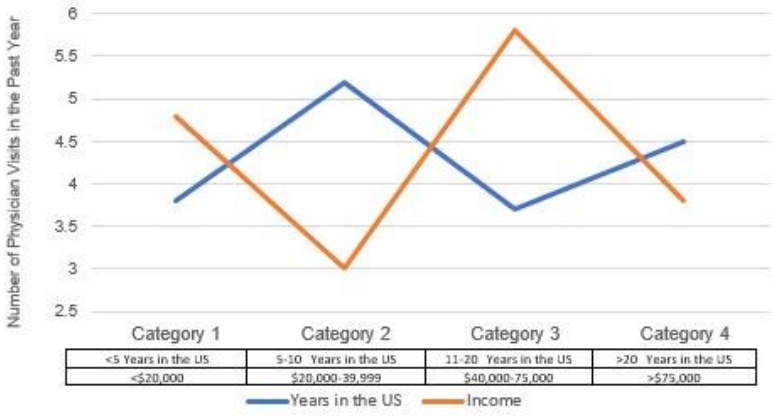


Figure 2.



VERSION 2 – REVIEW

REVIEWER	Cha-Nam Shin Arizona State University
REVIEW RETURNED	21-Sep-2019

GENERAL COMMENTS	Most of my comments in the original version have been adequately addressed.

REVIEWER	Carol Oladele Yale University, USA
REVIEW RETURNED	28-Aug-2019

GENERAL COMMENTS	The authors' revision of the manuscript was responsive to review feedback. The revisions

	greatly strengthened the manuscript. A few minor changes would make this manuscript ready for publication. Page 5 second paragraph. The last sentence uses the word impact twice. Consider changing the second “impact” to “influence.” Page 7 last sentence. Check the sentence structure for the sentence that describes how marital status was categorized. Page 8. #4 is missing the word “was.” Also check the structure of the sentences for this description of ECG measures. Page 9, first sentence under the subheading “Acculturation Measures,” could be clearer. Consider using “measured” instead of “characterized.” For example, “Acculturation was measured using several proxy measures.” Page 10. The authors mention using ANOVA for analyses; however, it appears that ANCOVA was also used based on the results presented in table S2. This information should be included in the statistical analysis section of the manuscript. I recommend making the table titles more descriptive to include information that lets the reader know what statistical test was performed. Page 10. The sentence referring to the inclusion of variables that were statistically significant in bivariate analyses is unclear. Suggestion: Only variables that were statistically significant in unadjusted analyses were included in multivariable analysis. Page 10. “exploratory analyses” should be changed to “sensitivity analyses” and a brief (one sentence) justification should be provided. Page 11. The word “regarding” is used twice in the first sentence at the top of the page. Page 11. The sentence that includes “which produce standard errors (SEs) not standard deviations” above “Results” should be deleted. The study is based on a sample and therefore all statistical procedures will produce standard errors. In the same sentence, “survey statistics” should be replaced with “proc survey procedures.” Page 12. The interpretation of part of table S1 is incorrect. The authors are comparing differences in means and language such as “was positively associated” is incorrect. You are testing whether there is a difference in mean values across categories. Therefore, interpretation should be something like “there was a statistically significant difference in mean LAVI values between categories of length of time spent in the US.” There is some residual use of the word “increasing” in places within the results section. The authors should review and determine the appropriateness of this word and determine instances where “higher” or “greater” should be used instead. Increasing, the way it is used here, suggests that temporal sequence can be determined. Page 12. The use of “statistically significantly lower” can be better stated as “Adjusted analyses

	demonstrated that greater time spent in the US is significantly associated with increased RWT and LAVI. The term statistical significance should always refer to the association itself. Page 12. The authors should confirm whether age of migration to US was associated with higher RWT. The table doesn't support that sentence. Page 12. Second sentence of the last paragraph should have a comparison group included in this sentence. For example, "compared to US born participants." Page 13. The word "statistically" should go before significant in the first sentence. The comment above about interpreting ANOVA results applies to this paragraph as well. Page 13. The last sentence of the first paragraph is difficult to interpret and should be revised. Page 13. The second paragraph needs a few words to let the reader know that these are results of the sensitivity analyses. This section could be reduced to just highlight the main results of the sensitivity analyses. Page 14. Section that describes acculturation seems out of place in the discussion. The authors should consider moving it to the introduction or removing if the explanation of acculturation in the introduction is deemed sufficient. Page 14. The end of the last sentence should be deleted. "despite long residence in the US" This is one of the authors' measures of acculturation. (re: length of time in the US). The results therefore cannot be "despite long residence in the US." Pages 14-15. Some of the content in paragraphs 2 and 3 are redundant. Consider consolidating the content. Page 15. The authors use language regarding the "magnitude of associations" when most analyses conducted do not permit evaluation of the magnitude of the association, with exception of odds ratio results. No other measures of association were presented. This statement should be modified to be more accurate. Page 16. The last part of the final paragraph that explains acculturative stress appears is unnecessary and does not add to the discussion. Consider removing or greatly reducing this content. Page 17. The first sentence of the second paragraph could be clearer. For example, "The statistically significant interaction between acculturation and SES may shed light…" Page 17. The authors should confirm whether reference to less acculturation meaning more retention of "host" culture is correct. This may be an error and should read "original" culture.

VERSION 2 – AUTHOR RESPONSE

Reviewer #1:

1. Page 5 second paragraph. The last sentence uses the word impact twice.

Response: This has been corrected.

2. Page 7 last sentence. Check the sentence structure for the sentence that describes how marital status was categorized.

Response: This has been corrected.

3. Page 8. #4 is missing the word “was.” Also check the structure of the sentences for this description of ECG measures.

Response: This has been corrected.

4. Page 9, first sentence under the subheading “Acculturation Measures,” could be clearer. Consider using “measured” instead of “characterized.” For example, “Acculturation was measured using several proxy measures.”

Response: This has been corrected.

5. Page 10. The authors mention using ANOVA for analyses; however, it appears that ANCOVA was also used based on the results presented in table S2. This information should be included in the statistical analysis section of the manuscript.

Response: We apologize but our analysis only consisted of unadjusted and adjusted regression analysis. We did not use ANOVA or ANCOVA for table S2 or any other analysis. Our statistical section has been edited to reflect this.

6. Page 10. The sentence referring to the inclusion of variables that were statistically significant in bivariate analyses is unclear. Suggestion: Only variables that were statistically significant in unadjusted analyses were included in multivariable analysis.

Response: This has been corrected.

7. Page 10. “exploratory analyses” should be changed to “sensitivity analyses” and a brief (one sentence) justification should be provided.

Response: This has been corrected.

8. Page 11. The word “regarding” is used twice in the first sentence at the top of the page.

Response: This has been corrected.

9. Page 11. The sentence that includes “which produce standard errors (SEs) not

standard deviations" above "Results" should be deleted. The study is based on a sample and therefore all statistical procedures will produce standard errors. In the same sentence, "survey statistics" should be replaced with "proc survey procedures."

Response: This has been corrected.

10. Page 12. The interpretation of part of table S1 is incorrect. The authors are comparing differences in means and language such as "was positively associated" is incorrect. You are testing whether there is a difference in mean values across categories. Therefore, interpretation should be something like "there was a statistically significant difference in mean LAVI values between categories of length of time spent in the US."

Response: This has been corrected.

11. Page 12. The use of "statistically significantly lower" can be better stated as "Adjusted analyses demonstrated that greater time spent in the US is significantly associated with increased RWT and LAVI. The term statistical significance should always refer to the association itself.

Response: This has been corrected.

12. Page 12. The authors should confirm whether age of migration to US was associated with higher RWT. The table doesn't support that sentence.

Response: This has been corrected.

13. Page 13. The last sentence of the first paragraph is difficult to interpret and should be revised.

Response: This has been corrected.

14. Page 13. The second paragraph needs a few words to let the reader know that these are results of the sensitivity analyses. This section could be reduced to just highlight the main results of the sensitivity analyses.

Response: This has been corrected.

15. Page 14. Section that describes acculturation seems out of place in the discussion. The authors should consider moving it to the introduction or removing if the explanation of acculturation in the introduction is deemed sufficient.

Response: The purpose of revisiting the definition of acculturation in the Discussion is to provide a more nuanced description of acculturation in the

context of our analysis. In response to the reviewer's suggestions, we shortened this description of acculturation but decided to not to remove it.

16. Page 14. The end of the last sentence should be deleted. "despite long residence in the US" This is one of the authors' measures of acculturation. (re: length of time in the US). The results therefore cannot be "despite long residence in the US."

Response: This has been corrected.

17. Pages 14-15. Some of the content in paragraphs 2 and 3 are redundant. Consider consolidating the content.

18. Page 15. The authors use language regarding the "magnitude of associations" when most analyses conducted do not permit evaluation of the magnitude of the association, with exception of odds ratio results. No other measures of association were presented.

Response: Our regression analyses does provide regression coefficients (β) as measures of association presented in the tables and in the text. We respectfully disagree with the reviewer and decided to leave this sentence largely intact.

19. Page 16. The last part of the final paragraph that explains acculturative stress appears is unnecessary and does not add to the discussion. Consider removing or greatly reducing this content.

Response: We have shortened this paragraph according to the reviewer suggestions. This paragraph serves to further familiarize the reader with the acculturative stress concept since in the subsequent paragraph we specifically connect our results regarding acculturation and SES to acculturative stress.

20. Page 17. The first sentence of the second paragraph could be clearer. For example, "The statistically significant interaction between acculturation and SES may shed light…"

Response: This has been corrected.

21. Page 17. The authors should confirm whether reference to less acculturation meaning more retention of "host" culture is correct. This may be an error and should read "original" culture.

Response: This has been corrected.