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Diabetes mellitus, hypertension and frailty: A population-based, cross-sectional study of Mexican older adults

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Aim: Chronic diseases are frequent in older adults, particularly hypertension and diabetes. The relationship between frailty and these two conditions is still unclear. The aim of the present analyses was to explore the association between frailty with diabetes and hypertension in Mexican older adults.

Methods: Analyses of the Mexican Health and Nutrition Survey, a cross-sectional survey, are presented. Data on diabetes and hypertension were acquired along with associated conditions (time since diagnosis, pharmacological treatment, among others). A 36-item frailty index was constructed and rescaled to z-values (individual scores minus population mean divided by one standard deviation). Multiple linear regression models were carried out, adjusted for age and sex.

Results: From 7164 older adults, 54.8% were women, and their mean age was 70.6 years with a mean frailty index score of 0.175. The prevalence of diabetes was of 22.2%, and 37.3% for hypertension. An independent association between diabetes, hypertension or both conditions (coefficients 0.28, 0.4 and 0.63, respectively, $P < 0.001$) with frailty was found. Having any diabetic complication was significantly associated with frailty with a coefficient of 0.55 (95% CI 0.45–0.65, $P < 0.001$) in the adjusted model. The number of years since diagnosis was also associated with frailty for both conditions.

Conclusions: Diabetes and hypertension are associated with frailty. In addition, an incremental association was found when both conditions were present or with worse associated features (any complication, more time since diagnosis). Frailty should be of particular concern in populations with a high prevalence of these conditions. **Geriatr Gerontol Int 2016; ••: ••–••.**

Keywords: diabetes, frailty, geriatric medicine, hypertension.

Introduction

The aging of the population is a global phenomenon that represents a challenge for societies, governments and health systems of countries worldwide.[1] One of the main challenges of older adult health is the so-called frailty syndrome, which is referred as a physiological state of increased vulnerability to inner and external stressors,[2–4] which predicts disability, dependence, long-term care use and mortality.[2,5–9] Early stages of this condition might not be evident; however, when it reaches a certain level, vulnerability appears from biological, clinical, functional and behavioral viewpoints.[2,8] The lack of a clear etiology along with the absence of early markers of frailty makes it difficult to be characterized in the clinical context. [7]

Diabetes and hypertension are two of the most frequent chronic diseases in older adults,[10–12] and also are the most common causes for hospitalization and mortality;[13–19] this is more evident in populations where high rates of obesity are found, such as the Mexican population. In addition, diabetes is associated with a higher risk of multiple coexisting medical conditions and geriatric syndromes in older persons.[20] In contrast, hypertension is a chronic disease with a slow and silent evolution; persons might not be aware of their condition before a related major event occurs.[21] Both conditions are associated with micro- and macrovascular complications,[18–20] which eventually could lead to dependency, increased need for long-term care use and death,[21] a similar path to that of frailty.

Diabetes and hypertension share common risk factors, and are frequently diagnosed earlier in life.[10,11,22] Along with other conditions (hypercholesterolemia,

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hypertriglyceridemia and obesity), diabetes and hypertension give rise to the so-called "metabolic syndrome," which represents a deterioration of a number of systems (endocrine, cardiovascular, gastrointestinal etc.), in which insulin resistance represents one of the main pathological features.[12,22] Furthermore, there is evidence that an altered glucose metabolism could lead to a frailty status, as shown by Kalyani *et al.*, where frail women had impaired glucose/insulin dynamics.[22] It is also noteworthy how inflammation is common to frailty, diabetes and hypertension, representing another possible link among these conditions.[22]

The aim of the present analyses was to explore the association between frailty with diabetes and hypertension (alone or in combination) in a representative sample of Mexican older adults participating in the last Mexican Health and Nutrition Survey 2012 (also known as ENSANUT). We here hypothesize that persons with diabetes and/or hypertension may have a higher probability of being frail than those who are not affected by them.

Methods

Sample and settings

This was a cross-sectional analysis of the last version of the Mexican Health and Nutrition Survey 2012, a nationwide survey of a probabilistic sample of Mexican population, the detailed description is available elsewhere.[23] From a total of 96 031 individuals of all ages, a representative subsample of older adults was included, gathering data of particular interest in older adult health, such as depressive symptoms, activities of daily living, cognitive assessment, falls and physical performance (gait speed and handgrip strength). This new set of information, along with the general questionnaire (including sociodemographic characteristics, comorbidity, healthcare use, psychosocial variables) was used for the present study.

Regarding the sample of older adults, after probabilistic sampling by country regions, from a total of 8874 eligible participants, 80% od respondents actually participated in the study, giving a final sample of 7164 older adults included in this report.

Measurements

A frailty index (FI) was generated following the indications provided by Searle *et al.*; that is, at least 30 deficits from different domains excluding those that could saturate early in life.[24] A total of 36 deficits were included from nine different domains (Table S1). The groups of items were: cognition (single question of memory problems), dependence on activities of daily living (including eight dichotomous questions), depressive symptoms (seven questions with a Likert scale for answer), comorbidities (including five self-reported and one measured [anemia] conditions), violence and accidents (falls, health-related problems because of violence and having suffered from aggression), senses (hearing and vision impairment), nutrition and anthropometry (eating less, weight loss, calf circumference, body mass index), physical performance tests (gait speed and handgrip strength), and satisfaction with life. This index did not include diabetes or hypertension, in order to avoid collinearity when comparing it with these two conditions and their related characteristics. In addition, a 30-item FI was also fitted to all the independent variables, adjusted and unadjusted to describe changes in estimates (Table S2).

In order to analyze the index as a continuous variable, but at the same time have an easier interpretation of the effects of diabetes and hypertension, it was further rescaled to z-values, subtracting from each individual value the sample mean and then dividing it by the standard deviation (SD); with this approach, beta coefficients are equivalent to one SD from the mean.[25]

To closely examine the components of both pathologies, some other features of each disease were also analyzed: the time since diagnosis and the use of pharmacological treatment. In addition, diabetic participants were further classified in the function of their diabetes-related complications (skin lesions, amputation, vision problems, heart attack, diabetic coma and neuropathy), and the number of times they visited a physician in the past year as a result of diabetic problems.

Statistical analysis

Descriptive statistics were carried out stratified by sex, with means and SD for continuous variables if normally distributed, and median with interquartile range (IQR) for not normally distributed variables; absolute and relative frequencies for categorical variables. Rescaled FI distribution was assessed for normality with the France test, in order to see if it was appropriate to use parametric statistics. Regarding multivariate analysis, multiple linear regression models unadjusted and adjusted (for age and sex) were carried out, with the rescaled FI as the dependent variable first for the disease groups (no diabetes or hypertension, diabetes only, hypertension only and both diseases), followed by the disease-related conditions (receiving pharmacological treatment, years since diagnosis, diabetic complications and number of physician visits related to diabetes). In addition, when the use of pharmacological treatment was analyzed, further adjustment was made for the time since the beginning of the disease. Complications were joined in a composite dichotomous variable, having or not having a diabetes-related complication; this variable was also further adjusted for time since the beginning of diabetes.

To test if the FI would behave the same with and without diabetes and hypertension, two procedures were carried out, the first one a simple correlation between the

36-item and the 30-item indexes. In addition, regressions were also carried out with both indexes in order to assess changes in the regression estimates. All analyses were run with the statistical software STATA version 13.1 (StataCorp, College Station, TX, USA).

Ethical issues

The research and ethics committee of the National Institute of Public Health (Mexico) approved this study, and it is registered by the committees of the National Institute of Geriatrics. All participants signed informed consent.

Results

From a total sample of 7164 older adults 54.8% ($n = 3923$) were women, with an overall mean age of 70.6 ± 8.1 years). The FI had a mean of 0.175 ± 0.093), significantly higher for women (mean 0.182 ± 0.097, $P < .001$). The highest mean for the components of FI was for vision impairment (0.496), followed by hearing impairment (0.473) and falls (0.356). Whereas deficits with the lowest means were having suffered aggression in the last year (0.014) and having heart failure (0.029; Table 1). The correlation between the 36-item and the 30-item FI was 0.929, $P < 0.001$, and rescaling of the FI resulted in a normal distribution.

Approximately half of the sample ($n = 3574$, 52.2%) did not present any of the diseases of interest. The prevalence of diabetes and hypertension were 22.2% ($n = 1596$) and 37.7% ($n = 2703$), respectively; in both cases, women showed a significantly higher proportion than men ($P < 0.001$). When categorizing participants by the presence of both conditions alone or simultaneously (mutually exclusive categories), the frequencies were: 52.3% ($n = 3745$) had neither diabetes nor hypertension, 9.9% ($n = 716$) had just diabetes, 25.4% ($n = 1823$) had just hypertension and 12.3% ($n = 880$) had both conditions. Among those with diabetes, 46.9% reported to have one or more complications (in decreasing order of prevalence): neuropathy (41%), vision problems (8.5%) and skin lesions (7%).

The median number of years since diabetes diagnosis was 10 (IQR 4–16), and the median for the number of visits in the past year due to diabetes care was 12 (IQR 4–12). Up to 91.6% of diabetic older adults received pharmacological treatment. Regarding hypertension, the median number of years since diagnosis was of 6 (IQR 2–15), and 89.6% of the older adults with hypertension received treatment (Table 1).

Estimates from the multiple regression models of the categories of diseases were significant in the majority of cases, and did not change from unadjusted to adjusted models (Table 2). A growing trend of the coefficient

Table 1 General characteristics of the population

Variable	Men, $n = 3241$ (45.2%)	Women, $n = 3923$ (54.8%)	Total ($n = 7164$)
Mean age, years (SD)	70.8 (8)	70.5 (8.1)	70.6 (8.1)
Mean frailty index (SD)†	0.159 (0.086)	0.188 (0.096)	0.175 (0.093)
No DM nor hypertension, *n* (%) †	1998 (61.6)	1747 (44.5)	3745 (52.2)
DM only, *n* (%)†	317 (9.8)	399 (10.1)	716 (9.9)
Hypertension only, *n* (%)†	624 (19.2)	1199 (30.5)	1823 (25.4)
DM and hypertension, *n* (%)†	302 (9.3)	578 (14.7)	880 (12.2)
Conditions associated with DM ($n = 1596$)			
Any complication from DM, *n* (%)†	268 (43.3)	481 (49.2)	749 (46.9)
No. years since DM diagnosis, median (IQR)	9 (4–15)	10 (4–17)	10 (4–16)
No. times visiting a physician last year due to DM, median (IQR)†	11 (3–12)	12 (4–12)	12 (4–12)
Receives pharmacological treatment for DM, *n* (%)	558 (90.1)	905 (92.6)	1463 (91.6)
Conditions associated with hypertension ($n = 2703$)			
No. years since hypertension diagnosis, median (IQR)†	5 (1–12)	7 (2–15)	6 (2–15)
Receives treatment for hypertension, *n* (%)†	810 (87.5)	1586 (90.7)	2396 (89.6)

†$P < 0.05$. CI, confidence interval; DM, diabetes mellitus; IQR, interquartile range.

Table 2 Multiple linear regression for scaled Frailty Index adjusted and unadjusted regression models predicting according to diabetes and hypertension status

Variables	Unadjusted		Adjusted*	
	Beta coefficient (95% CI)	*P*-value	Beta coefficient (95% CI)	*P*-value
None *vs* DM only	0.28 (0.2–0.35)	<0.001	0.3 (0.23–0.38)	<0.001
None *vs* hypertension only	0.4 (0.34–0.45)	<0.001	0.31 (0.26–0.36)	<0.001
None *vs* both DM and hypertension	0.63 (0.56–0.7)	<0.001	0.62 (0.55–0.69)	<0.001
DM only *vs* hypertension only	0.122 (0.03–0.2)	0.004	0.01(–0.07–0.08)	0.841
DM only *vs* both DM and hypertension	0.35 (0.26, 0.45)	<0.001	0.31 (0.22, 0.4)	<0.001
Hypertension only *vs* both DM and hypertension	0.23 (0.15–0.31)	<0.001	0.3 (0.23–0.38)	<0.001
Any complication of DM	0.59 (0.49–0.7)	<0.001	0.55 (0.45–0.65)	<0.001
No. years since DM diagnosis	0.012 (0.01–0.02)	<0.001	0.01 (0.003–0.01)	0.001
No. times visiting a physician last year due to DM	0.012 (0.002–0.022)	0.012	0.013 (0.003–0.022)	0.008
Receives treatment for DM	–0.003 (–0.08–0.08)	0.993	0.016 (–0.064–0.096)	0.694
No. years since hypertension diagnosis	0.006 (0.003–0.008)	<0.001	0.003 (0.001–0.006)	0.001
Receives treatment for hypertension	0.089 (–0.041–0.22)	0.179	0.03 (–0.094–0.155)	0.637

*Adjusted for age and sex. CI, confidence interval; DM, diabetes mellitus

estimates in the unadjusted model was observed when comparing the group without disease with any of the other categories: for the diabetes only group, the coefficient was of 0.28 (95% CI 0.2–0.35, $P < 0.001$), those with hypertension only 0.4 (95% CI 0.34–0.45, $P < 0.001$) and for older adults with both conditions 0.63 (95% CI 0.56–0.7, $P < 0.001$). Similar results were observed for the adjusted model. When contrasting the diabetes only group with the group of hypertension only, the coefficients were 0.122 (95% CI 0.03–0.2, $P = 0.004$) in the unadjusted model and 0.01 (95% CI –0.07–0.08, $P = 0.841$) after adjustment. The combination of the two conditions was again associated with higher FI, even after adjustment for potential confounders. Regarding the comparison of having hypertension only with having both conditions, the coefficient for the unadjusted model was of 0.23 (95% CI 0.15–0.31, $P < 0.001$), with similar results in the adjusted model.

The adjusted models of diabetes-related conditions were consistent with unadjusted models. Having any complication from diabetes had a coefficient of 0.55 (95% CI 0.45–0.65, $P < 0.001$), the coefficient for the number of years since diagnosis was 0.01 (95% CI 0.003–0.01, $P = .001$) and the coefficient for the number of times visiting a physician in the past year due to diabetic problems was 0.013 (95% CI 0.003–0.022, $P = 0.008$). Receiving treatment for diabetes or hypertension was not significant in any model. Finally, the number of years since hypertension diagnosis had a coefficient of 0.003 (95% CI 0.001–0.006, $P = .001$) in the adjusted model. Estimations of the models when using the 30-item FI had similar coefficients to those shown with the 36-item FI (Table S2); in this new FI, heart attack, heart failure, stroke hypercholesterolemia, hypertriglyceridemia and vision problems were excluded.

Discussion

The aim of the present analysis was to explore the association between frailty with diabetes and hypertension, both individually and combined, in a representative sample of Mexican older adults participating in the Mexican Health and Nutrition Survey 2012. Our data showed that there is an incremental trend of coefficients between groups, meaning that each of the diseases has its own specific impact on frailty. The meaning of the increasing coefficient values is that if the coefficient is close to 0.1, that means that having that condition would sum a standard deviation to the population mean of the FI (that is 0.175 [SD] + 0.093[mean]). This observation supports that previously proposed by Bales, who stated that "frailty is usually the result of a combination of problems rather than having a specific cause, and this combination expresses as a general functional decline".[26] In addition, using the FI allowed us to estimate not only the increase in vulnerability of the older adult, but also the burden of decline in the ability to carry out activities of daily living.[27] As stated by other authors, the FI captures a wider range of deficits including disability; therefore, when a disease,

such as hypertension or diabetes, has an independent association with the index, the burden on function could certainly be reflected.[28,29] This was shown in the present study, as there was a modest change in estimates when not including comorbidities related to both diabetes and hypertension, and excluding from the index, but keeping at least 30 deficits.

To our knowledge, this is the first work to emphasize features of particular diseases, and their impact on frailty. This approach might suggest the importance of carefully examining the results included as part of broader assessments, with the possible advantage of facilitating subsequent design and implementation of interventions. However, these diseases could simply resemble the impact of any other so-called deficit; these two chronic diseases are highly prevalent in our population, pointing to the fact that the prevention of highly prevalent conditions, such as hypertension and diabetes, might indirectly benefit the frailty status of older persons. Furthermore, the highly significant correlation between the two indexes (with and without diabetes and hypertension) and the unchanged estimations when using the 30-item FI are somehow a proof of concept of the FI; when the diseases are integrated into the sum of the other deficits, it interacts in a synergic way and no more as a unique disease impact; however, when the diseases are proved against the index, they act as a sole disease. Further research should aim to untangle the interactions and differential behavior of diseases when treated only as a deficit or vice versa.

In contrast, the present results should alert us to the fact that already presenting a single condition (such as diabetes or hypertension) is enough to increase the risk of frailty, and that worse manifestations of the diseases (complications, longer duration of the disease) can lead to even more detrimental conditions. From which we can reinforce the idea of individualizing treatments and not generalizing them when it comes to older adults' healthcare.

According to that, we can say that the accumulation of deficits occurs during the entire life, and these are not reversible. Then the prevention of frailty as a syndrome, as well as the development of disability and long-term care need, must be approached earlier in life, and have to be multidomain as well as multidisciplinary; having in mind not only mortality as the main adverse outcome, but a broader vision of how humans age, and which are the adverse outcomes in advanced age. This in turn could improve the care of older adults and not limit it to prevention of mortality, which becomes useless for subjects who already have a limited life expectancy. A surprising finding was the lack of association between pharmacological treatment and frailty, it would have been expected to have an inverse association with frailty. However, this could be the result of a highly variable pharmacological treatment, different adherence to treatment and use of other alternative treatments, among others. However, treatments for specific conditions, such as diabetes and hypertension, that are targeted to diminish mortality and somehow complications in a linear fashion, might not improve frailty, which has non-linear dynamics.[30] Further research including more information about treatment-specific chronic diseases could better clarify this association.

We must highlight that this was a cross-sectional analysis, with limitations for the interpretation of the results; however, there are no previous publications analyzing these two conditions in a representative sample of Mexican older adults (which in turn is a model of a population with a high prevalence of diabetes and hypertension). We are aware of the need for longitudinal approaches for causal relationship between these variables; however, there is a clear temporal relationship between the diagnosis for diabetes or hypertension and frailty, which allow us to derive certain conclusions about it, always respecting the limitations of the design.

Finally, it could be said that just as hypertension and diabetes are a matter of public health in younger adults, in highly prevalent populations it would be expected that frailty would appear in an accelerated manner.

Disclosure statement

The authors declare no conflict of interest.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site.

Table S1. Variables in the 38-item Frailty Index and their respective scores and mean values.
Table S2. Multiple linear regression for the 30-item Frailty Index adjusted and unadjusted regression models predicted according to diabetes and hypertension status (excluding heart attack, heart failure, stroke hypercholesterolemia, hypertriglyceridemia and vision problems).