



# The Journal of Latin American Geriatric Medicine

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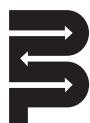
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## Correlation of the SARC-F questionnaire with muscle mass in Colombian elderly with osteosarcopenia

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### Abstract

**Aim:** The aim of the study was to determine the association between low muscle mass evaluated by Dual-energy X-ray absorptiometry (DXA) and the SARC-F questionnaire. **Methods:** This was a cross-sectional study of patients over 60 years sent to bone densitometry between April and November 2018. The SARC-F questionnaire and body assessment measures were applied using DXA. The presence of low muscle mass was determined using the European criteria EWGSOP2 and osteoporosis according to the WHO. **Results:** Fifty-two patients were included, with a mean age of 74.27 years ( $SD \pm 7.04$ ), 88.4% were women, and mean body mass index 21.89 ( $SD \pm 3.36$ ). About 28.85% had a SARC-F > 4. The mean skeletal muscle mass index was 6.54 kg/m<sup>2</sup> ( $SD \pm 0.92$ ). About 32.69% of the patients had low muscle mass according to the EWGSOP2 criteria. The prevalence of osteosarcopenia was 7.69% (Osteopenia/osteoporosis plus sarcopenia with SARC-F > 4 and low muscle mass). **Conclusions:** The ability of the SARC-F instrument to discriminate low muscle mass was not found in this cohort of Colombian older adults. The prevalence of osteoporosis and sarcopenia presented a distribution similar to that described in the literature. It is necessary to carry out research in Colombia aimed at defining the muscle mass reference values.

**Key words:** Aged. Dual-energy X-ray absorptiometry. Geriatric medicine. Osteoporosis. SARC-F. Sarcopenia.

### Correlación del cuestionario SARC-F con la masa muscular en adultos mayores colombianos con osteosarcopenia

### Resumen

**Objetivo:** Determinar la relación entre una masa muscular baja evaluada por DXA en una población cribada para osteoporosis y el cuestionario SARC-F. **Métodos:** Estudio de corte transversal en individuos mayores de 60 años enviados a densitometría ósea entre abril y noviembre de 2018. Se aplicó el cuestionario SARC-F y medidas de evaluación corporal con DXA. La masa muscular baja se determinó a través de los criterios europeos EWGSOP2 y la osteoporosis según los parámetros de la OMS. **Resultados:** Se incluyó a 52 pacientes, con edad promedio de 74.27 años ( $DE \pm 7.04$ ) y 88.4% correspondió a mujeres, con IMC promedio de 21.89 ( $DE \pm 3.36$ ). El 28.85% presentó un SARC-F ≥ 4. El promedio del índice de masa muscular esquelética (IMME) fue de 6.54 kg/m<sup>2</sup> ( $DE \geq 0.92$ ). El 32.69% del total de la muestra tenía una masa muscular baja según los criterios EWGSOP2. La prevalencia de osteosarcopenia fue del 7.69% (osteopenia/osteoporosis más sarcopenia [SARC-F > 4] y masa muscular baja). **Conclusión:** No se encontró capacidad del instrumento SARC-F para diferenciar la masa muscular baja en esta cohorte de adultos mayores colombianos. La prevalencia de osteoporosis y sarcopenia mostró una distribución similar a la descrita en las publicaciones médicas. Son necesarias más investigaciones en Colombia para definir los valores de referencia de la masa muscular.

**Palabras clave:** Anciano. DXA. Geriatría. Osteoporosis. SARC-F. Sarcopenia.

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## INTRODUCTION

Osteosarcopenia (OS) is a geriatric syndrome characterized by the coexistence of bone mineral loss (defined as T Score < -1 according to WHO criteria) and sarcopenia<sup>1</sup>. The sum of these conditions increases the probability of adverse outcomes in elderly patients in terms of functional performance and vital prognosis. Patients with hip fractures with OS have been found to have 1.8 times more risk of mortality in the 1<sup>st</sup> year<sup>2</sup>. The prevalence of OS reported in different studies is between 5 and 37%, being more common in women and patients over 65 years old<sup>3</sup>. Huo et al.<sup>4</sup> described a higher prevalence of sarcopenia in people with osteoporosis, compared with those with osteopenia (62.7% vs. 47.4%) in Penrith, Australia. To date, there are no data on the incidence or prevalence of OS in Colombia.

Much of the studies published so far in international literature, define sarcopenia considering the low muscle mass as the main diagnostic criteria, also, they base the cutoff points on those established by the 2010 European consensus<sup>5</sup>: a appendicular muscle mass index < 5.5 kg/m<sup>2</sup> in women and 7.26 kg/m<sup>2</sup> in men, by Dual Advanced X-ray Energy (DXA). The cutoff point is based in Baumgartner's study<sup>6</sup>, where low muscle mass was established as a value of 2 standard deviations (SD) below the mean of a young reference group. On the other side, reference values proposed by the 2018 European consensus<sup>7</sup> for the appendicular muscle mass index are based on an Australian population<sup>8</sup>. In Colombia, DXA appendicular mass measurement is not widely available, and for this reason, finding a screening tool that allows the clinician better decision-making at the patient's bedside can improve both diagnostic suspicion and use of the health resource. Comparatively, in the Latin American context, there is available data in Chile and Mexico. The data found in the southern country for the cutoff points of the skeletal muscle mass index obtained by DXA were 5.77 kg/m<sup>2</sup> in women and 7.19 kg/m<sup>2</sup> in men. This data were retrieved from a geriatric population (over 60 years old) without values estimated from a group of younger people<sup>9</sup>. The values obtained in Mexico reported cutoff points of the DXA appendicular skeletal muscle mass index in a population of young patients, by locating two SD below average<sup>10</sup>. Globally, the most used cutoff points for OS are 6 kg/m<sup>2</sup> in women and 7 kg/m<sup>2</sup> in men, proposed by the European consensus in 2018.

On the other hand, SARC-F is a questionnaire developed to identify people at risk of sarcopenia. It consists

of five items considering cardinal findings or consequences of sarcopenia. It has been validated through different cohorts, demonstrating internal consistency, and adequate reproducibility. People with scores of 4 or higher are more likely to have a deficit in daily life activities, lower performance in execution-based measures, lower scores in short performance physical battery (SPPB), and an increased risk of hospitalization and mortality according to Baltimore's longitudinal study (odds ratio 3.0 Confidence interval 95% 1.57-5.73)<sup>11</sup>. Regarding the correlation of SARC-F specifically with muscle mass, it has been proven poor association with appendicular mass evaluated by Bioimpedanciometry ( $r = 0.34$ )<sup>12</sup>. The sensitivity of SARC F has been reported between 14 and 21% with high specificity, above 90%, which makes it an important questionnaire to discriminate probable cases of Sarcopenia that would require a full assessment<sup>13</sup>.

Due to the great variability of cutoff points and the absence of studies that estimate the applicability of the SARC-F questionnaire and its correlation with the objective muscle mass assessment estimated by DXA, this study was conducted. The main objective is to determine the association between low muscle mass determined by DXA and the score obtained in the SARC-F questionnaire in a population of Colombian older adults with suspected osteoporosis. The secondary objective is to know the prevalence of OS in this population.

## METHODS

A cross-sectional observational study was designed, with a sample of patients attending bone densitometry for osteoporosis screening or monitoring during 2018, at International FOSCAL Clinic Escanografía S.A. Center (Scanography Public Limited Company). A non-probabilistic sampling of consecutive cases of all subjects who met the inclusion criteria was performed.

The inclusion criteria were having 60 years or more and signing informed consent. Patients with severe dementia, Barthel Index < 60 points, active cancer except for skin, recent use in the past 3 months of steroids (equivalent to 10 mg daily of prednisolone), and amputation of some limbs were excluded from the study. Body composition determination was made using GE Healthcare's Lunar Prodigy Advance dual-energy absorption (DXA) equipment using enCORE 13.2 software. Osteoporosis was defined according to the WHO criteria through the T score value. A t value

$\leq -2.5$  was classified as osteoporosis and a T value between  $-1$  and  $-2.4$  as osteopenia.

The day of the test validated to the Mexican Spanish SARC F questionnaire<sup>13</sup> was applied by a team of doctors previously trained by a specialist in Geriatrics. Appendicular muscle mass was determined with the Relative Musculoskeletal Index (weight in Kg/size in m<sup>2</sup>) based on the Baumgartner equation, which was automatically calculated by the equipment. To determinate the presence of low muscle mass, the reference values of the second European consensus (values  $<7$  kg/m<sup>2</sup> in men,  $<6$  kg/m<sup>2</sup> in women)<sup>7</sup> were considered. The presence of Sarcopenia was defined by the summation of a score in SARC F of 4 or more associated with low muscle mass. Variables of physical performance from the EWGSOP2 Sarcopenia Criteria such as gait speed, short physical performance battery, and timed-up-and-go test were not measured. On the other hand, patients who had a bone mineral density with a T score value of  $< -1$  and sarcopenia were classified as OS. All participants signed written informed consent. The study received the endorsement from the ETHICS Committee CEI FOSCAL according to Act No. 30 of 2017.

### Statistical analysis

Descriptive analysis was performed with the central trend and dispersion measurements (mean and SD or median and interquartile ranges), depending on the normality distribution of quantitative variables. Qualitative variables were expressed with absolute and relative frequencies. Subsequently, group comparison analysis was performed using t-test or Wilcoxon statistical tests for quantitative variables based on the distribution of the variables; Chi-square statistical tests or Fisher's exact test was used for qualitative variables, depending on the amount of data for each category.

## RESULTS

The study included 52 patients. The general characteristics are summarized in table 1. About 88.46% of the participants were women. The most common indication of DMO was osteoporosis screening. About 25.49% of participants had a previous fracture; however, only 17.3% of them knew they had osteoporosis and were under treatment. It should be noted that  $< 2\%$  of people knew the term Sarcopenia. On the other hand, only 21.15% of subjects performed

physical activity at least 3 times/week. The most common comorbidity was osteoarthritis, followed by Diabetes mellitus and chronic obstructive pulmonary disease. The mean body mass index (BMI) was 21.89. All participants had a sufficient functional capacity in Activities of Daily Living. Concerning bone mineral density, 53.85% had density in osteoporosis range according to the WHO criteria. About 16.67% of the population had evidence of morphometric vertebral fracture.

### SARC-F and muscle mass

Applying the SARC-F questionnaire, 28.8% of people had 4 or more points. Body composition assessment through the relative Appendicular Muscle Mass Index had a mean of 6.53 kg/m<sup>2</sup>. According to EWGSOP2 criteria, 32.69% of participants had low muscle mass, and the prevalence of Sarcopenia and OS was 9.62% and 7.69%, respectively. However, this prevalence varies in the scenario of different cutoff points published in Latin America (Table 2). In subjects listed as osteosarcopenic, the mean Appendicular Muscle Mass was 5.23 kg/m<sup>2</sup> ( $SD \pm 0.97$ ) versus 6.65 kg/m<sup>2</sup> ( $SD \pm 0.83$ ) in patients without OS ( $p = 0.0024$ ). Concerning the correlation between the SARC-F questionnaire with muscle mass, there are no statistically significant differences between the SARC F Value and the prevalence of low muscle mass (Table 3), or between the SARC F Value and mean Appendicular Muscle Mass Index (Table 4). Therefore, in our region, we found inappropriate discrimination of the SARC-F questionnaire for DXA Estimated Muscle mass.

## DISCUSSION

Our findings demonstrate there is no association between the SARC F questionnaire and values of appendicular muscle mass index, lacking in the proper discrimination of patients that, with positive screening, does not have OS.

Bahat et al., on a Turkish validation study of SARC-F, described the poor capacity of discrimination of the questionnaire for the detection of low muscle mass, according to EWGSOP2 Criteria, with a sensitivity of 20% and a specificity of 81%. This sensitivity was lower compared with the one for grip strength, reported in 33.7% by the National Institutes of Health, the Up and Go Test, reported in 58.3%, and the SPPB reported in 55.2%<sup>14</sup>. However, SARC-F was an excellent tool for excluding the altered muscle

**Table 1.** Patient characteristics  
VSARC F > 4, n (%)

Characteristic	Total (n = 52)
Age, mean (SD), y	74.27 ( $\pm$ 7.04)
Women, n (%)	46 (88.46)
Urban, n (%)	47 (90.38)
Weight mean (SD), kg	68.29 (10.21)
Height mean (SD), m	1.56 (0.06)
BMI mean (SD)	21.89 (3.36)
Previous fracture, n (%)	13 (25.49)
Forearm	4 (7.69)
Hip	3 (5.77)
Vertebral	2 (3.85)
Knee and foot	2 (3.85)
Hand	1 (1.92)
Other	1 (1.92)
Treatment for osteoporosis with previous fracture, n (%)	9 (17.3)
Densitometry's indication, n (%)	
Osteoporosis screening	39 (75)
Osteoporosis monitorization	4 (7.69)
Previous fracture	3 (5.77)
Unknown	5 (9.62)
Physical activity 3 or more times per week, n (%)	11 (21.15)
Comorbidities, n (%)	
Osteoarthritis	16 (30.77)
Diabetes mellitus	11 (21.57)
Chronic obstructive pulmonary disease	7 (13.46)
Chronic use of steroids	7 (13.46)
Heart failure	6 (11.76)
Chronic kidney disease	5 (9.62)
Cancer	4 (7.69)
Rheumatoid arthritis	3 (5.77)
Stroke	1 (1.92)
Charlson Comorbidity index $\geq$ 3, n (%)	5 (10.2)
Comprehensive geriatric assessment, median (IQR)	
Barthel Index	100 (95-100)
Lawton's Instrumental Activities of Daily Living Scale	7 (6-8)
Mini Mental State Examination (MMSE)	25 (24-27)
Mini Nutritional Assessment Short Form (MNA-SF)	8 (7-10)
VSARC F > 4, n (%)	15 (28.85)

**Table 1.** Patient characteristics (continued)

Characteristic	Total (n = 52)
Low muscle mass EWGSOP2, n (%)	17 (32.69)
Men	13 (28.26)
Women	4 (66.67)
Bone Mineral Density, g/cm <sup>2</sup>	
Hip, median (IQR)	0.74
Lumbar spine, mean (SD)	(0.69-0.88)
Radius 33%, mean (SD)	0.95 (0.17)
Osteopenia (T score < -1.0--2.4), n (%)	0.68 (0.127)
Osteoporosis (T score < -2.5), n (%)	22 (42.31)
Morphometric vertebral fracture, n (%)	28 (53.85)
No	40 (83.33)
1 vertebra	6 (12.5)
2 or more vertebrae	2 (4.17)

**Table 2.** Prevalence of Sarcopenia and Osteosarcopenia in the cohort, according to different criteria of low muscle mass

Criteria of low muscle mass	Sarcopenia <sup>a</sup>	Osteosarcopenia <sup>b</sup>
EWGSOP2	9.62%	7.69%
Mexico <sup>10</sup>	1.92%	1.92%
Colombia (BIA) <sup>11</sup>	17.31%	15.38%

<sup>a</sup>Sarcopenia: SARC F > 4 AND low muscle mass.<sup>b</sup>Osteosarcopenia: Sarcopenia AND BMD < -1.0 in T score.

function in Sarcopenia. In this study, the assessment of the muscle mass was made with bioimpedanceometry and not with DXA<sup>15</sup>. Besides, Nguyen et al. documented in the SARC-F Vietnam Validation Study, with 764 participants from a geriatric hospital (mean age of  $71.5 \pm 8.9$  years), a discriminatory capacity of 0.72 for Sarcopenia criteria (EWGSOP2). They evaluated appendicular muscle mass with DXA. The mean appendicular muscle mass index was  $4.7 \text{ kg/m}^2$ , and the BMI was  $21.7 \text{ kg/m}^2$ . 64.9% of patients with sarcopenia had SARC-F of 4 or more, while 31.8% of

(Continues)

**Table 3.** Correlation of SARC F questionnaire with muscle mass according to different criteria of low muscle mass

Criteria of Low Muscle Mass	All patients (n = 52)	SARC F Questionnaire		p value
		< 4 (n = 37)	≥ 4 (n = 15)	
EWGSOP2 <sup>a</sup> , n (%)	17 (32.69)	12 (32.4)	5 (33.3)	0.95
Mexico <sup>b</sup> , n (%)	2 (3.85)	1 (2.7)	1 (6.6)	0.501
Colombia (BIA) <sup>c</sup> , n (%)	31 (59.62)	22 (59.4)	9 (60)	0.97

<sup>a</sup>EWGSOP2 (European Working Group on Sarcopenia in Older People 2 Consensus): Women < 6 kg/m<sup>2</sup>, Men < 7 kg/m<sup>2</sup>.

<sup>b</sup>Mexico: Women < 4.72 kg/m<sup>2</sup>, Men < 5.86 kg/m<sup>2</sup>.

<sup>c</sup>Manizales, Colombia (Bioimpedanciometry): Women < 6.42 kg/m<sup>2</sup>, Men < 8.39 kg/m<sup>2</sup>.

**Table 4.** Mean muscle mass, according to SARC F Questionnaire

Muscle mass	All patients (n = 52)	SARC F Questionnaire		p value
		< 4 (n = 37)	≥ 4 (n = 15)	
All patients, mean (SD)	6.54 (0.92)	6.606 (0.85)	6.38 (1.09)	0.4301
Women, mean (SD)	6.47 (0.93)	6.51 (0.85)	6.4 (1.12)	0.7102

patients without sarcopenia had these values on the questionnaire<sup>16</sup>.

Because of this, SARC F is a tool easily used by the clinician for the screening of patients with suspected sarcopenia, given its high specificity for the detection of the compromised muscle function. However, this measure cannot be fully assumed as a specific surrogate of the composition of the muscle fiber, considering the multiple factors that influence its generation, development, maintenance, and function.

Studies conducted in Brazil and China with older adults demonstrate better sensitivity of SARC-F combined with an indirect measure of muscle mass such as calf circumference, increasing sensitivity to 60.7%,

and discriminatory capacity (AUC) to 0.92. However, in this publication, the calf perimeter cutoff was 33 cm for women and 34 cm for men<sup>17</sup>. Our study did not check whether the calf perimeter association improved SARC-F sarcopenia discrimination capacity, although it may be useful to improve the tool performance.

The prevalence of OS in our study (7.69%) is similar to the one published by Rubek – Nielsen et al.<sup>3</sup>, reflecting the need for optimizing diagnostic criteria in each region of the world. Furthermore, the frequency of osteopenia and osteoporosis in this study is like that described by Szlejf et al. in Mexico City<sup>18</sup>, where they reported a prevalence of 77.8% of these conditions, and a 33.7% of sarcopenia.<sup>14</sup> While Hologic equipment was used for DXA, it does not present much variability with the methods used in our research for DMO evaluation. Unfortunately, the cutoff points taken for muscle mass assessment were those of the US National Institute of Health, which are not equivalent with sarcopenia data obtained in this study, a situation widely described in other papers as a relevant limitation for comparing different values of this condition<sup>19</sup>.

In Colombia, available muscle composition data were found in Manizales and Bogota, but these were not performed with DXA. The research group of the University of Caldas reported muscle body composition data by the bioimpedance method with values corresponding to 6.42 kg/m<sup>2</sup> in women and 8.39 kg/m<sup>2</sup> in men, based on the cutoff point of 2 SD below the average of young patients<sup>20</sup>. It should be noted that the calculation of body composition performed by bioimpedance requires a conversion equation that is calibrated regarding the lean mass value measured with DXA in a specific population<sup>7</sup>. Researchers of the SABE Colombia group of the Javeriana University in Bogota have defined Sarcopenia taking into account the grip strength (cutoff point of 30 kg for men and 20 kg for women), the walking speed (in the lowest quintile between the 2<sup>nd</sup> and 5<sup>th</sup> group), and the calf perimeter (< 31 cm), showing a prevalence of 11.5% in the population studied, with the first EWGSOP criteria<sup>21</sup>. This study lacks ideal body composition measurements and did not concomitantly evaluate bone mineral density and therefore does not allow the estimation of OS. The new EWGSOP2 criteria, when strictly applied, should also be considered to decrease the prevalence of sarcopenia, compared with the first ones<sup>22</sup>.

Due to the diagnostic modalities for the determination of body composition, the different cutoff points, its heterogeneity, and the interindividual variability of the population, we consider that the sum of these factors makes it hard to find a correlation between the SARC-F questionnaire and the body composition in this group of patients.

This one is the first study that evaluates both muscle and bone body composition in older adults in Colombia, from a reference center in the formation of radiologists and primary care physicians, with great experience in densitometric diagnosis. The main limitations of the study are the sample size, and the absence of longitudinal follow-up to evaluate the prediction of OS with fractures and functional impairment. Besides, our definition of OS lacks information about physical performance measures included in the European consensus. However, this way reveals low potency and muscle efficiency as self-reporting. This information, in addition to the assessment of muscle mass, gives a conceptual approximation to the identification of subjects as sarcopenic.

## CONCLUSION

No association was found between low muscle mass and the SARC-F questionnaire demonstrating a limited ability of the instrument to discriminate this muscle alteration. The prevalence of osteoporosis and sarcopenia had a distribution similar to that described in the literature. This one is the first study that explores the prevalence of OS in Colombia estimated by DXA, with limitations for the extrapolation of results given the absence of physical performance variables. Further investigations are needed to defining reference values of muscle mass for Colombia in young people using DXA.

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## CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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## ETHICAL DISCLOSURES

**Protection of people and animals.** The authors declare that no experiments were performed on humans or animals for this research.

**Confidentiality of the data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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## Relationship of functionality before hip fracture with mortality in older adults

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### Abstract

**Background:** Functionality before hip fracture (HF) is considered a predictor of mortality. At the end of the post-fracture 1<sup>st</sup> year, 60% do not regain ambulation, and immobility is a predictor of complications and mortality. **Objective:** The objective of the study was to analyze the relationship of pre-HF functionality with immediate, early, and late post-operative mortality. **Material and methods:** Retrospective cohort study in old adults in a concentration hospital. Immediate (before 1-month post-fracture), early (2-12 months post-fracture), and late (after 1 year post-fracture) mortality were defined; functionality was assessed by Barthel scale: dependent or independent. Cox regression was used to determine survival trend. **Results:** Seventy-five patients were included (66% women), 37 patients were between 80 and 89 years of age, and 12 subjects were categorized as dependent. In the immediate mortality group ( $n = 18$ ), the risk of death was similar between dependents and independents; in early mortality ( $n = 19$ ) dependents had a risk of dying (Relative Risk [RR] 0.18), and in late mortality ( $n = 39$ ) the risk persisted higher in dependent patients (RR 0.14) than in independents. **Conclusion:** Dependence is a risk factor for early and late mortality, but not relevant for immediate mortality.

**Key words:** Functionality. Pre-fracture. Mortality. Hip fracture.

### Relación de la funcionalidad anterior a la fractura de cadera con mortalidad en adultos mayores

### Resumen

**Antecedentes:** La funcionalidad anterior a la fractura de cadera (FC) se considera predictor de mortalidad. Al término del primer año posterior a la fractura, el 60% no recupera la deambulación y la inmovilidad es un factor predictor de complicaciones y mortalidad. **Objetivo:** Analizar la relación de la funcionalidad antes de la FC con mortalidad inmediata, temprana y tardía posquirúrgica. **Material y métodos:** Estudio de cohorte retrospectivo realizado en adultos mayores en un hospital de concentración. Se definieron: mortalidad inmediata (antes del primer mes posterior a la fractura), temprana (2° a 12° meses posteriores a la fractura) y tardía (>1 año después de la fractura); se valoró la funcionalidad mediante la escala de Barthel: dependiente o independiente. Se empleó regresión de Cox para determinar la tendencia de supervivencia. **Resultados:** Se incluyó a 75 pacientes (66% mujeres), 37 se encontraban entre 80 y 89 años y 12 se categorizaron como dependientes. En el grupo de mortalidad inmediata ( $n = 18$ ), el riesgo de muerte fue similar entre dependientes e independientes; en el de mortalidad temprana ( $n = 19$ ), los dependientes tenían un riesgo de morir (RR, 0.18) y en el de mortalidad tardía ( $n = 38$ ), el riesgo persistió mayor en los pacientes dependientes (RR, 0.14) que en los independientes. **Conclusión:** La dependencia es un factor de riesgo para mortalidad temprana y tardía, pero no relevante para la mortalidad inmediata.

**Palabras clave:** Funcionalidad anterior a la fractura. Mortalidad. Fractura de cadera. Adulto mayor.

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## INTRODUCTION

The increase in the older adult population has generated a higher incidence of osteoporosis<sup>1,2</sup>, an important health problem due to its social and health impact, high cost, and high disability<sup>3</sup>. Worldwide, more than 200 million people are reported to have osteoporosis, of which 8.9% will present a fracture<sup>4-6</sup>.

Hip fracture (HF) due to fragility stands out for its multifactorial origin and its bio-psycho-social affection, due to complications such as cognitive impairment, functional impairment, immobility, sarcopenia, and depression, among others; generating an impact on quality of life and increasing disability in the elderly<sup>3,7,8</sup>.

In Mexico, at the end of the 20<sup>th</sup> century, an average of 100 HF/day was reported, affecting the female gender 4 times more, with a risk of between 8.5% and 18% of HF during their lifetime<sup>9,10</sup>. In 2005, an incidence of 169 women and 98 men with HF per 100,000 population-years was reported<sup>11</sup>.

Patients with HF show an increase in mortality when compared to non-fractured patients of the same age and gender<sup>12,13</sup>. Mortality is observed between 6% and 10% in the 1<sup>st</sup> year, 30% after the 1<sup>st</sup> year post-fracture, and 40% 2 years after the event<sup>14,15</sup>. The male gender has a higher mortality risk (HR 1.64 [95% Confidence Interval, 1.3-2.06])<sup>16,17</sup>.

In the field of Geriatrics, a "functionally healthy" older adult is defined as one capable of facing a process of change, with an adequate level of functional adaptation and personal satisfaction<sup>1,2</sup>. Therefore, a dependent elderly person will have a lower capacity to adapt to HF and with this, a higher risk of complications and death.

It is reported that 40% of patients with HF will recover their ambulation 1-year post-fracture, 60% will use a walking aid, and 33% will not recover their independence<sup>18-20</sup>. However, no mention is made of the degree of functionality of these patients before their injury.

It is assumed that independent patients with preserved ambulation will have a greater chance of recovering gait and avoiding the complications associated with immobility.

In a study carried out in a Japanese population<sup>21</sup>, it was identified that a low Barthel index before the fracture generated a greater risk of poor recovery and higher mortality.

Therefore, it is necessary to know whether in our environment, pre-fracture functionality plays a role

in increased mortality, to carry out measures such as expediting surgical intervention and rehabilitation therapy in those patients with greater vulnerability, that is, with greater dependence before HF.

The aim of this study is to analyze the relationship of functionality before HF with immediate, early, and late post-surgical mortality.

## MATERIALS AND METHODS

Analytical observational retrospective study which included 389 patients with HF, and were admitted to the Central Hospital "Dr. Ignacio Morones Prieto" in the city of San Luis Potosí, Mexico from the period of June 2014 to July 2019. We selected 75 patients who met the following inclusion criteria: age older than 60 years, with fragility HF, undergoing surgical fixation or hemiarthroplasty, with functional assessment by Barthel scale on admission, who died within the period of interest, and registered in the state base of death certificates.

Surviving patients, patients with incomplete information, and patients with pathological fractures, bilateral fractures, history of HF, periprosthetic fracture, or with non-surgical management were excluded from the study.

The Barthel Scale score, months of discharge-function (defined as time from date of surgical event to date of death), age, gender, and cause of death were studied.

The study was approved by the Ethics Committee (24-CEU-001-20160427) and the Research Committee (Reg. 17CI24028093) of the central hospital Dr. Ignacio Morones Prieto, with permission to access patient records.

### **Determination of mortality and functionality**

The sample was divided into three groups: patients with immediate mortality, was defined as the event occurring within the 1<sup>st</sup> month after HF surgery, patients with early mortality, when it occurred within the 2<sup>nd</sup> and 12<sup>th</sup> months, and patients with late mortality when it occurred after 1 year after the surgical event.

The degree of functionality of the patient during admission was determined by means of the Barthel scale, that patient with a score < 60 points was defined as a dependent patient, and that patient with a score ≥ 60 points as an independent patient.

**Table 1.** Demographic characteristics of study population

Characteristics	Immediate mortality (n = 18) (%)	Early mortality (n = 19) (%)	Late mortality (n = 39) (%)
Female	11 (61)	16 (84)	24 (61)
Condition "Dependence"	4 (22)	3 (15)	5 (12)
Age			
60-69	0	0	3 (7)
70-79	2 (11)	9 (47)	13 (33)
80-89	10 (55)	8 (42)	19 (48)
90-100	6 (33)	2 (10)	4 (10)
Death's diagnosis			
Pneumonia	6 (33)	7 (36)	11 (28)
Cardiac insufficiency	2 (11)	4 (21)	2 (5)
Sepsis	2 (11)	3 (15)	3 (7)
Renal illness	0	1 (5)	2 (5)
Thromboembolic	3 (16)	0	0
Myocardial Infarction	5 (27)	4	17 (43)
Others	0	0	4 (10)

## Statistical analysis

Sequential non-probabilistic sampling was done. A sample size was calculated for the state of San Luis Potosí, considering 308,000 old adults (State Government, 2016)<sup>22</sup>, and a reported maximum prevalence of HF of 1.1% (2009)<sup>23</sup>; margin of error 5%, with a confidence of 95%. The required sample was 17 patients. However, since the causes are multifactorial, more patients were included in a period of time in accordance with Hanke and Wichern<sup>24</sup> you want to recommend that this type of sample should be at least 50 individuals. No randomization method was applied. Through Cox regression, the risk of mortality was determined by comparing dependent versus independent patients over time.

## RESULTS

Of the 75 patients studied, 50 subjects (66.67%) were female. Age ranged from 60 to 100 years, most subjects were between 80 and 89 years of age (n = 37, 49.3%), 12 subjects (16%) categorized as previously dependent. They were divided into the three groups, according to their respective date of death: immediate, early, and late post-fracture mortality, and related to their state of functionality. In the immediate death group (No. 18,

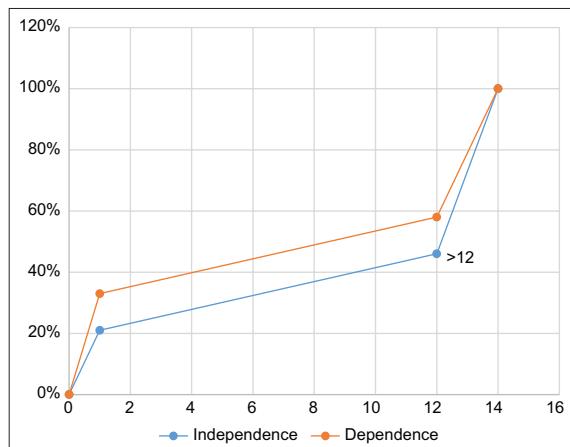
24%), four patients were categorized as dependent, in the early death group (no. 19, 25%) three patients were dependent, and in the late mortality group (no. 38, 52%), with five dependent patients (Table 1). The proportion of risks is protective for the group of independent patients over dependents. A trend of the same risk of dying among dependents and independents was observed during the 1<sup>st</sup> post-operative month. In the early mortality group, an increased risk of dying with Relative Risk (RR) 0.18 (0.065-0.539 p = 0.001, CI 95%) was observed in dependent patient compared to independents; similarly, in late mortality, the group of dependents had an increased risk of death (RR 0.14 [0.064-0.336 p < 0.001 CI 95%]) compared to independent patients (Table 2). In relation to death diagnoses, in the immediate mortality group the most common causes were: Pneumonia (33%) e Acute Myocardial Infarction (27%). In the early mortality group, pneumonia was the most common cause of death at 36%, followed by heart failure with 21%. And in the late mortality group, that is, after the 1<sup>st</sup> year after 100, acute myocardial infarction was the first cause (43%), followed by pneumonia (28%).

## DISCUSSION

In this study, the sample studied has characteristics to other studies in terms of age, gender, and causes

**Table 2.** Relative risk (with 95% CI) of mortality in relation with de functionality before the hip fracture

	Dependent patients	Total patients	Relative risk (RR)	CI 95%	p value
Immediate mortality	4	18	0.34	0.1150-1.037	0.05
Early mortality	3	19	0.18	0.0652-0.5393	0.001
Late mortality	5	38	0.14	0.0643-0.3363	< 0.001

**Figure 1.** Mortality by functionality over time.

of death<sup>3,6,7,11</sup>. There is evidence of an increased risk of falling in independent patients with preserved wandering, during their mobilization outside or inside the home<sup>25</sup>. For this reason, our work obtained sample 5 times more independent patients than dependent patients. A higher incidence of the female gender was observed, being the most physiologically vulnerable to this pathology<sup>26,27</sup>. The most common age was 80-89 years, as reported by studies in the American population<sup>28</sup>. Of the total sample of 76 patients in this study, 18 older adults (23%) were observed to have died within the 1<sup>st</sup> month of post-fracture, subsequently there was a distribution of 19 patients (25%) throughout the 2<sup>nd</sup>-12<sup>th</sup> months; and finally, 51% of the sample died after the post-show year (Fig. 1). Similar results were obtained in a recent meta-analysis where the magnitude and duration of excess post-fracture mortality were explored in the first 3 months, and remained high for the 1<sup>st</sup> year, gradually descending to even 10 years<sup>29,30</sup>. In the immediate mortality group (< 1 year), dependency was not observed to contribute as a risk factor for mortality, because it was similar among independent and dependent

patients. Unlike the results obtained in the ishidou<sup>21</sup> study, where the low Barthel index was a significant determinant of mortality risk after adjusting to age and gender. Within the 2<sup>nd</sup>-12<sup>th</sup> months of post-fracture, defined as early mortality, independence was observed to be a protective factor in maintaining survival in this period. In our knowledge, there are no studies evaluating these same criteria, although it is reported that within the 1<sup>st</sup> year post-fractura there is a mortality of 20-24%<sup>31,32</sup>; however, the level of functionality of the samples is unknown. In early and late mortality groups, the trend remains that pre-FC independence is a protective factor of mortality. Similar to the Haentjens study et al.<sup>29</sup>, it was observed that the risk of mortality decreased substantially over time, especially in those functional patients. However, in our study, we find ourselves as limiting: sample size and inequality in the proportion in number between dependents and independents. A larger sample will be required to obtain conclusive data.

## CONCLUSION

Our study found that independence, with a Barthel index > 60 points, is a protective factor for post-fracture mortality when compared to dependent patients. However, this protection was not evident within the 1<sup>st</sup> month.

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## CONFLICTS OF INTEREST

All authors declare that they have no conflicts of interest.

## ETHICAL DISCLOSURES

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

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## Deficiencia de vitamina B<sub>12</sub> y fragilidad en adultos mayores del centro de México

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### Resumen

**Introducción:** La fragilidad se relaciona con caídas, fracturas, limitación de las actividades de la vida diaria y aumento de la hospitalización en adultos mayores. El objetivo de este estudio fue investigar el nexo entre la fragilidad y la vitamina B<sub>12</sub>. **Metodología:** Se realizó un estudio de corte transversal y de relación; se incluyó a 240 adultos mayores de 60 a 70 años, de ambos géneros, que acudieron a la consulta. Se consideraron criterios de exclusión enfermedades neurológicas y pacientes que no completaron las pruebas. Todos los pacientes se evaluaron con los criterios de Fried para fragilidad. La deficiencia de vitamina B<sub>12</sub> se definió como una cifra <400 pg/ml. Se utilizó la prueba t de Student, la prueba U de Mann-Whitney y la prueba no paramétrica Kruskal-Wallis. **Resultados:** A los pacientes se les estratificó por grupos. El 86.6% de los participantes presentaba por lo menos alguna enfermedad crónico-degenerativa. Los valores de vitamina B<sub>12</sub> decrecieron respecto de la fragilidad. Se mostró una relación significativa entre las cifras de vitamina B<sub>12</sub>, la debilidad y la baja actividad física. **Conclusión:** La disminución de vitamina B<sub>12</sub> es un posible factor de riesgo para experimentar fragilidad en el adulto mayor.

**Palabras clave:** Fragilidad. Vitamina B<sub>12</sub>. Adulto mayor. Micronutrientes.

### Vitamin B<sub>12</sub> deficiency and frailty in older adults from central Mexico

### Abstract

**Background:** Frailty is associated with recurrent falls, fractures, limitation of activities of daily living, and increased hospitalization in older adults. The aim of this study was to investigate the association between frailty and vitamin B12, which has been shown to be related to numerous geriatric syndromes. **Methodology:** A cross-sectional and association study was carried out; including 240 adults aged 60 to 70 years, of both genders, who wandered to the outpatient clinic and without cognitive alterations. Neurological diseases and patients who did not complete the tests were considered exclusion criteria. All patients were evaluated with the Fried criteria for frailty. Vitamin B<sub>12</sub> deficiency was defined as a serum level less than 400 pg/ml. Student's t test, the Mann-Whitney U test and the non-parametric Kruskal-Wallis test were used. **Results:** The patients were stratified in a fragile, prefragile and robust group. 86.6% of the patients had at least some chronic degenerative disease. Vitamin B12 levels decreased as severity increased with respect to frailty. A significant association between vitamin B12 levels, weakness and low physical activity was shown. **Conclusion:** The decrease in vitamin B<sub>12</sub> is a possible risk factor for frailty in the elderly.

**Key words:** Frailty. Vitamin B<sub>12</sub>. Elderly. Micronutrients.

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## INTRODUCCIÓN

La fragilidad es un síndrome de causa múltiple y se caracteriza por una disminución de la fuerza, resistencia y función fisiológica reducida que acentúa la vulnerabilidad de un individuo para desarrollar dependencia o muerte<sup>1</sup>. En todo el mundo, la prevalencia de fragilidad entre la población geriátrica es hasta de un 48%<sup>2</sup>. La fragilidad se vincula con caídas, fracturas, restricción de actividades de la vida diaria, disminución de la movilidad, pérdida de la función cognitiva, aumento de la frecuencia de hospitalización e institucionalización en residencias, además de mortalidad<sup>3</sup>. Por lo tanto, la identificación de los factores que causan fragilidad son aspectos muy importantes de investigar.

El mal estado nutricional se reconoce como un factor de riesgo para muchas afecciones relacionadas con la edad y, en fecha más reciente, ha surgido el papel de la deficiencia de la vitamina B<sub>12</sub> en el desarrollo de varias enfermedades crónicas.

La vitamina B<sub>12</sub> o cobalamina es una vitamina hidrosoluble que contiene cobalto que no puede sintetizar el cuerpo humano y, por lo tanto, debe extraerse de los alimentos o sintetizarse a partir de la microbiota intestinal<sup>4</sup>.

La vitamina B<sub>12</sub> en la dieta se une por lo regular a las proteínas en los alimentos y requiere para su liberación los ácidos gástricos y la pepsina en el estómago. Una vez que la vitamina B<sub>12</sub> se libera, se une a la haptocorrina salival (HC) que protege a la vitamina del ambiente ácido del estómago mientras se desplaza hacia el intestino delgado. En el intestino delgado, la vitamina B<sub>12</sub> se une al factor intrínseco (IF) producido por las células parietales gástricas. En el íleon, el complejo IF-vitamina B<sub>12</sub> se une al receptor cubam, lo que facilita la endocitosis en el lisosoma. En este último, el IF se degrada y la vitamina B<sub>12</sub> se libera al citosol y luego se moviliza al torrente sanguíneo. La mayor parte de la vitamina B<sub>12</sub> (80%) está unida al HC, en tanto que el resto lo hace a la transcobalamina<sup>5</sup>.

Los adultos mayores están en riesgo de mostrar una deficiencia de vitamina B<sub>12</sub> debido a una prevalencia elevada de atrofia gástrica, que a su vez perjudica la liberación de la vitamina B<sub>12</sub> de las proteínas de los alimentos para su absorción, una inflamación crónica del estómago que afecta hasta un 30% de los adultos mayores de 60 años<sup>6</sup>.

La gastritis atrófica se caracteriza por una atrofia de la mucosa que conduce a una secreción reducida de ácido gástrico y, por lo tanto, a una disminución de

la absorción de la vitamina B<sub>12</sub>, ya que el ácido clorhídrico y la pepsina son esenciales para su liberación de las proteínas alimentarias<sup>7</sup>.

Además, cierta evidencia muestra que la deficiencia de vitamina B<sub>12</sub> se relaciona con varias enfermedades crónicas, como el accidente cerebrovascular<sup>8</sup>, deterioro cognitivo<sup>9</sup>, osteoporosis<sup>10</sup>, desacondicionamiento físico<sup>11</sup>, neuropatías, alteraciones de la marcha y equilibrio, caídas recurrentes, depresión, hipotensión ortostática, valores elevados de homocisteína, y aumento del riesgo cardiovascular<sup>12</sup>; otros investigadores refieren que ciertas conductas como el alcoholismo crónico, o una mala absorción debido a la dieta o una operación<sup>13</sup>, consumo de largo plazo de inhibidores de la bomba de protones y antagonistas de los receptores de histamina H<sub>2</sub><sup>14</sup>, así como consumo de metformina<sup>15</sup>, han incrementado la prevalencia de deficiencia de vitamina B<sub>12</sub> en poblaciones de edad avanzada.

Otros investigadores demostraron que los pacientes con sarcopenia tienen cifras más bajas de vitamina B<sub>12</sub> circulante en comparación con los controles, lo que sugiere que la deficiencia de vitamina B<sub>12</sub> podría afectar la función del músculo esquelético<sup>16</sup>.

Sin embargo, la correlación entre la deficiencia de micronutrientes y la fragilidad no es clara. La incidencia de deficiencia de vitamina B<sub>12</sub> aumenta con la edad<sup>17</sup> y muy pocos estudios se han realizado para revisar si la deficiencia de vitamina B<sub>12</sub>, tiene algún efecto directo sobre el desarrollo de la fragilidad<sup>18</sup>. El objetivo de este estudio fue investigar el nexo entre los valores de vitamina B<sub>12</sub> y la fragilidad cuantificados con los criterios de Fried en los adultos mayores.

## MATERIAL Y MÉTODOS

Se condujo un estudio de corte transversal y de relación en adultos mayores de 60 a 70 años, de ambos géneros, que acudieron a la consulta externa del IMSS 4 de enero del 2018 a diciembre del 2019, con su participación libre y voluntaria, previa firma de consentimiento informado. Los resultados se le entregaron con recomendaciones o con referencia a un médico especialista, según correspondiera.

Se realizó un muestreo no probabilístico, con la participación de 240 pacientes. Los criterios de inclusión fueron: edad de 65 a 70 años, no poseer alteraciones cognitivas y ser capaz de deambular. Se consideraron criterios de exclusión enfermedades neurológicas que imposibilitaran efectuar las evaluaciones y pacientes que no completaran todas las pruebas. El poder

estadístico calculado para las relaciones entre los terciles de vitamina B<sub>12</sub> en suero fue del 82%.

Los participantes se entrevistaron sobre las variables sociodemográficas, neurocognitivas, psicosociales y biológicas; se tomaron muestras de sangre periférica, previo ayuno de 8 h, para medir los valores de concentración sérica de vitamina B<sub>12</sub> y ácido fólico, además de glucosa, urea, creatinina y albúmina.

Las muestras se procesaron antes de cuatro horas desde el momento de la punción venosa, antes de lo cual se mantuvieron en refrigeración a 4°C. Las cifras séricas de vitamina B<sub>12</sub> se determinaron mediante inmunoanálisis competitivo por quimioluminiscencia directa (ADVIA Centaur®). A los adultos mayores se les clasificó de acuerdo con los criterios de Fried para la fragilidad y se clasificaron en tres grupos: robustos ( $n = 80$ ), prefrágiles ( $n = 80$ ) y frágiles ( $n = 80$ ).

El estado de fragilidad física de Fried se evaluó de acuerdo con los cinco componentes del síndrome propuestos y se validaron en el Estudio de Salud Cardiovascular<sup>19</sup>.

La pérdida de peso involuntaria o no intencional se definió como un índice de masa corporal <18.5 kg/m<sup>2</sup> o pérdida de peso no intencional >4.5 kg en los últimos seis meses.

La lentitud se clasificó en concordancia con los valores del quintil más bajo (estratificados por sexo y altura) en el promedio de dos mediciones de la prueba de velocidad de marcha rápida de 4.6 m. Tiempo de caminata, estratificado por género y altura. Hombres: límite de tiempo para caminar 4.6 m como criterio de fragilidad: altura ≤ 173 cm ≥ 7 s; altura ≥ 173 cm ≥ 6 s. Mujeres: altura ≤ 159 cm ≥ 7 s; altura ≥ 159 cm ≥ 6 s.

La debilidad se midió por la extensión dominante de la rodilla. Los participantes en el quintil más bajo de un valor promedio ajustado por género e índice de masa corporal de tres estudios se definieron como débiles. La fuerza de extensión de rodilla se estratificó por sexo y cuartiles de índice de masa corporal.

El agotamiento se determinó por medio de dos preguntas de la *Center for Epidemiologic Studies Depression Scale*. Se preguntó a los participantes si en la última semana sentían que todo lo que hacían era un esfuerzo y no tenían ganas de hacer nada. Los participantes podían responder: 0 = nunca o casi nunca (menos de un día); 1 = a veces (1-2 días); 2 = con frecuencia (3-4 días); 3 = siempre o casi siempre (5-7 días). Los participantes que contestaron con frecuencia o siempre en alguna de las dos preguntas se clasificaron como frágiles para este criterio.

La actividad física se evaluó con el tiempo autoinformado medido en horas, dedicado diariamente a actividades ligeras, moderadas y vigorosas. Las kilocalorías gastadas por semana se calculan mediante un algoritmo estandarizado. Esta variable está estratificada por género. Los hombres con 383 kilocalorías gastadas por actividad física por semana son frágiles, mientras que las mujeres se consideraron frágiles si consumían 270 kilocalorías por semana.

Los pacientes con tres o más componentes se agruparon en el grupo frágil; con la presencia de uno o dos componentes se agruparon como prefrágiles y cuando el paciente no tenía ninguno de los componentes se agrupó como robusto.

Además, los pacientes se dividieron en dos grupos: valor de vitamina B<sub>12</sub> por encima y por debajo de 200 pg/ml. Luego se compararon los grupos en términos de los criterios de Fried.

Se excluyó a los pacientes con diagnóstico reciente de cáncer, insuficiencia cardíaca, insuficiencia renal, insuficiencia hepática e insuficiencia respiratoria aguda y pacientes que recibieron vitamina B<sub>12</sub> o complementos de folato antes de tomar la muestra de vitamina B<sub>12</sub> en sangre.

Asimismo, todos los pacientes se evaluaron para las funciones cognitivas y se excluyó a los individuos con un miniexamen del estado mental <23 (clasificado como deterioro cognitivo).

El estudio se inició después de recibir la aprobación del comité de ética del IMSS HGZ No. 4. Los participantes fueron informados de los procedimientos, beneficios y riesgos potenciales de los estudios a efectuar, en consonancia con la Declaración de Helsinki sobre investigación en seres humanos. Se realizó solo con los adultos mayores que decidieron participar tras obtener su consentimiento informado por escrito, concedido libremente.

## ANÁLISIS ESTADÍSTICO

Para lograr un grado de confianza del 95% y un margen de error del 5% se requirió un tamaño de muestra de 240 pacientes. Los datos se analizaron con SPSS para Windows, versión 25.0 (SPSS, Inc., Chicago, IL, EE.UU.). Para la estadística descriptiva, las variables medibles se evaluaron con la prueba de bondad de ajuste de Kolmogorov-Smirnov para determinar la normalidad de la distribución.

Las variables con distribución normal se expresaron como media y desviación estándar y las variables que no siguieron una distribución normal se presentaron

como mediana. Cuando se consideraron dos grupos, se revisó la diferencia entre las medias con la prueba de Student, en tanto que la importancia de la diferencia entre medianas se analizó al aplicar la prueba U de Mann-Whitney.

Cuando se consideraron más de dos grupos, la diferencia entre las medias se evaluó con el análisis paramétrico de la prueba de varianza, en tanto que la importancia entre los valores medios se investigó a través de la prueba no paramétrica de Kruskal-Wallis. Una  $p <0.05$  se consideró estadísticamente significativa.

Para la comparación de más de dos grupos se utilizó ANOVA unidireccional, seguido de la prueba de comparación múltiple de Bonferroni.

## RESULTADOS

Se estudió a un total de 240 adultos mayores. La edad promedio de los participantes fue de 68.9 años (60-70 años); el 60.4% de la muestra correspondió a mujeres. El 23% de los pacientes tenía hasta cinco años de escolaridad primaria. El 4% no sabía leer o escribir. El 76% pertenecía a un estrato socioeconómico medio o bajo. La fragilidad se observó con más frecuencia en los pacientes que vivían acompañados o con su pareja (Tabla 1). Respecto del estado nutricional, la media de IMC fue de  $27.0 \text{ kg/m}^2 \pm 4.0 \text{ DE}$ , con límites inferior y superior de 16.4 y  $37.9 \text{ kg/m}^2$ , respectivamente. Un 27% de los pacientes estudiados tuvo obesidad de grado I (Tabla 2).

Para determinar la fragilidad, los pacientes se evaluaron mediante los criterios de Fried. La Tabla 2 muestra las diferencias significativas entre los grupos.

Como se muestra en la Tabla 3, cuando se comparó a los grupos prefrágil y frágil con un grupo control, se observó que la hipertensión arterial sistémica, la insuficiencia venosa periférica, la osteoporosis, la diabetes mellitus de tipo II, la enfermedad pulmonar obstructiva crónica y la sarcopenia se presentaban con mayor frecuencia en estos grupos ( $p <0.05$ ). El 86.6% de los pacientes geriátricos tenía por lo menos alguna enfermedad crónico-degenerativa.

Los valores de vitamina B<sub>12</sub> se redujeron de acuerdo con el incremento de la gravedad respecto de la fragilidad ( $p <0.001$ ); por su parte, los valores de ácido fólico y vitamina D no mostraron diferencias significativas entre los grupos (Tabla 4).

La Tabla 5 muestra la relación entre los valores de vitamina B<sub>12</sub> y la debilidad medida con la fuerza de extensión de la rodilla y la baja actividad física ( $p <0.001$ ).

**Tabla 1.** Características demográficas de los pacientes

Variable	Robusto (n = 80)	Prefragil (n = 80)	Frágil (n = 80)	p
Edad (años)	65.9 ± 4.8	65.7 ± 5.3	63.6 ± 4.6	0.190
Género				0.149
Masculino (%)	33	27	35	
Femenino (%)	47	53	45	
Escalaridad (%)	13/44/23 0-5/6-11/≥11 años	17/41/22	27/35/18	0.440
Estado civil				
Acompañado (%)	39	52	72	0.197
Solo (%)	41	28	8	

Los datos se expresan como media ± desviación estándar. Mediana y frecuencia. \*p <0.05.

**Tabla 2.** Comparación de los criterios de Fried entre los pacientes

Componentes de fragilidad	Robusto (n = 80)	Prefragil (n = 80)	Frágil (n = 80)	p
IMC (kg/m <sup>2</sup> )	26.4 ± 2.60	24.0 ± 3.05	21.8 ± 1.70	0.180
Lentitud/ velocidad de marcha (m/s)	4.6 ± 0.26	6.04 ± 1.23	9.91 ± 1.29	0.001
Debilidad/fuerza de extensión de rodilla (kg)	16.31 ± 5.01	13.84 ± 4.53	5.71 ± 3.94	0.001
Agotamiento (%)	1.65 ± 0.80	1.93 ± 0.47	2.65 ± 0.12	0.001
Actividad física (kcal)	1,391.0 ± 985.5	655.4 ± 363.8	257 ± 125	0.001

Los datos se expresan como media ± desviación estándar. \*p <0.05.

## DISCUSIÓN

En este estudio se buscó la correlación entre la cifra sérica de vitamina B<sub>12</sub> y la fragilidad en pacientes geriátricos y se determinó que el valor de vitamina B<sub>12</sub> podría vincularse con la fragilidad en este tipo de pacientes.

La prevalencia de la deficiencia de vitamina B<sub>12</sub> entre los pacientes geriátricos que se evaluaron fue del 66.6%, en comparación con otros estudios que alcanzaron el 40%<sup>20</sup>.



complicaciones. Se ha pensado que la relación entre la deficiencia de vitamina B<sub>12</sub> que se observa con frecuencia en la población anciana, y que se vincula con síndromes geriátricos, como deficiencia cognitiva, trastornos del equilibrio y la marcha, caídas frecuentes, depresión e hipotensión ortostática, se correlaciona con la fragilidad<sup>28</sup>.

Sin embargo, la comparación de la deficiencia de vitamina B<sub>12</sub> con los subparámetros de los criterios de Fried mostró diferencias entre los grupos. En la bibliografía se han hallado muy pocos estudios que investiguen la relación entre la cifra de vitamina B<sub>12</sub> y la fragilidad. En un estudio conducido en 2010 se demostró la correlación entre diferentes variaciones genéticas que afectan el mecanismo de transporte de la vitamina B<sub>12</sub> y la fragilidad. Los autores plantearon la hipótesis de que la deficiencia de vitamina B<sub>12</sub> podría inducir el desarrollo de fragilidad a través de mecanismos que aumentan el valor de la homocisteína y causan daño celular a través de la hipometilación del DNA y el RNA<sup>29</sup>, lo que conduce a una disminución del metabolismo energético y posiblemente desencadena la activación de vías inflamatorias<sup>30</sup>.

Los puntos fuertes de este estudio incluyen el diseño prospectivo, el número adecuado de muestras y la evaluación detallada de todos los pacientes. Las limitaciones del estudio incluyen el diseño transversal y la evaluación de la deficiencia de vitamina B<sub>12</sub> basada tan sólo en la cifra sérica de la vitamina B<sub>12</sub>. Además, no se cuantificaron los valores de ácido metilmalónico y homocisteína.

En conclusión, en este análisis transversal realizado con una gran población de estudio se identificó la correlación entre la fragilidad, que se observa con frecuencia en casos geriátricos con múltiples resultados adversos, y el valor sérico de la vitamina B<sub>12</sub>. Los estudios se han concentrado en la fragilidad durante los últimos 20 años; sin embargo, una mayor comprensión de la correlación requiere la conducción de estudios longitudinales en el futuro.

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## CONFLICTO DE INTERESES

Los autores declaran no tener conflicto de intereses.

## RESPONSABILIDADES ÉTICAS

**Protección de personas y animales.** Los autores declaran que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

**Confidencialidad de los datos.** Los autores declaran que han seguido los protocolos de su centro de trabajo sobre la publicación de datos de pacientes.

**Derecho a la privacidad y consentimiento informado.** Los autores han obtenido el consentimiento informado de los pacientes o sujetos referidos en el artículo. Este documento obra en poder del autor de correspondencia.

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## Mexican hip fracture audit (ReMexFC): 2019 annual report

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### Abstract

**Background:** Hip fracture (HF) is associated with negative outcomes, functional decline, and high costs. HF audits helped improving compliance in key performance indicators (KPI) and achieving better health-care outcomes. **Objective:** The aim of the audit is to know socio-demographic characteristics of HF in Mexico, the compliance to KPI and outcomes. **Methodology:** Prospective multicentric, observational, and descriptive study in seven public hospitals in Mexico. We included patients 60 years and older with fragility HF. We measured socio-demographic characteristics, pre fracture gait and functional status, in-hospital KPI and outcomes after 30 days. The authors used descriptive statistics for analysis. **Results:** We included 220 patients, mean age was 81 years, 75% were women. The most frequent fracture was transtrochanteric. Mean surgical delay was of 144 h. After 30 post-discharge, 18% had an independent gait, mean mortality was 11.4%. **Conclusions:** Our compliance to KPI is low, and our health-care outcomes could be improved. A national audit will help to know our current status in HF care and built policies to improve quality of care and outcomes.

**Key words:** Hip fracture. Audit. Fragility fractures. Orthogeriatrics.

### Registro Mexicano de Fractura de Cadera (ReMexFC): informe anual 2019

### Resumen

**Introducción:** La fractura de cadera causa múltiples efectos negativos en la salud, tiene altos costos y provoca dependencia con frecuencia. Los registros de fractura de cadera han promovido el apego a indicadores de calidad y mejorado los resultados asistenciales. **Objetivo:** Conocer las características sociodemográficas de la fractura de cadera en México, apego a indicadores de calidad y resultados asistenciales. **Metodología:** Estudio prospectivo, multicéntrico, observacional y descriptivo en siete hospitales públicos de México. Se incluyó a mayores de 60 años con fractura de cadera por fragilidad. Se midieron las variables prefractura, al ingreso, apego a indicadores de calidad en fase aguda, al alta y resultados asistenciales a los 30 días. Se usó estadística descriptiva. **Resultados:** Se incluyó a 220 pacientes y la edad media fue de 81 años. El 75% correspondió a mujeres. La fractura más frecuente fue la transtrocantérica con 54%. La demora quirúrgica fue de 144 horas. A los 30 días, el 18% caminaba independientemente y la mortalidad fue de 11.4%. **Conclusiones:** Se observa una baja adherencia a los indicadores de calidad. Un registro nacional ayudará a conocer el estado actual de la asistencia de fractura de cadera y generar políticas para la atención y mejorar los resultados. Existen muchos puntos de oportunidad para mejorar la atención.

**Palabras clave:** Fractura de cadera. Registro. Fractura por fragilidad. Ortogeriatría.

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## INTRODUCTION

In the past decades, we faced an increase in the number of elders; consequently, the number of chronic non-communicable diseases such as osteoporosis is increasing<sup>1</sup>. Fragility fractures are the most important complication of osteoporosis<sup>2</sup> and hip fracture (HF) is the most serious because its high mortality, costs, and functional decline<sup>3-5</sup>.

HF has a in hospital mortality between 2% to 8% and 25% to 35% after the 1<sup>st</sup> year<sup>6-8</sup>. In the Latin American region, a study in Chile reported in-hospital mortality of 3%<sup>9</sup> and of 27% in the 1<sup>st</sup> year in Colombia<sup>10</sup>. In Mexico, the pilot phase of the Mexican HF audit (ReMexFC) reported an in-hospital mortality of 7.4% and 14% after 30 days<sup>11</sup>. Other negative consequences of HF a decline in quality of life<sup>12</sup> as well as very high costs<sup>13</sup>.

The HF audits began in the United Kingdom with the National HF Database (NHFD), this registry managed to capture more than 60,000 HFs<sup>4</sup>. These registries improve mortality, surgical delay, early mobilization and increased the involvement of geriatricians<sup>14-19</sup>. The ReMexFC started in 2018, its objectives and methodology were recently earlier<sup>20</sup> followed by the pilot phase<sup>11</sup>.

## Objectives

The main objective of ReMexFC is to know the socio-demographic characteristics of HF in Mexican in older adults with HF, as well as compliance to key performance indicators (KPI) and health-care outcomes.

The secondary objectives of ReMexFC are to acknowledge individual compliance from the participating hospitals to be able to generate health policies and quality improvement projects in HF care, with follow-up throughout the next years.

## METHODS

ReMexFC is a national project with the participation of multiple hospitals in different states of Mexico. It began with its pilot phase in 2018. This paper corresponds to the results of 2019. Each hospital has an investigator responsible for capturing data and sending information all HFs patients admitted to their hospital.

We conducted a multicenter, prospective, longitudinal, and observational study in seven public hospitals of different health systems in Mexico. The hospitals

of the Mexican Institute of Social Security (IMSS) were the General Hospital of Zone 1, IMSS, Colima and the General Hospital of Zone 83 IMSS, Morelia. From the Institute of Social Security and Services for State Workers (ISSSTE), the Regional Hospital of León and the High Specialty Hospital of Morelia were included in the study. The National Health Minister, the participating hospitals were the General Hospital of Zacatecas, and the General Hospital of Mexico "Dr. Eduardo Liceaga," finally, from the Petróleos Mexicanos (PEMEX) healthcare system, the Reynosa Regional Hospital. All of them received authorization from their respective ethics and research committees.

The study included patients 60 years or older with diagnosis of fragility HF, defined as those who suffered a low-energy trauma or a fall from their own standing position. All information was captured by the senior investigator of each hospital and sent to a digital platform, without including any personal information. Only the data manager had access to the cloud in which the data were stored during the study. Each hospital received an identification letter from "A" to "G" to guarantee the anonymity of the center when the results were published, and only the main researcher from each hospital and the data manager were aware of the identity of each letter. After the individual descriptive analysis of hospitals, feedback was sent regarding their performance.

We measured the variables suggested by the Fragility Fracture Network<sup>21</sup> (FFN) in their minimum common dataset (MCD)<sup>22</sup>. These included demographical and pre-fracture characteristics, in-hospital KPI, outcomes at discharge and after a 30-day follow-up period (Table 1). The gait was assessed by the Functional Ambulatory Category<sup>23</sup>, mental state at admission with the Pfeiffer scale<sup>24</sup>, surgical risk through the American Society of Anesthesiology (ASA) scale<sup>25</sup>. To measure functional status we used Barthell scale<sup>26</sup> and finally the Confusion Assessment Method (CAM) was used for the diagnosis of delirium<sup>27</sup>.

## Statistical analysis

Descriptive statistics were used for the analysis of the variables. In the case of qualitative, frequencies and percentages are reported. In the case of quantitative variables, means ± standard deviations or medians with interquartile range are reported, depending on the variable in the normality tests (Kolmogorov-Smirnov or Shapiro). The SPSS statistical package from IBM (Inc., Chicago, IL, version 24) was used.

**Table 1.** Minimum common database or MCD

In-hospital phase	
Patient's General Information	Pre-Fracture Characteristics
Gender	Place of residence
Age	Mobility <sup>γ</sup>
City and State	Gait aids
Hospital	Mental status <sup>α</sup>
Private or public hospital	Surgical risk <sup>β</sup>
In-Hospital	Side of the fracture
Date and time of arrival to emergency room	Type of fracture
Date and time of admission to traumatology ward	Osteoporosis treatment <sup>Σ</sup>
Sore ulcers before admission	Functional satuts <sup>χ</sup>
Delirium <sup>π</sup>	Discharge
Date and time of surgery	Destination after discharge
Orthopedic implant used in surgery	Date of discharge
Surgical delay in hours	Hospital length of stay
Use of femoral blocking	Osteoporosis treatment
Anesthesia modality used	In-hospital mortality
Specialist	30-day follow-up
Weight bearing the day after surgery	Readmission
	Surgical reintervention
	Mortality
	Gait and need for aids
	Osteoporosis treatment <sup>Σ</sup>
	Functional status

γ Functional Ambulatory Category (FAC): FAC 0= Unable to walk FAC 1= Requires great help from one person.

FAC 2 = Requires little help from one person. FAC 3 = walks independently in interiors but needs supervision.

FAC 4 = Walks independently in interiors without supervision. FAC 5= Walks in interiors and exteriors independently.

α Pfeiffer's scale.

β American Society of Anesthesiology (ASA).

Σ calcium, vitamin D and antiresorptive or anabolic drugs.

χ Barthel index.

π Confusion assessment method.

## RESULTS

Between January and December 2019, a total of 220 patients with hip fragility fracture were admitted in all of the hospitals. The socio-demographic and baseline prefracture characteristics are presented in table 2. The mean age was 81 years, most of the patients lived at home and had an independent gait. More than half of the patients had a high surgical risk and 58% and at admission were had disorientation or with cognitive dysfunction. The most frequent fracture was transtrochanteric and only 10% received treatment for osteoporosis before the fracture.

Regarding the KPI and health-care outcomes are shown in table 3. The median surgical delay was 144 h (interquartile range 96-214) and only 4.5% of patients had surgery in the first 48 h after admission. Almost

half of them were evaluated during their stay by a geriatrician. In the post-operative period, 26.8% sat out of bed and 15.3% started partial weight bearing as tolerated during hospitalization. Length of stay was 8 days (interquartile range 6-12), and after discharge only 4.1% entered long-term care.

The most frequently used device was the dynamic hip screw system (DHS) with 44% of cases, followed by partial prostheses with 35.1%. The intracapsular patients received prostheses or hemiprostheses in 64.9% of the cases. In the case of transtrochanteric, 50.4% of the cases received a DHS system and 2.4% a centromedullary nail (CCM). Finally, the subtrochanteric 61.5% were treated with the DHS system and 7.6% with CCM.

The health-care outcomes are shown in table 4. The most frequent causes of the surgical delay were the



**Table 3.** In-hospital health-care outcomes and key performance indicators

	<b>General (n = 220)</b>	<b>A (n = 43)</b>	<b>B (n = 51)</b>	<b>C (n = 23)</b>	<b>D (n = 18)</b>	<b>E (n = 16)</b>	<b>F (n = 45)</b>	<b>G (n = 24)</b>
Surgical delay (h)	144 (96-214)	128 (88-164)	168 (114-251)	301.7 ± 157.1	206 ± 123	105 (90-113)	163 (135-237)	98 (88-163)
Surgery in the first 48 h	10 (4.5)	5 (11.6)	1 (2)	-	-	2 (12.5)	1 (2.2)	1 (4.2)
Type of surgery								
Total prostheses	16 (7.2)	2 (4.7)	4 (7.8)	-	1 (5.5)	1 (6.2)	6 (13.3)	2 (8.4)
hemiprostheses	79 (35.9)	18 (41.8)	17 (33.3)	5 (21.7)	8 (44.4)	8 (50.0)	18 (40.2)	5 (20.8)
DHS <sup>9</sup>	97 (44.1)	19 (44.1)	23 (45.1)	14 (60.9)	6 (33.3)	7 (43.8)	11 (24.4)	17 (70.8)
Centromedular nail	5 (2.2)	2 (4.6)	-	-	-	-	3 (6.6)	-
Anesthesia technique								
Regional	168 (76.4)	40 (93)	47 (92.2)	12 (57.1)	15 (93.8)	16 (100)	14 (36.8)	24 (100)
General	8 (3.9)	1 (2.3)	1 (2)	-	1 (6.2)	-	5 (13.2)	-
Femoral blockage	3 (1.36)	-	1 (2)	-	-	-	2 (4.4)	-
Evaluated by geriatrician	99 (45.4)	38 (88.4)	7 (13.7)	9 (39.1)	-	9 (56.3)	14 (31.1)	22 (91.7)
Sat the day after surgery	59 (26.8)	23 (53.5)	15 (29.4)	2 (8.7)	-	1 (6.3)	6 (14.6)	12 (50)
Weight bearing as tolerated the day after surgery	32 (15.3)	-	8 (15.7)	3 (13.0)	-	5 (31.3)	4 (9.8)	12 (50)
Osteoporosis treatment at discharge	57 (26.9)	23 (53.5)	1 (2.2)	2 (8.7)	-	6 (37.5)	10 (22.2)	15 (62.5)
Length of stay	8 (6-12)	7 (6-9)	9.9 (7.3-13.8)	14.5 ± 6.6	9.1 ± 4.9	5.7 ± 1.7	9 (7-12)	7.3 ± 1.8
Destination after discharge								
Home	196 (89.1)	35 (81.4)	45 (88.2)	20 (87.0)	17 (100)	15 (93.8)	41 (91.1)	23 (95.8)
Long-term care	9 (4.1)	-	1 (1.9)	3 (13)	-	1 (6.3)	3 (6.7)	1 (4.2)

Continuous variables are reported as mean ± standard deviation or median (interquartile range). Categorical variables are reported in N (%).

9 DHS=Dynamic hip screw.

The median surgical delay is 144 h, and only 4.5% of patients underwent surgery in the first 48 h of stay. This is one of the most relevant issues in HF care, because of its implications in the health-care outcomes, mortality, and costs. Furthermore, it is a modifiable factor in the patient pathway. International standards suggest that surgery should be performed in the first 36 to 48 h<sup>31-33</sup>. The main cause of delay was administrative situations unrelated to the clinical condition of the patient.

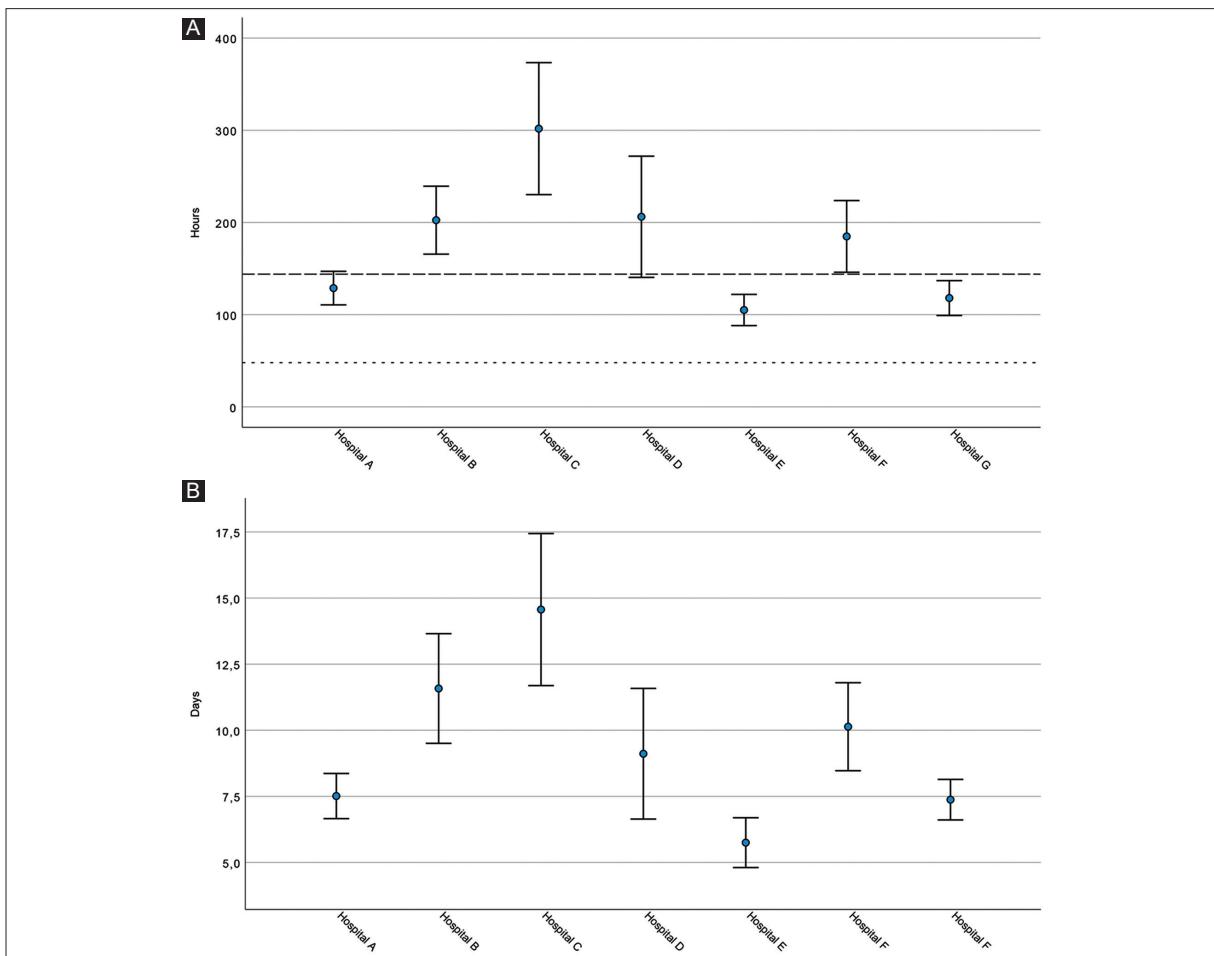
The HIP ATTACK study<sup>34</sup> suggests that the surgical delay is justified in cases where the patient's clinical status is unstable.

Our surgical delay contrasts with other countries, for example, in Scotland 72% of patients undergo surgery in the first 36 h<sup>34</sup>, 70% in Ireland<sup>17</sup>, and 40% in Spain<sup>16</sup>. A review of HF work in Mexico from 2000 to 2018 did not find any paper focused in surgical delay, which suggests that it is a point of opportunity in our country<sup>35</sup>. Our audit found that 25% of patients

**Table 4.** Main causes of surgical delay, in-hospital mortality and morbidity

	General (n = 220)	A (n = 43)	B (n = 51)	C (n = 23)	D (n = 18)	E (n = 16)	F (n = 45)	G (n = 24)
Cause for surgical delay <sup>a</sup>								
No theater available	121 (57.9)	29 (67.4)	26 (51.0)	4 (17.4)	2 (11.5)	13 (81.3)	28 (71.8)	19 (79.2)
No surgical material available	47 (22.5)	5 (11.6)	18 (35.8)	9 (39.1)	13 (76.5)	-	2 (5.1)	-
anticoagulation	7 (3.3)	-	-	4 (17.4)	-	-	-	3 (12.5)
Unstable clinical status	16 (7.7)	4 (9.3)	3 (5.9)	3 (13)	1 (5.6)	-	4 (8.9)	1 (4.2)
Complications								
Delirium	67 (31.3)	16 (37.2)	16 (31.4)	7 (30.4)	4 (25)	5 (31.3)	14 (31.3)	5 (20.8)
Sore ulcers	56 (25.5)	18 (41.9)	18 (35.3)	2 (8.7)	1 (11.2)	1 (6.3)	14 (31.1)	2 (8.3)
Mortality	8 (3.7)	1 (2.3)	5 (9.8)	-	1 (5.6)	-	1 (2.2)	-
Pre-surgery	5 (2.3)	-	3 (5.9)	-	1 (5.6)	-	1 (2.2)	-
Post-surgery	3 (1.4)	1 (2.3)	2 (3.9)	-	-	-	-	-

<sup>a</sup>191 patients included in this analysis (5 died before surgery, 10 non-surgical patients, and 14 with no delay). Categorical variables are reported in n (%).



**Figure 1.** Comparative surgical delay **A:** length of stay **B:** and main complications. The dotted line corresponds to the 48-h standard for surgical delay. The dashed lines correspond to the overall median.

**Table 5.** Healthcare outcomes after 30 days of follow-up

	General (n = 145)	A (n = 15)	B (n = 43)	C (n = 16)	D (n = 11)	E (n = 19)	F (n = 31)	G (n = 10)
Barthel index	35(15-55)	26.7 ±16	42 ± 27.6	35 (30- 48)	37.7 ± 20	26.8 ± 25.1	40.3 ± 30.2	33.5 ± 18.6
Gait								
Not able to walk	59 (40.7)	13 (86.7)	20 (46.5)	12 (75)	8 (72.7)	12 (63.2)	12 (38.7)	9 (90)
Independent gait <sup>a</sup>	18 (12.4)	1 (6.7)	8 (18.6)	-	-	-	9 (29)	-
Osteoporosis treatment	37 (25.5)	12 (80)	7 (16.3)	1 (6.3)	-	8 (42.1)	5 (16.1)	4 (40)
Residence								
Home	136 (93.8)	15 (100)	43 (100)	13.8 (81.3)	11 (100)	16 (84.2)	28 (90.3)	10 (100)
Long-term care	9 (6.2)	-	-	3 (18.8)	-	3 (15.8)	3 (9.7)	-
Readmission	11 (7.6)	-	1 (2.3)	1 (6.3)	-	4 (21.1)	4 (12.9)	1 (10)
Mortality	19 (11.6)	1 (0.6)	7(4.3)	2 (1.2)	1 (0.6)	3 (1.8)	4 (2.4)	1 (0.6)

Continuous variables are reported as mean ± standard deviation or median (interquartile range). Categoric variables are reported in N (%).

<sup>a</sup> FAC 3-5.

developed sore ulcers. This contrasts with the 2% of the German audit, or 4% in Spain<sup>16</sup>.

Another important topic is the device used. The British guidelines for clinical excellence or NICE<sup>31</sup> for its acronym in English suggest sticking to certain types of devices based on the type of fracture.

In the ReMexFC, the most frequently used device was the DHS with 44%, followed by partial prosthesis with 35.1%. Of the intracapsular patients, 54.3% had a hemiprosthesis and 10.5% a total prosthesis. About 50.4% of the transtrochanteric fractures received DHS system. Europe has given much more weight to devices such as centromedullary nails in subtrochanteric fractures; England reported in the NHFD 91.6% used a centromedullary nail for this type of fracture<sup>4</sup>. In the ReMexFC, this device was only used in 2.4% of all fractures, corresponding to 17.8% of subtrochanteric ones. This may be explained by the budgets of public hospitals that does not include in most of our health-care systems centromedullary nails because of the high costs compared with DHS.

Early mobilization and rehabilitation are also associated with HF outcomes. We reported that 15% of patients started weight bearing as tolerated the day after surgery, and 30 days after discharge 40% were not able to walk yet. This contrasts with the FONDA cohort at the Hospital Universitario de la Paz, Madrid, where almost half of their patients started weight bearing ambulation during the acute phase of the HF, and who at 3 months 3 out of 4 have independent gait<sup>8</sup>.

Regarding mortality, in the acute phase it is relatively low, 3.7%, with a range of 2.2% to 9.8%. Spain, Scotland, Germany, and the United Kingdom oscillate between 4 and 5% mortality in the in-hospital phase<sup>16</sup>, however at 30 days it increased to 11.6%. This contrasts with Spain reporting 7%<sup>36</sup> and Australia 5%<sup>37</sup>. This disparity may be due to multiple causes; however, we consider that the main reason is compliance to KPI such as surgical delay, early mobilization, and weight bearing.

Finally, osteoporosis treatment at discharge has been one of the most important points in the secondary prevention model, considering the imminent risk of fracture in the 1<sup>st</sup> weeks after a fragility fracture. In the ReMexFC, 26.9% of the patients received treatment for osteoporosis at discharge, and it remains almost without change at 30 days. In England in the NHFD they have a 50% adherence to discharge<sup>4</sup>, but it drops to 34% at 30 days. There are hospitals in Mexico that did not provide treatment, which is a point of enormous opportunity of improvement.

The main weaknesses of the registry is that we do not have yet representation at the national level, in addition to the fact that the participating hospitals have a relatively low number of cases, we have < 1% of the estimated HFs annually in Mexico<sup>38</sup>. In Mexico there are very few orthogeriatric units in the country, so that the clinical contribution of geriatrics to HF care is not available nationwide. Efforts should be made to increase the centers in the country with orthogeriatric wards.

The main strengths of the study are that as far as the authors know, it is the first Latin American registry of its type, in addition to being the first multicenter study that includes different health-care systems (IMSS, ISSSTE, PEMEX, and the Ministry of Health). Therefore, we may think that the reality of other hospitals and cities is not so different, and it gives us a great opportunity to improve KPI and health-care outcomes in HF in Mexico.

## CONCLUSIONS

We have a low compliance to KPI in HF patients in Mexico; this happens in different healthcare institution, there are not enough structured orthogeriatric wards. This phenomenon has a negative impact on healthcare outcomes, such as mortality, morbidity, gait, and development of dependency.

Having a national registry will help us understand this gap and generate policies to increase compliance to KPI. Surgical delay, early mobilization, and osteoporosis treatment are of great concern. We should continue with the ReMexFC project, increase participating hospitals so that we can have a better overview of the reality of HF in Mexico.

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## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

## ETHICAL DISCLOSURES

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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## Validation of the frontal assessment battery in Mexican older adults with cognitive impairment

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### Abstract

**Background:** Cognitive impairment (CI) can produce frontal dysfunction. Frontal Assessment Battery (FAB) is a brief cognitive and behavioral battery. **Objectives:** The objective of the study was to validate the FAB in Mexican older adults with CI. **Methods:** This was a observational, cross-sectional, and comparative study. It included 90 participants: Dementia ( $n = 30$ ), Mild CI (MCI) ( $n = 30$ ), and Cognitively Healthy ( $n = 30$ ). The neuropsychological battery included Neuropsi, MoCA-E, and FAB. The categorical variables were reported in proportions and percentages, and the continuous in mean and standard deviation. ANOVA was used for continuous variables and Chi-square for categorical variables. Pearson's Correlation Coefficient (CC) was calculated. Yield was established by Receiver Operating Characteristic and Area Under the Curve (AUC) calculation. **Results:** The mean age was  $76.2 \pm 7.2$  years, 63.3% women ( $n = 57$ ). Cronbach's alpha coefficient was 0.71. FAB obtained positive and strong CC for Neuropsi ( $r = 0.617$ ,  $p < 0.05$ ) and total MoCA-E ( $r = 0.795$ ,  $p < 0.05$ ). The dementia AUC was 0.80 (95% CI, 0.70-0.89;  $p < 0.001$ ) with a cutoff point of  $\leq 14$  (sensitivity 73% and specificity 70%). The AUC of MCI was 0.74 (95% CI, 0.61-0.86;  $p = 0.001$ ) with a cutoff point of  $\leq 16$  (sensitivity 83.3% and specificity 63.3%). **Conclusions:** FAB is a valid tool in Mexican older adults with CI.

**Key words:** Frontal assessment. Cognitive impairment. Frontal assessment battery. Frontal dysfunction.

### Validación de la batería de evaluación frontal en adultos mayores mexicanos con deterioro cognitivo

### Resumen

**Antecedentes:** El deterioro cognitivo (DC) puede producir disfunción frontal. La batería de evaluación frontal (FAB, Frontal Assessment Battery) es una batería cognitiva breve y conductual. **Objetivos:** Validar la FAB en adultos mayores mexicanos con DC. **Métodos:** Estudio observacional, transversal y comparativo. Incluyó a 90 participantes: demencia ( $n = 30$ ), deterioro cognitivo leve (DCL) ( $n = 30$ ) y cognitivamente saludable ( $n = 30$ ). La batería neuropsicológica incluyó Neuropsi, MoCA-E y FAB. Las variables categóricas se informaron en proporciones y porcentajes, y las continuas en media y desviación estándar. ANOVA para las variables continuas y  $\chi^2$  para las categóricas. Se calculó el coeficiente de correlación de Pearson (CCP). **Resultados:** La edad media fue de  $76.2 \pm 7.2$  años, con 63.3% de mujeres ( $n = 57$ ). El coeficiente alfa de Cronbach fue de 0.71. La FAB obtuvo CCP positiva y fuerte para Neuropsi ( $r = 0.617$ ,  $p < 0.05$ ) y MoCA-E total ( $r = 0.795$ ,  $p < 0.05$ ). La AUC de demencia fue 0.80 (IC 95%, 0.70-0.89;  $p < 0.001$ ) con punto de corte de  $\leq 14$  (sensibilidad, 73%; especificidad, 70%). La AUC de DCL fue de 0.74 (IC 95%, 0.61-0.86;  $p = 0.001$ ) con punto de corte de  $\leq 16$  (sensibilidad, 83.3%; especificidad, 63.3%). **Conclusiones:** La FAB es una herramienta válida en adultos mayores mexicanos con DC.

**Palabras clave:** Evaluación frontal. Deterioro cognitivo. Batería de evaluación frontal. Disfunción frontal.

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## INTRODUCTION

As a consequence of population aging, cognitive impairment (CI) represents a public health problem. In 2015, it affected more than 47 million people in the world, and it is estimated that by 2030 it will affect 75 million, a figure that will triple by 2050. In Mexico, 3.5 million people with CI could be reached, which will undoubtedly have an impact on the health system<sup>1</sup>. The World Health Organization and the Alzheimer's Association International recommend increasing basic and clinical research that allows early detection of CI<sup>2</sup>. Dementia is characterized by a progressive loss of cognition that impacts the individual's performance<sup>3</sup>, while Mild CI (MCI) represents a prodromal stage that can potentially progress to dementia<sup>4</sup>.

CI can affect various brain regions, including the frontal lobes; their function is to maintain cognitive, behavioral, and motor functions. The prefrontal area involves connections with other cortical and subcortical areas<sup>5</sup>, so the damage to these networks affects behavior and executive function<sup>6</sup>. CI can produce executive dysfunction to varying degrees, establishing cognitive patterns for its approach<sup>7,8</sup>. There are various tests to assess frontal function, however, they are extensive tests and require prior training, limiting their application<sup>9,10</sup>.

Dubois et al. designed a specific test, called Frontal Assessment Battery (FAB), with the aim of evaluating the cognitive and behavioral function of the frontal lobe<sup>11</sup>. This test has been used in various clinical situations, such as Frontotemporal Dementia (FTD)<sup>12</sup>, Alzheimer's Disease (AD)<sup>13</sup>, and Vascular Dementia, among others<sup>14</sup>. Socio-cultural factors can modify the performance of this test, so validations are necessary in each country<sup>15-18</sup>. Brief tests, such as the FAB, could help evaluate patients with frontal dysfunction.

The objective of our study was to determine the validity of FAB in Mexican older adults with CI, as well as to know the cutoff points of the test.

## METHODS

### *Study design*

This was a observational, cross-sectional, and comparative study carried out in a Memory Clinic of a tertiary hospital in Mexico City. The study was approved by the Institutional Ethics Committee. All participants signed an informed consent.

## Participants

Men and women older than 65 years were included in the study. The selection of the participants was non-probabilistic and for convenience. Three groups were established: dementia group, MCI group, and Cognitively Healthy (CH) group. The diagnosis of dementia was determined by the criteria of DSM-5<sup>19</sup> and/or NINCDS-ADRDA<sup>20</sup>. The criteria of Petersen et al.<sup>14</sup> is used for the diagnosis of MCI. The CH group was established through a standardized clinical and neuropsychological evaluation that ruled out a cognitive alteration according to education and gender<sup>21</sup>.

Those with uncontrolled or untreated depressive symptoms were excluded from the study, defined with a score > 5 by the 15-item version of Geriatric Depression Scale<sup>22</sup>, delirium, visual or hearing impairment, illiterate, history of neurological or psychiatric disease, severe rheumatoid arthritis, motor sequelae of cerebrovascular disease, uncontrolled hypertension, untreated thyroid disease, glycosylated hemoglobin ≥ 9%, history of severe hypoglycemia, presence of heart failure severe, or recent traumatic brain injury.

## Measurements

All participants were evaluated by a specialist in geriatrics and/or neurology, considering the clinical criteria of the expert as the gold standard, later all participants were subjected to a neuropsychological evaluation. In addition, a clinical history and comprehensive geriatric evaluation were carried out, from which socio-demographic data and functional status were obtained through scales that measure: Basic Activities of Daily Living<sup>23</sup> and Instrumented Activities of Daily Living (IADL)<sup>24</sup>. The neuropsychological evaluation included two tests: the Brief Neuropsychological test in Spanish (Neuropsi), standardized in the Mexican population by age, sex, and education<sup>21</sup>, and the MoCA-E test<sup>25,26</sup>. Both tests were compared against the FAB<sup>11</sup>.

## FAB

The FAB is a brief cognitive and behavioral battery that can be used at the bedside, useful to assess frontal lobe functions, and consists of six subtests that explore conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. Each subtest

**Table 1.** Clinical and socio-demographic characteristics of the participants

	Total (n = 90)	CH (n = 30)	MCI (n = 30)	Dementia (n = 30)	p
Age (years) <sup>A,C</sup>	76.2 ± 7.2	72.8 ± 6.5	77.9 ± 6.3	78.1 ± 7.6	0.005
Female n (%)	57 (63.3)	25 (83.3)	17 (56.7)	15 (50)	0.018
Education (years)	13.2 ± 5.0	14.0 ± 4.0	12.0 ± 5.6	13.6 ± 5.3	0.293
BADL (Katz)	5.7 ± 0.5	5.7 ± 0.4	5.7 ± 0.7	5.8 ± 0.3	0.427
IADL (Lawton and Brody) <sup>B,C</sup>	6.2 ± 2.3	7.5 ± 1.0	7.0 ± 1.5	4.2 ± 2.5	<0.001
Neuropsi <sup>A,B,C</sup>	93.0 ± 20.7	110.4 ± 7.7	91.6 ± 20.3	77.1 ± 16.3	<0.001
MoCA-E <sup>A,B,C</sup>	22.0 ± 5.6	26.1 ± 2.0	22.9 ± 3.7	16.9 ± 5.8	<0.001
FAB <sup>A,B,C</sup>	13.8 ± 3.9	16.7 ± 1.5	14.0 ± 3.0	10.8 ± 4.2	<0.001

Data are Media ± Standard Deviation. CH: cognitively healthy; MCI: mild cognitive impairment; BADL: basic activities of daily living; IADL: Instrumented activities of daily life; MoCA-E: montreal cognitive assessment; FAB: frontal assessment battery. Data are analyzed with ANOVA for continuous variables and Chi-square for categorical variables, a Post-hoc analysis with Tukey test is performed. <sup>A</sup>CH versus MCI, p < 0.05; <sup>B</sup>MCI versus Dementia, p < 0.05; <sup>C</sup>CH versus Dementia, p < 0.05.

has a value from 0 to 3, so the maximum score is 18, with the lowest one indicating greater frontal dysfunction<sup>11</sup> (Annex 1 in Spanish). To determine the convergent correlation, the subtests that specifically evaluate frontal lobe functions of each of the instruments were selected.

### Statistical analysis

The categorical variables were reported in proportions and percentages, and the continuous variables in mean and standard deviation. The analysis of tests and subtests was performed with a Z score. ANOVA was used to compare means, and for categorical Chi-square. A *post hoc* analysis with Tukey's test is performed. For internal consistency, Cronbach's Alpha was calculated. Construct validity was determined by the original author<sup>11</sup>. Pearson's Correlation Coefficient (CC) was calculated for concurrent validity. The performance was established by means of the Receiver Operating Characteristic (ROC), the calculation of Area Under the Curve (AUC) was performed to establish cutoff point, as well as sensitivity and specificity. p < 0.05 was considered statistically significant. The SPSS statistical package (SPSS, Inc., Chicago IL, version 20.0 for Windows) was used.

## RESULTS

The validation process was carried out on 90 participants. The mean age was 76.2 ± 7.2 years, 63% women (n = 57), and the mean education was 13.2 ± 5.0 years. The CH group was significantly younger than the MCI

group (p < 0.05) and dementia group (p < 0.05), respectively. The group with dementia had a lower score in IADL compared to the CH (p < 0.05) and MCI group (p < 0.05), as well as a worse performance in Neuropsi, MoCA-E, and FAB compared to the rest of the groups (p < 0.001), while the MCI group had a better performance than the dementia group, but worse performance compared to the CS group (p < 0.001). Table 1 shows the clinical and socio-demographic characteristics of the groups. Cronbach's Alpha Coefficient was 0.71 for the FAB. The characteristics of frontal function performance by groups are presented in table 2.

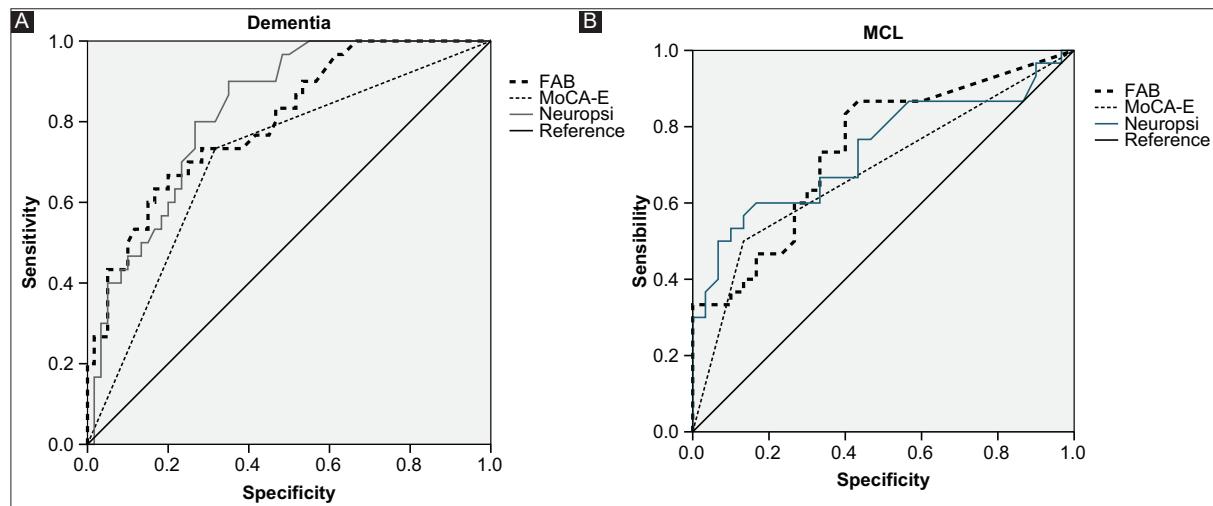
Regarding the correlation, it is observed that the FAB obtained a high CC for Neuropsi ( $r = 0.617$ ,  $p < 0.05$ ) and MoCA-E ( $r = 0.795$ ,  $p < 0.05$ ), while the mental flexibility subtests ( $r = 0.422$ ,  $p < 0.05$ ), motor programming ( $r = 0.437$ ,  $p < 0.05$ ), and sensitivity to interference ( $r = 0.357$ ,  $p < 0.05$ ) obtained a moderate correlation, unlike the conceptualization subtests ( $r = 0.228$ ,  $p < 0.05$ ), inhibitory control ( $r = 0.262$ ,  $p < 0.05$ ), and environmental autonomy ( $r = 0.278$ ,  $p < 0.05$ ) where the correlation was weak (Table 3).

The ROC curve for FAB in relation to the dementia group showed an AUC of 0.800 (95% CI, 0.70-0.89;  $p < 0.001$ ), with a cutoff point of ≤14, sensitivity of 73% (95% CI, 0.89-0.57), and specificity of 70% (95% CI, 0.81-0.58), PPV of 55%, NPV of 84%. The ROC curve for FAB in relation to the MCI group showed an AUC of 0.742 (95% CI, 0.61-0.86;  $p = 0.001$ ), with a cutoff point of ≤ 16, sensitivity of 83.3% (95% CI, 0.96-0.69), and specificity of 63.3% (95% CI, 0.71-0.35), PPV of 64%, and NPV of 76%. Figure 1 shows the ROC curves of the FAB in CI.

**Table 2.** Performance of the frontal function

	<b>Subtest</b>	<b>CH (n = 30)</b>	<b>MCI (n = 30)</b>	<b>Dementia (n= 30)</b>	<b>p</b>
Neuropsi	Similarities <sup>A,C</sup>	0.54 ± 0.38	-0.15 ± 1.10	-0.39 ± 1.09	< 0.001
	Phonological verbal fluency <sup>C</sup>	0.33 ± 0.65	0.09 ± 1.27	-0.42 ± 0.83	0.010
	MF, change hand position <sup>A,B,C</sup>	0.70 ± 0.65	0.14 ± 0.83	-0.84 ± 0.82	< 0.001
	MF, opposite reactions <sup>A,B,C</sup>	0.57 ± 0.25	0.01 ± 0.86	-0.58 ± 1.24	< 0.001
	MF, alternating movements <sup>C</sup>	0.41 ± 0.56	-0.03 ± 0.93	-0.38 ± 1.24	0.007
	Total <sup>A,B,C</sup>	0.83 ± 0.37	-0.07 ± 0.98	-0.76 ± 0.78	< 0.001
MoCA-E	Trail Making Test Part B <sup>A,C</sup>	0.64 ± 0.69	-0.08 ± 1.01	-0.55 ± 0.89	< 0.001
	Total <sup>A,B,C</sup>	0.73 ± 0.35	0.16 ± 0.66	-0.89 ± 1.04	< 0.001
FAB	Conceptualization	0.18 ± 0.53	-0.17 ± 0.91	-0.01 ± 1.37	0.374
	Mental flexibility <sup>A,C</sup>	0.47 ± 0.45	-0.23 ± 1.17	-0.23 ± 1.06	0.006
	Motor programming <sup>B,C</sup>	0.48 ± 0.58	0.28 ± 0.78	-0.76 ± 1.08	< 0.001
	Sensitivity to interference <sup>B,C</sup>	0.54 ± 0.39	0.12 ± 0.89	-0.66 ± 1.15	< 0.001
	Inhibitory control <sup>A,B,C</sup>	0.71 ± 0.67	-0.04 ± 0.94	-0.67 ± 0.84	< 0.001
	Environmental autonomy	0.19 ± 0.31	0.19 ± 0.31	-0.38 ± 1.62	0.032
	Total <sup>A,B,C</sup>	0.72 ± 0.38	0.04 ± 0.77	-0.76 ± 1.07	< 0.001

CH: cognitively healthy; MCI: mild cognitive impairment; MF: motor functions; MoCA-E: montreal cognitive assessment; FAB: frontal assessment battery. The data are analyzed with ANOVA, and a Post-hoc analysis with Tukey's test is performed. <sup>A</sup>CH versus MCI, p < 0.05; <sup>B</sup>MCI versus Dementia, p < 0.05; <sup>C</sup>CH versus Dementia, p < 0.05. Group means are expressed in Z scores.



**Figure 1.** Receiver operating characteristic curve performance of FAB with CI. **A:** Dementia, FAB AUC 0.800 (95% IC, 0.70-0.89; p < 0.001), MoCA AUC 0.708 (95% IC, 0.59-0.82; p < 0.001); Neuropsi AUC 0.827 (95% IC, 0.74-0.91; p < 0.001). **B:** MCI, FAB 0.742 (95% IC, 0.61-0.86; p = 0.001); MoCA 0.683 (95% IC, 0.54-0.82; p = 0.015; Neuropsi AUC 0.738 (95% CI, 0.60-0.86; p = 0.002). MCI: mild cognitive impairment; FAB: Frontal assessment battery.

## DISCUSSION

The results of our study show that the FAB has a moderate internal consistency, and that it is a valid test in Mexican older adults with CI, both for dementia

and MCI, similar to that published by Iavarone et al.<sup>16</sup>, Wong et al.<sup>27</sup>, and Dubois et al.<sup>11</sup>.

A strong correlation was observed between the FAB and the global assessment tests, MoCA-E, and Neuropsi. A study by Abrahámová et al. demonstrated

		FAB						
	Specific subtests	Conceptualization	Mental flexibility	Motor programming	Sensitivity to interference	Inhibitory control	Environmental autonomy	Total
Neuropsi	Similarities	0.228*						
	Phonological verbal fluency		0.422*					
	MF, change hand position			0.437*				
	MF, opposite reactions				0.357*			
	MF, alternating movements					0.262*		
	Total						0.617*	
MoCA-E	Trail Making Test Part B					0.278*		
	Total						0.795*	

FAB: frontal assessment battery; VF: verbal fluency; MF: motor functions; MoCA-E: montreal cognitive assessment; \* , p < 0.05.

similar findings between MoCA-E and FAB<sup>28</sup>. The correlation between MoCA-E and FAB can be explained as a consequence of the psychometric ability of MoCA-E to evaluate executive function from specific tests such as working memory, abstract reasoning, planning, inhibition, attention, and mental flexibility<sup>8</sup>.

Comparing the FAB, MoCA-E, and Neuropsi subtests, the domains of conceptualization, inhibitory control, and environmental autonomy demonstrated a weak correlation, while mental flexibility, motor programming, and sensitivity to interference demonstrated a moderate correlation. For all the above, an adequate convergent validity was observed between the FAB, MoCA-E, and Neuropsi. Our findings could be explained because most of the executive function tasks in these tests activate neural networks prominently distributed in the prefrontal cortex<sup>8</sup>.

Regarding the different types of CI, FAB allowed to discriminate between MCI and dementia in the subtests of motor programming, sensitivity to interference, and inhibitory control. The decrease in scores on the motor programming subtests could be explained as a consequence of the fact that individuals with poor motor function are associated with a higher risk of dementia<sup>29</sup>. On the other hand, those with self-behavior deficits and lesions in the ventral frontal regions could be unable to inhibit inappropriate responses and show greater frontal dysfunction<sup>11</sup>. Therefore, the FAB could discriminate between subtypes of CI when the subtests are qualitatively analyzed<sup>30,31</sup>.

Our findings suggest that FAB has good diagnostic precision for dementia, with an AUC of 0.800 (95% CI, 0.70-0.89, p < 0.001), with a cutoff point of ≤ 14, sensitivity of 73%, and specificity of 70%. The cutoff point found is similar to that reported by Custodio et al. who propose a cutoff point ≤ 14.5, although with a sensitivity of 97.7%, and specificity of 81.1% in the Peruvian population<sup>32</sup>. Chong et al. also showed a cutoff point similar to ours, but in the Chinese population, with a sensitivity of 91% and specificity of 70.3%<sup>33</sup>. In the case of MCI, FAB demonstrated an adequate AUC, with a cutoff point of ≤ 16, a sensitivity of 83.3%, and a specificity of 63.3%. It is possible that FAB is useful for detecting MCI, although it is convenient to complement it with another test, this as a result of its low specificity. Bezdicek et al. demonstrated a cutoff point of ≤ 16 to discriminate patients with MCI from those of CH (sensitivity 84.4% and specificity 81.2%)<sup>34</sup>. Hurtado et al. reported a cutoff point of ≤ 12.5, with a sensitivity of 74.1%

**Table 3.** Pearson's correlation coefficient

and specificity of 72.2%<sup>30</sup>. Chong et al. improved diagnostic accuracy when combining MMSE and FAB to identify MCI in a Chinese population (sensitivity 91.3% and specificity 77%)<sup>33</sup>.

### **Strengths and limitations**

The main strength of our study is based on the fact that it is the first study to validate FAB in Mexican older adults with CI. Likewise, it also provides information regarding the performance of the test for its application in the clinical field. Another relevant aspect is that participants with MCI and dementia were included. On the other hand, the main limitation of our study is that it was not possible to differentiate between the subtypes of dementia, in addition the test-retest validity was not performed, and the average level of education could limit the external validity of the study.

## **CONCLUSIONS**

The findings of our study show that the FAB is a useful test for the diagnosis of CI in the Mexican population. With respect to dementia, FAB was useful as a diagnostic test by showing good sensitivity and specificity, while for MCI it obtained a low specificity, so the test should be complemented with some other cognitive test.

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## **AUTHOR CONTRIBUTION**

SGAN, LAGG y AJMA designed the study, MJSO review the literature, and JODF collect data and perform statistical analysis. All authors interpreted the data and commented on the manuscript. All authors contributed and approved the final manuscript.

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## **CONFLICTS OF INTEREST**

The authors declare that they have no conflict of interest.

## **ETHICAL DISCLOSURES**

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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## Annex 1. The Frontal Assessment Battery (FAB)

**Subprueba 1. Conceptualización** (semejanzas). “*¿En qué se parece... un plátano y una naranja?” ... ¿una mesa y una silla?*” ... *¿una rosa, un tulipán y una margarita?*”. En caso de un fallo total (por ejemplo: “*no son iguales*”) o fallo parcial (por ejemplo: “*ambos tienen cáscara*”), ayude al sujeto diciendo: “*tanto un plátano como una naranja son...*” pero puntúe 0 para el ítem, no ayude al sujeto con los siguientes dos ítems. Cuente como correctas únicamente las respuestas categóricas (frutas, muebles, flores).

3 correctas	3 puntos
2 correctas	2 puntos
1 correcta	1 punto
0 correctas	0 puntos

**Subprueba 2. Flexibilidad mental** (fluidez verbal). “*Diga tantas palabras como pueda que comiencen con la letra F, cualquier palabra, excepto nombres propios y derivados*”. Si el sujeto no responde en los primeros 5 segundos diga “*por ejemplo, frío*”. Si el sujeto hace una pausa de 10 segundos, estimúlelo diciendo “*cualquier palabra que comience con la letra F*”. El tiempo permitido es de 60 segundos. Puntúe únicamente las palabras correctas, no tome en cuenta las repeticiones o palabras derivadas.

Más de 9 palabras	3 puntos
6 a 9 palabras	2 puntos
3 a 5 palabras	1 punto
Menos de 3 palabras	0 puntos

**Subprueba 3. Programación motora** (series motrices). “*Fíjese bien en lo que hago...*” [examinador con su mano izquierda realiza 3 series puño-canto-palma]. “[Con su mano derecha haga las mismas series, primero conmigo y luego usted solo” [3 repeticiones más junto al paciente] “*Ahora, hágalo usted solo*”.

3 correctas	El paciente lleva a cabo 6 series consecutivas por sí solo
2 correctas	El paciente lleva a cabo al menos 3 series consecutivas solo
1 correcta	El paciente falla solo, pero hace las 3 series con el examinador
0 correctas	El paciente no puede llevar a cabo al menos 3 series consecutivas

**Subprueba 4. Sensibilidad a la interferencia** (instrucciones conflictivas). “*Toque 2 veces cuando yo toque una vez*” [para asegurarse que el sujeto ha entendido las instrucciones, se realiza una serie de 3 ensayos 1-1-1]. “*Toque una vez cuando yo toque 2 veces*” [para asegurarse de que el sujeto ha entendido las instrucciones, se realiza una serie de 3 ensayos 2-2-2]. [El examinador entonces lleva a cabo la siguiente serie 1-1-2-1-2-2-2-1-1-2].

Sin errores	3 puntos
1-2 errores	2 puntos
≥ 2 errores	1 punto
Golpea como el examinador ≥ 4 veces consecutivas	0 puntos

**Subprueba 5. Control inhibitorio** (Go-No Go). “*Toque una vez cuando yo toque una vez*” [para asegurarse de que el sujeto ha entendido las instrucciones, se realiza una serie de 3 ensayos 1-1-1]. “*No toque cuando yo toque 2 veces*” [para asegurarse de que el sujeto ha entendido las instrucciones, se realiza una serie de 3 ensayos 2-2-2]. [El examinador entonces lleva a cabo la siguiente serie 1-1-2-1-2-2-2-1-1-2].

Sin errores	3 puntos
1-2 errores	2 puntos
≥ 2 errores	1 punto
Golpea como el examinador ≥ 4 veces consecutivas	0 puntos

**Subprueba 6. Autonomía ambiental** (conducta de prensión). [Examinador está sentado frente al paciente y coloca las manos del mismo palmas arriba sobre sus rodillas. Sin hablar o ver al paciente, el investigador acerca sus manos a las del paciente y toca sus palmas, para ver si el sujeto las toma espontáneamente. Si el paciente las toma, el examinador intenta de nuevo después de pedirle] “*Ahora, no tome mis manos*”.

El paciente no toma las manos del examinador	3 puntos
El paciente duda y pregunta qué debe hacer	2 puntos
El paciente toma las manos sin dudar	1 punto
Toma las manos a pesar de pedirle explícitamente que no lo haga	0 puntos

Puntuación total \_\_\_\_\_