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## ORIGINAL ARTICLES

**Sensitivity and specificity of the Global Leadership Initiative on Malnutrition criteria for the detection of malnutrition in geriatric patients** **1**

*Jorge E. Chavarría-Favila, Gerardo Ávila-Butrón, Denisse Prone-Olazabal, and Yohami S. Ortiz-López*

**Implementation of an orthogeriatric model in a second-level hospital in Mexico** **7**

*José O. Duarte-Flores, Jaime A. Espinoza-Ávila, Cynthia G. Solís-Silva, Lorena Ávila-Cázar, Julián Abraham-Mancilla, María del C. Arellano-Correa, and Horacio Vargas-Jiménez*

**Relation between adverse drugs reactions with potentially inappropriate prescription in hospitalized older adults** **14**

*Klissman López-Cruz, Jesús A. Gómez-García, Virginia A. Ortiz-Ruiz, Nancy E. Guzmán-Delgado, and Luis A. Arboine-Aguirre*

**Quality of life in elderly adults with infarct code in cardiac rehabilitation** **23**

*Alicia M. Negrete-Cruz, Jesús A. Gómez-García, Eder E. Aguilar-y Méndez, Roxela Botello-López, and Nancy E. Guzmán-Delgado*

## BRIEF COMMUNICATION

**Nephrotic syndrome secondary to Sjögren syndrome in an older adult: a clinical case analysis** **29**

*Antonio González, Fernanda Aviña, Dario Sandoval, Andrea Higareda, and Gretell Henríquez-Santos*

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# Sensitivity and specificity of the Global Leadership Initiative on Malnutrition criteria for the detection of malnutrition in geriatric patients

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## Abstract

**Aim:** This study aimed to determine the specificity and sensitivity of the Global Leadership Initiative on Malnutrition (GLIM) criteria as a diagnostic tool compared to a full version of the Mini-Nutritional Assessment (MNA) in hospitalized geriatric patients. **Methods:** The prospective observational cross-sectional study in older adults hospitalized between March 2021 and May 2022. The MNA full version and GLIM criteria will be applied. **Results:** The prevalence of malnutrition in the study population according to GLIM was 6.8% moreover, according to MNA was 1.58%. The results of GLIM versus MNA diagnostic tests were: 100% sensitivity, 94.6% specificity and an accuracy of 94.7%. **Conclusion:** The GLIM criteria have good sensitivity and specificity. It is recommended to continue with studies to validate the use of GLIM as a tool to support the diagnosis of malnutrition in older people hospitalized in conditions of the study population.

**Keywords:** Older adult. Global Leadership Initiative on Malnutrition. Mini-Nutritional Assessment. Malnutrition.

## Sensibilidad y especificidad de los criterios de Iniciativa de Liderazgo Global sobre Desnutrición para la detección de desnutrición en pacientes geriátricos

## Resumen

**Objetivo:** Determinar la especificidad y sensibilidad de los criterios GLIM como herramienta diagnóstica respecto a MNA versión completa en pacientes geriátricos hospitalizados. **Métodos:** Estudio transversal observacional prospectivo en adultos mayores hospitalizados entre marzo 2021 y mayo 2022. Se aplicaron los cuestionarios MNA versión completa y GLIM. **Resultados:** La prevalencia de desnutrición en la población de estudio según GLIM de 6.8% y según MNA de 1.58%. Los resultados de prueba diagnóstica de GLIM vs MNA fueron una sensibilidad del 100%, una especificidad de 94.6% y una precisión de 94.7%. **Conclusión:** Los criterios GLIM tienen una buena sensibilidad y especificidad se recomienda continuar con estudios para la validación del uso de GLIM como herramienta para apoyo en el diagnóstico de desnutrición en personas mayores hospitalizadas en condiciones similares a la población de estudio.

**Palabras clave:** Persona Mayor. GLIM. MNA. Desnutrición.

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## INTRODUCTION

Hospital malnutrition is a highly prevalent problem from the first studies published by Butterworth in 1974<sup>1</sup> to the present, despite the multiple efforts made for its early detection and monitoring, it is a problem that affects between 56% and 63% of hospitalized patients<sup>2</sup>.

Hospitalized older adults have a higher risk of malnutrition compared to those cared at home or nursing home care. Among the factors that stand out for the development of malnutrition, we can highlight: the lack of appetite that goes together with reduced intake and leads to an energy imbalance, as well as stress due to illness, especially respiratory diseases<sup>3</sup>.

To prevent and treat malnutrition in the hospital ambit, first, it is necessary to detect and diagnose it. One of the most accepted nutritional assessments to evaluate hospitalized older adults is the Mini-Nutritional Assessment (MNA), which detects malnutrition risk and malnutrition since it emphasizes weight loss, intake, mobility, self-perception of nutritional status, and dietary analysis, recommended by ESPEN due to its degree of specificity and sensitivity in this population<sup>4</sup>.

Derived from the lack of a globalized classification to detect hospital malnutrition, in 2016, the Global Leadership Initiative on Malnutrition (GLIM) was proposed and, in 2018, the criteria were formally launched<sup>5</sup>.

So that, despite the fact that, there are multiple methods for the diagnosis of malnutrition and its categorization in hospitalized patients, currently, there is no method that is globally accepted and that has proven studies in different populations. The current studies that include the GLIM criteria in geriatric patients are limited, therefore the great relevance of continuing to search for studies that implement them<sup>6</sup>.

The GLIM criteria are a consensus proposal of multiple societies worldwide to globalize the criteria for the diagnosis of malnutrition, this initiative is very useful to formalize and unify the aspects evaluated by all health professionals worldwide, these actions will contribute to obtain standardized and objective results when providing nutritional care in the different hospital stays.

The importance of the use of GLIM for detection of malnutrition in the hospital environment lies in the fact that GLIM considers the five most important factors when it comes to detecting malnutrition, which is weight loss, body mass index (BMI) reduction, and muscle mass reduction, in the intake or absorption of nutrients and inflammation, according to ESPEN, ASPEN AND among other institutions<sup>7</sup>.

## METHODS

A prospective observational cross-sectional study with a descriptive scope was conducted. All patients admitted to hospitalization were taken as the universe; as a population of all hospitalized geriatric patients. The inclusion criteria were patients aged 60 years or over, in a conscious state 15/15 according to the GLASGOW coma scale and exclusion criteria were patients with a traumatic event in the upper extremities, inflammatory or neurological diseases, diseases that make it difficult to mobility of hands and/or arms, patients within the COVID area. The information available in the clinical record was used, as well as the assessment for filling out the GLIM and MNA (Fig. 1).

### Statistical analysis

The sample size was calculated with the following formula<sup>1</sup>:

$$n = \frac{Z^2 pq}{d^2}$$

n = Sample size.

Z = Critical Z value, calculated in the normal curve area tables with 1.96 with a confidence level of 93%

d = 0.07 absolute precision level.

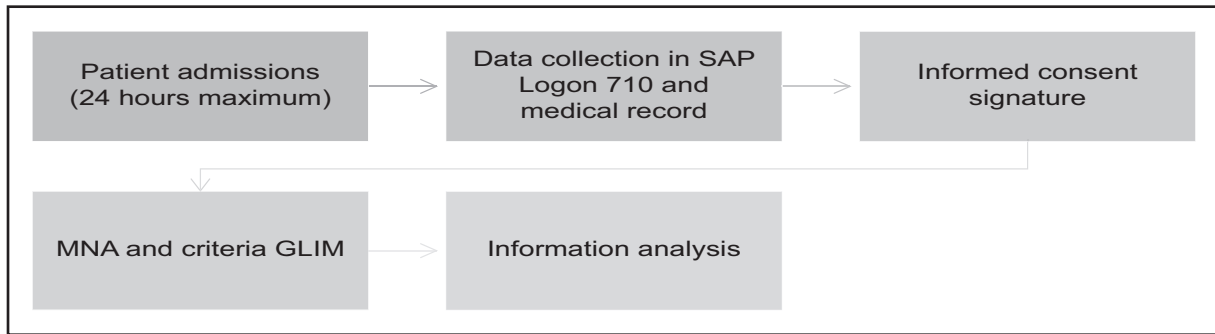
p = Approximate proportion of the phenomenon under study in the reference population of 40%.

q = Proportion of the reference population that does not present the phenomenon under study 60%.

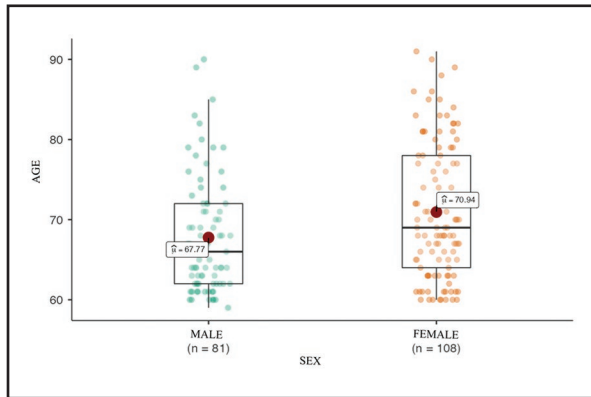
The normality of the variables was evaluated using the Kolmogorov–Smirnov test, the variables with normal distribution were presented in mean and standard deviation and those with different distributions in median and ranges. The differences between measurements were evaluated using the t-student and Mann Whitney U tests depending on the distribution of the data. As well as Spearman's correlation analysis. To evaluate the prognostic efficacy, sensitivity and specificity under the ROC curve was performed ( $p < 0.05$  has been considered statistically significant). For data analysis, the statistical program Jamovi version 2.2.5 was used.

## RESULTS

A total of 189 patients were studied, of which 43% corresponded to men and 57% to women (Fig. 2). The average age of male participants was between 60 and 65 years, and in the female gender from 65 to 70 years (Table 1).



**Figure 1.** Methods for collecting, classifying, and analyzing information obtained from patients. The patient must be admitted to a medical clinic where they must have a maximum hospitalization period of 24 h, afterward the data were collected in the SAP Logon 710 medical record database, to obtain the data, authorization is requested from each patient to participate in this project for which the informed consent form was filled out. Once the data was obtained, MNA and GLIM criteria were obtained according to specific characteristics of each patient to finally analyze the information and reach the conclusions for the purposes of this research. MNA: Mini-Nutritional Assessment; GLIM: Global Leadership Initiative on Malnutrition.



**Figure 2.** Analysis of the total sample of patient gender and age relationship. Comparison of male and female patients and their relationship with the age of the total sample of patients. In the analysis of general characteristics, we found a total sample of 189 patients, of which 43% were male and 57% were female. The distribution in relation to age and gender is as follows, with a prevalence of males between 60 and 65 years old and women between 65 and 70 years old.

**Table 1.** Distribution of participants by gender and age

Age	Male	Female
81-90	5	20
71-80	19	25
60-70	57	63
Total	81	108

From a sample of 81 male and 108 female patients, the highest prevalence in men was between 60 and 65 years old, and in women between 65 and 70 years old, data that will be useful for the purposes of further research.

Analysis of the population is carried out with respect to criteria of sex, age, weight, and BMI, finding a higher average age for female sex (70 years) with respect to male gender (68 years), female population presented a BMI of 26.1 (18.2-45.2), and male 27 (18.8-28.2) (Table 2).

According to the three final GLIM criteria: normal, moderate malnutrition, and severe malnutrition, a relationship was found between the severity of malnutrition and a decrease in grip strength with dynamometry. An analysis of the data was carried out, including

in a single group called “patients without malnutrition according to MNA” patients with a normal nutritional status and patients at risk according to MNA, which were compared with the GLIM results, obtaining a total of three patients with malnutrition and 186 patients without malnutrition according to MNA and a total of 13 patients with malnutrition and 176 patients without malnutrition according to GLIM. The prevalence of malnutrition was found to be 1.58% according to MNA, and 6.8% according to the GLIM criteria (Table 3).

The sensitivity and specificity obtained from the analysis of the data (n = 189), using the full version of the MNA assessment as the standard in comparison with the GLIM criteria, and grip strength as a measure of muscle mass, were as follows: sensitivity of 1.00, specificity of 0.946, and precision of 0.947. When analyzing the patients who were malnourished according to MNA and with moderate or severe malnutrition



**Table 2.** Analysis of gender, age, body mass index, weight, and grip strength

Variable	Malnutrition	Without malnutrition	p-value
Age	72 (66-79)	68 (63-74)	0.137
Weight	65 (58-80)	72 (58-84)	0.076
Body mass index	21.8 (20.8-26.4)	26.3 (24.0-26.4)	0.008*
Grip strength	20 (14-28)	26 (20-34)	0.031*

\*Values lower than 0.05 are statistically significant. The smaller p-value, the more reliable the results obtained. p-value obtained for body mass index is less than 0.05, which indicates that the result is clinically significant for the next study.

**Table 3.** Analysis of MNA malnutrition versus GLIM malnutrition

GLIM criteria	MNA in malnutrition	MNA without malnutrition	Total
GLIM in malnutrition	3	10	13
GLIM without malnutrition	0	176	176
Total	3	186	189

MNA: Mini-Nutritional Assessment; GLIM: Global Leadership Initiative on Malnutrition.

Analysis of data encompassing into a single group called "patients without malnutrition according to MNA" the patients with a normal nutritional status and the patients at risk according to MNA, which were compared with the results of GLIM. Obtaining a total of three patients with malnutrition and 186 patients without malnutrition according to MNA, according to GLIM a total of 13 patients with malnutrition and 176 patients without malnutrition, a prevalence of malnutrition according to MNA of 1.58% and according to GLIM criteria of 6.8% was found.

according to GLIM criteria, an area under the curve of 0.9731 was obtained (Fig. 3). So that, according to the analysis of the previous data, we can presume that the sensitivity, specificity, and precision of the GLIM criteria for the diagnosis of malnutrition is good compared to the long version MNA tool.

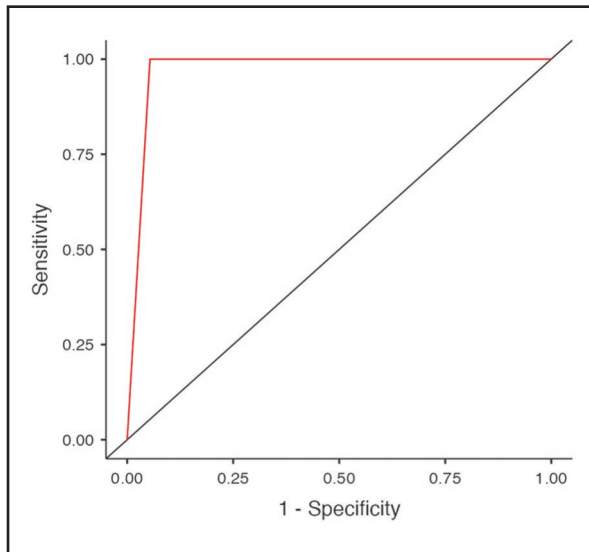
## DISCUSSION

Several studies have emerged since the publication of the GLIM criteria in 2018 to date, describing their usefulness in clinical practice in different populations and specific situations. The present study focused on the study of the population of hospitalized older adults, whose nutritional evaluation is of great importance due to multiple factors that can contribute to malnutrition during hospitalization, so having diagnostic tools for nutritional care process is important, essential.

Different authors have highlighted the usefulness and value of the GLIM criteria in the diagnosis of malnutrition in the elderly, even above assessment tools such as the Subjective Global Assessment (PG-SGA) or ESPEN 2015 criteria due to their predictive capacity of in-hospital complications in elderly patients<sup>8</sup>.

Although it has also been determined that the concordance between diagnostic tools such as PG-SGA, ESPEN, ASPEN/AND, and GLIM depends on the nutritional screening tool and the combinations of diagnostic criteria used, highlighting as less valid the combinations of indicators that use BMI as diagnostic criteria<sup>9</sup>. As mentioned by Huo et al., in an extensive systematic review and meta-analysis, the GLIM criteria have the potential to be used as the "gold standard" for the diagnosis of malnutrition in clinical practice<sup>10</sup>.

To our knowledge and date, there are no previous studies examining the predictive value of the GLIM criteria using MNA as a comparison to nutritional assessment. On the other hand, there is evidence of the evaluation of the MNA against the GLIM criteria, finding variable results. In general and as expected, GLIM has shown superior detection of cases with malnutrition compared to MNA; however, MNA has stood out for its usefulness in detecting patients "at risk of malnutrition." These results show agreement with the objectives of the use of MNA and GLIM, as screening and detection tools for malnutrition, respectively. For example, Lengelé et al. demonstrated that the GLIM criteria, unlike the MNA, are useful in predicting the



**Figure 3.** Sensitivity and specificity of MNA full version versus GLIM criteria assessment. The sensitivity and specificity obtained from the analysis of the data of the 71 patients studied, using the MNA full version as the standard compared to GLIM criteria, using grip strength as a measure of muscle mass, were as follows: a sensitivity of 0.44, a specificity of 0.98, and an accuracy of 0.91 were obtained by analyzing patients who were at nutritional risk or malnutrition according to MNA and moderate or severe malnutrition according to GLIM criteria, with an area under the curve of 0.9731. MNA: Mini-Nutritional Assessment; GLIM: Global Leadership Initiative on Malnutrition.

incidence of sarcopenia at 5 years<sup>11</sup>. Even though the populations included in these studies may not be comparable due to their characteristics, for example, European ethnicity, non-hospitalized patients, belonging to community centers or diagnosed with cancer, if they show a trend in terms of the comparison of MNA and GLIM in this age group<sup>12</sup>.

One of the main disadvantages of using MNA for the detection of malnutrition is that this tool has a very large number of questions, as well as not taking into account inflammatory factors related to the disease and malabsorption. Although there is a short version of MNA (MNA sf), it continues without taking these factors into account<sup>7</sup>.

The measurement of muscle mass by a validated method is essential in the elderly since it can contribute to the diagnosis of sarcopenia or cachexia and giving a value of more weight to this indicator, unlike MNA, can be beneficial for the prognosis of adults' hospitalized seniors.

One of the most noteworthy aspects of this research is that GLIM was used using dynamometry

as a measurement of muscle mass, an easily reproducible and very low-cost method, which can facilitate reproducing said determination in most hospitals<sup>13</sup>.

Regarding weaknesses, the determination of force by dynamometry is an indirect measurement of muscle mass, so patients with decreased strength in upper limbs, arthritis, or in a state of sedation cannot be evaluated by this method. However, due to the characteristics of the population studied, the determination of grip strength was a viable method to obtain said marker.

It is important to highlight that the results obtained in this study may not be ideal in terms of generalization to the bulk of older adults in Mexico, since our population presents characteristics that may not be representative of them. The presence of social factors as the lack of economic resources, poor education in nutrition aspects, unsupportive social environments, among others, increases the risk of malnutrition<sup>14</sup>.

There are still deficiencies in the knowledge about the sensitivity of the tool to detect changes in the nutritional status after a treatment, as well as the restrictiveness of the normal values, but as a tool to obtain a diagnosis of malnutrition in geriatric patients taking it as a step. After nutritional screening, as the consensus mentions, it is quite useful and easy to apply, as well as having excellent diagnostic capacity according to the results obtained from this investigation.

## CONCLUSION

According to the results of the present study, it is suggested that GLIM could be a very useful tool for the diagnosis of malnutrition in hospitalized geriatric patients in similar conditions to the study population since adequate sensitivity and specificity were found when compared with the diagnosis of malnutrition by MNA.

Carrying out larger studies with the objective of validating the use of the GLIM criteria in the Mexican population would be of great value.

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## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.



## ETHICAL DISCLOSURES

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

**Data Confidentiality.** The authors declare that patient data does not appear in this article.

**Right to privacy and informed consent.** The authors declare that patient data does not appear in this article.

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## Implementation of an orthogeriatric model in a second-level hospital in Mexico

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### Abstract

Hip fracture (HF) is a health problem and orthogeriatric models improve care indicators. **Objective:** The objective of this study was to determine the indicators of care in older people (OP) with HF due to frailty in an orthogeriatric model. **Materials and methods:** This study was a longitudinal, prospective, and comparative study. The orthogeriatric model included a multidisciplinary team. **Results:** Thirty-eight cases were analyzed. The mean age was  $79.6 \pm 9.2$  years, 78.9% were women ( $n = 30$ ). The orthogeriatric model was more likely to sit postoperatively (28.6% vs. 2.9%,  $p < 0.001$ ), has post-operative rehabilitation (34.3% vs. 5.7%,  $p = 0.00$ ), and receives secondary prevention at discharge (38.9% vs. 22.2%,  $p = 0.00$ ). Hospital stay was shorter in the orthogeriatric model (5.5 vs. 7.5 days,  $p = 0.04$ ). **Conclusions:** Cases with HF due to frailty in the orthogeriatric model were more likely of sitting down in the post-surgical period, having rehabilitation, shortening the hospital stay, and receiving secondary prevention.

**Keywords:** Older people. Hip fracture. Orthogeriatric.

### Implementación de un modelo de ortogeriatría en un hospital de segundo nivel en México

#### Resumen

La Fractura de Cadera (FC) es un problema de salud y los modelos de ortogeriatría mejoran los indicadores de atención. **Objetivo:** Determinar los indicadores de la atención en Personas Mayores (PM) con FC por fragilidad en un modelo de ortogeriatría. **Material y métodos:** Estudio longitudinal, prospectivo y comparativo. El modelo de ortogeriatría incluyó un equipo multidisciplinario. **Resultados:** Se analizaron 38 casos. La edad media fue de  $79.6 \pm 9.2$  años, 78.9% mujeres ( $n = 30$ ). El modelo de ortogeriatría tuvo mayor probabilidad de sentarse en el postquirúrgico (28.6% vs. 2.9%,  $p < 0.001$ ), tener rehabilitación postquirúrgica (34.3% vs. 5.7%,  $p = 0.00$ ) y recibir prevención secundaria al egreso (38.9% vs. 22.2%,  $p = 0.00$ ). La estancia hospitalaria fue menor en el modelo de ortogeriatría (5.5 vs. 7.5 días,  $p = 0.04$ ). **Conclusiones:** Los casos con FC por fragilidad en el modelo de ortogeriatría tuvieron mayor probabilidad de sentarse en el postquirúrgico, recibir rehabilitación, disminución de tiempo intra-hospitalario y recibir prevención secundaria.

**Palabras clave:** Persona mayor. Fractura de cadera. Ortogeriatría.

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## INTRODUCTION

Due to the demographic transition, there is an increase in the demand for surgical services by older people (OP)<sup>1,2</sup>. Health systems should adapt to the needs of their population. OP benefits from person-centered care<sup>3</sup>. The Comprehensive Geriatric Evaluation establishes a management plan in OP with hip fracture (HF) due to frailty. It is estimated that 30% of OP suffer at least one fall per year and, therefore, have a higher risk of having an HF, being a public health problem that implies high institutional costs and higher morbidity and mortality<sup>4,5</sup>.

There are various models of care in OP with HF<sup>6</sup>. The traditional model guided by on-demand consultations is the most common, while the orthogeriatric co-management model is an ideal model in which a multidisciplinary team participates in a coordinated manner<sup>7-9</sup>. The models seek to preserve the autonomy of the individual after HF, reduce the length of hospital stay, and promote a coordinated discharge plan together<sup>6,10</sup>.

The National Institute for Health and Care Excellence recommends the early involvement of a multidisciplinary orthogeriatric team<sup>11</sup>. Unlike the traditional model, the co-management orthogeriatric model describes a form of cooperation between orthopedists and geriatricians, including other areas such as rehabilitation, physiotherapist, anesthesiology, social work, and nutrition, among others<sup>12-15</sup>. Routine implementation of orthogeriatric models in the UK has been linked to a significant decrease in 30-day mortality in its national HF registry<sup>16</sup>. It has been shown that orthogeriatric collaboration is effective in terms of a reduction in hospital stay compared to traditional models<sup>17</sup>.

There is little information in Mexico about the impact of orthogeriatric in our health system<sup>18</sup>. Orthogeriatric models are not yet common practice. There is evidence that orthogeriatric models improve health care indicators compared to the traditional model<sup>19</sup>. The described indicators include the length of hospital stay, mortality, pre-surgical time, medical and surgical complications, readmission, mobility, and place of residence on discharge<sup>10,20</sup>. The objective of our study was to determine the health care indicators in OP with HF in a co-management orthogeriatric model versus a traditional model in a public hospital with a second level of care.

## MATERIALS AND METHODS

A longitudinal, prospective, and comparative study was carried out in a second level of care public hospital. A longitudinal analysis was contemplated for 1 year.

Individuals older than 65 years who were admitted to the emergency department for HF due to frailty were included in the study. The participants signed informed consent. Individuals who did not agree to participate and who did not have HF due to frailty were excluded from the study.

The population was divided into two groups: a control group made up of a traditional model that included an orthopedic doctor who requested assessment by other specialists on demand; and an intervention group made up of an orthogeriatric team that included coordination between an orthopedic doctor and a geriatrician, including geriatric nursing, social work, and rehabilitation medicine. The type of sampling was non-probabilistic at convenience. Clinimetry was applied in both groups by a geriatric nurse. A survey was applied to determine the sociodemographic variables, including pre-fracture mobility, functionality, and fall situation. The orthogeriatric model was co-managed since its admission. The geriatric area was in charge of carrying out a Comprehensive Geriatric Assessment on admission and optimized perioperative management that included analgesic adjustment, thromboprophylaxis, early detection and management of in-hospital complications, and antibiotic prophylaxis, among other interventions. Orthopedics was in charge of the surgical moment. Geriatric nursing routinely reinforced non-pharmacological interventions. After the geriatric surgical procedure, he requested rehabilitation intervention. Since there is no physiotherapy in the unit, the rehabilitation physician trained the primary caregiver with visual material. On discharge, the orthogeriatric team gave the family a plan that included a reconciliation of pharmacological treatment and non-pharmacological care measures. Pre-surgical time, complications and in-hospital mortality, delirium, and pressure ulcers (PU) were assessed during his stay. Both groups received a follow-up phone call 30 days after discharge to assess mortality, post-fracture mobility, complications, and continuity of secondary prevention. There was approval by the local bioethics committee.

Data were analyzed from October 2019 to February 2020 due to the conversion to Hospital 100% COVID, for which the study was prematurely suspended. Data were presented as measures of central tendency and dispersion (mean  $\pm$  SD or percentages according to the variable). To compare categorical variables,  $\chi^2$  was used, while *U Mann-Whitney* was used to compare

quantitative variables. Statistical analysis was performed using the Statistical Package for the Social Sciences version 22.0 package.

## RESULTS

Thirty-eight of 41 cases were analyzed. Three cases were excluded because HF was ruled out. The mean age of the population was  $79.6 \pm 9.2$  years, with women ( $n = 30$ , 78.9%) who came from the community ( $n = 36$ , 94.7%). The orthogeriatric model had a smaller sample than the traditional one (17 vs. 21) and more longevity (84.0 vs. 76.6,  $p = 0.009$ ). About 44.7% of the entire population was diabetic and 63.2% was hypertensive. About 26.3% of the population had a previous diagnosis of dementia. The traditional model had greater pre-fracture mobility than the orthogeriatric model (FAC-5, 18.4 vs. 36.8,  $p = 0.04$ ), but there was no difference in functionality between the two groups, with a moderate degree of dependence (Barthel  $73.9 \pm 27.8$ ). The most common place of fall was the bedroom ( $n = 12$ , 31.6%). The most common fracture was pertrochanteric ( $n = 24$ , 63.2%). About 92.1% ( $n = 35$ ) had not previously received osteoprotective treatment. The total population tended to have an abnormal cognitive screening at admission (Pfeiffer  $5.2 \pm 4.0$ ) (Table 1).

There was a tendency to have less surgical delay in the orthogeriatric model (89.3 vs. 113.0 h,  $p = 0.10$ ). The most common surgical procedure was dynamic hip screw (DHS) placement ( $n = 20$ , 52.6%). The most common reason for the delay was lack of surgical time ( $n = 33$ , 94.3%). The American Society of Anesthesiologists risk classification was  $2.6 \pm 0.5$ , with regional anesthesia predominating ( $n = 31$ , 88.6%). In-hospital pressure ulcers (PU) developed in 11.1% ( $n = 4$ ) and delirium in 32.4% ( $n = 12$ ). The orthogeriatric model during hospitalization was more likely to sit postoperatively (28.6% vs. 2.9%,  $p < 0.001$ ), has postoperative rehabilitation (34.3% vs. 5.7%,  $p = 0.00$ ), and is more likely to receive secondary prevention (38.9% vs. 22.2%,  $p = 0.00$ ). Hospital stay was shorter in the orthogeriatric model (5.5 vs. 7.5 days,  $p = 0.04$ ). There was no difference in the place of residence at discharge (institutionalization 2.7% vs. 2.7%,  $p = 0.906$ ). Mortality in the acute phase was 2.6% ( $n = 1$ ), with no difference between the two models (Table 2).

Thirty days after discharge, an individual from the traditional model was readmitted due to surgical infection. About 89.2% of the population lived up to 30 days. There was no difference in mobility in

the population ( $p = 0.20$ ) or in functionality (Barthel  $29.8 \pm 25.3$ ,  $p = 0.92$ ). 93.9% ( $n = 31$ ) lived in the community and 60.6% ( $n = 20$ ) of the population continued with secondary prevention, with no difference between the models (33.3% vs. 27.3%,  $p = 0.35$ ) (Table 3).

## DISCUSSION

In Mexico, there is a few information regarding orthogeriatric models<sup>21</sup>. Our study fulfilled its objective by determining that some indicators in OP with HF due to frailty can be improved in orthogeriatric models compared to the traditional model, revealing the viability of an orthogeriatric model in a second-level hospital in our country. Orthogeriatric models must be adapted to the needs of each hospital unit; therefore, there may be variability in the form of organization between the same second-level hospital units<sup>22,23</sup>.

We found that a quarter of the population had a previous diagnosis of dementia, similar to Mukherjee et al. that found a third of its population with prior cognitive impairment<sup>24</sup>. This finding is related to abnormal cognitive screening in our population, considering that the prevalence of falls is high in subjects with cognitive alterations<sup>25</sup>. One-third of the population had hospital-acquired delirium, and it is possible that the prevalence of cognitive impairment in our population is even higher.

One of the main goals of orthogeriatric is an early surgical procedure<sup>22</sup>. In our study, there was a tendency for a shorter surgical delay in the orthogeriatric model compared to the traditional one, but there was no statistical difference. Despite being considered a surgical emergency, in our hospital, the pre-surgical time was outside the international recommendations<sup>26</sup>. In this case, more factors related to the schedule and availability of operating rooms had an influence, a situation very similar to the rest of the country. We show that the length of stay can be shortened and possibly indirectly reduce in-hospital complications. A meta-analysis by Grigoryan et al. demonstrated that orthogeriatric services reduce the length of stay, a result similar to what we found<sup>27</sup>. A reduction in length of stay could also reduce hospitalization costs, which were not reviewed in our study.

No difference was observed in mortality either in-hospital or 30 days after discharge, unlike other studies that have shown a reduction in mortality in orthogeriatric models<sup>28</sup>. Total in-hospital mortality in

<b>Table 1. Demographic characteristics</b>				
<b>Variable</b>	<b>Orthogeriatric (n = 17)</b>	<b>Traditional (n = 21)</b>	<b>Total (n = 38)</b>	<b>p = 0.001</b>
Age	84.05 ± 10.1	76.42 ± 7.0	79.66 ± 9.21	0.009
Sex				0.709
Female	14 (36.8%)	16 (42.1%)	30 (78.9%)	
Male	3 (7.9%)	5 (13.2%)	8 (21.1%)	
Comorbidity				
DM	8 (21.1%)	9 (23.7%)	17 (44.7%)	0.796
SAH	10 (26.3%)	14 (36.8%)	24 (63.2%)	0.618
Ischemic heart disease	3 (7.9%)	3 (7.9%)	6 (15.8%)	0.778
Heart failure	3 (7.9%)	5 (13.2%)	8 (21.1%)	0.643
Chronic lung disease	2 (5.3%)	1 (2.6%)	3 (7.9%)	0.426
Dementia	5 (13.2%)	5 (13.2%)	10 (26.3%)	0.727
Place of residence				1.00
Community	16 (42.1%)	20 (52.6%)	36 (94.7%)	
Institutionalized	1 (2.6%)	1 (2.6%)	2 (5.3%)	
Pre-fracture mobility				0.042
FAC-0	0 (0.0%)	1 (2.6%)	1 (2.6%)	
FAC-1	3 (7.9%)	0 (0.0%)	3 (7.9%)	
FAC-2	4 (10.5%)	0 (0.0%)	4 (10.5%)	
FAC-3	0 (0.0%)	1 (2.6%)	1 (2.6%)	
FAC-4	3 (7.9%)	5 (36.8%)	8 (21.1%)	
FAC-5	7 (18.4%)	14 (36.8%)	21 (55.3%)	
Barthel pre-fracture	72.94 ± 28.01	74.76 ± 28.34	73.95 ± 27.80	0.847
Gait aid				0.089
Not required	6 (15.8%)	14 (36.8%)	20 (52.6%)	
Walking stick	10 (26.3%)	10 (26.3%)	15 (39.5%)	
Walker	1 (2.6%)	1 (2.6%)	3 (7.9%)	
Drop place				0.307
Bathroom	2 (5.3%)	1 (2.6%)	3 (7.9%)	
Bedroom	5 (13.2%)	7 (18.4%)	12 (31.6%)	
Stairs	0 (0.0%)	4 (10.5%)	4 (10.5%)	
Kitchen	0 (0.0%)	2 (5.3%)	2 (5.3%)	
Garage	1 (2.6%)	2 (5.3%)	3 (7.9%)	
Room	1 (2.6%)	0 (0.0%)	1 (2.6%)	
Courtyard	2 (5.3%)	3 (7.9%)	5 (13.2%)	
Hall	2 (5.3%)	1 (2.6%)	2 (5.3%)	
Another place in the house	2 (5.3%)	0 (0.0%)	2 (5.3%)	
Public road	2 (5.3%)	1 (2.6%)	3 (7.9%)	
Fracture side				0.740
Right	7 (18.4%)	7 (18.4%)	14 (36.8%)	
Left	10 (26.3%)	14 (36.8%)	24 (62.2%)	
Fracture type				0.311
Non-displaced sub-capital	1 (2.6%)	0 (0.0%)	1 (2.6%)	
Displaced Subcapital	4 (10.5%)	3 (7.9%)	7 (18.4%)	
Per-trochanteric	10 (26.3%)	14 (36.8%)	24 (63.2%)	
Subtrochanteric	0 (0.0%)	3 (7.9%)	3 (7.9%)	
Other	2 (5.3%)	1 (2.6%)	3 (7.9%)	
Pre-fracture osteoporosis treatment				0.679
No prior treatment	16 (42.1%)	19 (50.0%)	35 (92.1%)	
Pfeiffer	5.3 ± 3.8	5.19 ± 4.2	5.26 ± 4.04	0.870
Stay in the ED (h)	44.7 ± 34.2	39.4 ± 24.7	41.8 ± 29.04	0.918
Pre-admission PU	0 (0.0%)	3 (7.9%)	3 (7.9%)	0.238
Pre-admission delirium	4 (10.5%)	4 (10.5%)	8 (21.1%)	0.736

To compare categorical variables,  $\chi^2$  was used, while *U Mann-Whitney* was used to compare quantitative variables. DM: diabetes mellitus; SAH: systemic arterial hypertension; FAC: functional ambulation categories; ED: emergency department; PU: pressure ulcers.

**Table 2.** Hospital phase

Variable	Orthogeriatric	Traditional	Total	p
Type of surgery				
Partial prosthesis	6 (15.8%)	6 (15.8%)	12 (31.6%)	0.534
Total prosthesis	0 (0.0%)	2 (5.3%)	2 (5.3%)	
DHS	9 (23.7%)	11 (28.9%)	20 (52.6%)	
Non-surgical	1 (2.6%)	2 (5.3%)	3 (7.9%)	
Other	1 (2.6%)	0 (0.0%)	1 (2.6%)	
Surgical delay (h)	89.3 ± 47.99	113.0 ± 58.66	102.20 ± 54.59	0.101
Cause of delay				
Lack of surgical time	16 (45.7%)	17 (48.6%)	33 (94.3%)	0.489
Clinical instability	0 (0.0%)	2 (5.7%)	2 (5.7%)	
ASA	2.59 ± 0.618	2.71 ± 0.463	2.66 ± 0.534	0.587
Type of anesthesia				
Regional	15 (42.9%)	16 (45.7%)	31 (88.6%)	0.409
General	0 (0.0%)	2 (5.7%)	2 (5.7%)	
Mixed	1 (2.9%)	1 (2.9%)	2 (5.7%)	
In-hospital PU	1 (2.8%)	3 (8.3%)	4 (11.1%)	0.605
In-hospital delirium	6 (16.2%)	6 (16.2%)	12 (32.4%)	0.732
Pre-surgical	5 (13.5%)	5 (13.5%)	10 (27.0%)	0.763
Sat post-surgical	10 (28.6%)	1 (2.9%)	11 (31.4%)	0.001
Post-surgical rehabilitation	12 (34.3%)	2 (5.7%)	14 (40.0%)	0.000
Destination at discharge				
Community	16 (43.2%)	19 (51.4%)	35 (94.5%)	0.906
Institutionalization	1 (2.7%)	1 (2.7%)	2 (5.4%)	
Secondary prevention at discharge	14 (38.9%)	8 (22.2%)	22 (61.1%)	0.006
Hospital stays (days)	5.59 ± 2.00	7.50 ± 3.03	6.62 ± 2.75	0.041
Acute phase mortality	0 (0.0%)	1 (2.6%)	1 (2.6%)	0.362
Pre-surgical	0 (0.0%)	1 (2.6%)	1 (2.6%)	0.362

To compare categorical variables,  $\chi^2$  was used, while *U Man Whitney* was used to compare quantitative variables. DHS: dynamic hip screw; ASA: American Society of Anesthesiology; PU: pressure ulcers.

our study is even lower compared to that described in the literature (5-24%)<sup>24,29</sup>. There was a trend toward higher mortality 30 days after discharge in the traditional model; however, our sample was small, and we found no statistical difference.

The orthogeriatric model had a greater possibility of sitting down and having post-surgical rehabilitation, this may be the result of greater coordination between the medical areas. The lack of specialized personnel may influence this result and must be adapted to the particularities of each hospital unit. We did not find a difference in post-surgical autonomy; however, at the beginning of the study, the individuals in the orthogeriatric model had worse autonomy than the traditional model, which could have influenced the result. Post-surgical rehabilitation has great evidence; however, the activities that we provide are based on training the family members and depend

on their cooperation, which could modify the results, since, in the literature, there is a clear benefit<sup>30</sup>.

Finally, the orthogeriatric model was more likely to provide secondary prevention after HF, a finding like that found in some meta-analyses<sup>31</sup>. However, we found no treatment difference 30 days after discharge which can be explained by high dropout rates. Implementation of increased follow-up is likely to help improve adherence<sup>32</sup>.

Our study had major limitations. The first limitation is related to the duration of the study. Due to the pandemic situation, it was not possible to continue with the study as planned. Second, there are few geriatric and rehabilitative medical personnel, which limits coverage in shifts. We do not have physiotherapists, which limits the strategies that are proposed in rehabilitation. A third limitation is that we do not consider variables that include in-hospital complications,



**Table 3.** Phase of 30 days after hospital discharge

Variable	Orthogeriatric	Traditional	Total	p
Readmission 30 days	0 (0.0%)	1 (2.8%)	1 (2.8%)	0.364
Mortality 30 days	1 (2.7%)	3 (8.1%)	4 (10.8%)	0.355
Reoperation 30 days	0 (0.0%)	1 (3.0%)	1 (3.0%)	0.325
Reason for re-intervention				
Surgical wash	0 (0.0%)	1 (3.0%)	1 (3.0%)	0.325
FAC at 30 days				
FAC-0	6 (18.2%)	9 (27.3%)	15 (45.5%)	0.203
FAC-0.1	0 (0.0%)	2 (6.1%)	2 (6.1%)	
FAC-1	3 (9.1%)	1 (3.0%)	4 (12.1%)	
FAC-2	4 (12.1%)	2 (6.1%)	6 (18.2%)	
FAC-3	3 (9.1%)	1 (3.0%)	4 (12.1%)	
FAC-4	0 (0.0%)	2 (6.1%)	2 (6.1%)	
FAC-5	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Residence at 30 days				
Community	15 (45.5%)	16 (48.5%)	31 (93.9%)	0.965
Institutionalization	1 (3.0%)	1 (3.0%)	2 (6.1%)	
Gait assistant at 30 days				
Walking stick	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.343
Walker	8 (24.2%)	5 (15.2%)	13 (39.4%)	
Secondary prevention at 30 days	11 (33.3%)	9 (27.3%)	20 (60.6%)	0.353
Barthel at 30 days	28.13 ± 20.96	31.47 ± 29.5	29.85 ± 25.38	0.928

To compare categorical variables,  $\chi^2$  was used, while *U Mann-Whitney* was used to compare quantitative variables.  
FAC: functional ambulation categories.

frailty, and sarcopenia that could modify the results. Frailty increases the risk of adverse events, and its prevalence increases with older age groups<sup>33</sup>. The intervention group was older than the control group, so the intervention group might be expected to have a higher prevalence of frailty and a higher risk of adverse events compared to the control group, which could alter the results. We also do not consider the time from fracture to admission to the emergency department. This data may be related to family abandonment and could modify the results. Fourth, the follow-up was only 30 days. A longer follow-up could demonstrate other types of results related to autonomy, quality of life, and fear of falling<sup>34</sup>. Finally, non-probability sampling for convenience has the risk of sampling bias that could have an impact on our results.

Up to now, our study is one of the few carried out in the country and lays the foundations for the development of similar studies that generate more evidence. The results will help generate better care protocols within second-level hospitals. Having similar studies will help to generate consensus in our environment.

## CONCLUSIONS

The orthogeriatric model in a second-level hospital in our environment is related to a decrease in the length of hospital stay, a greater possibility of sitting down in the post-surgical period, and having rehabilitation. We also found that the orthogeriatric model was more likely to receive secondary prevention after discharge. No difference in in-hospital or discharge mortality was identified. The results lay the foundations to develop a better care protocol in second-level hospitals; however, each unit must individualize their care according to the available resources.

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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 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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# Relation between adverse drugs reactions with potentially inappropriate prescription in hospitalized older adults

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## Abstract

**Endpoint:** The aim of the study was to analyze the relationship between adverse drug reactions (ADRs) and potentially inappropriate prescriptions (PIPs) in hospitalized older adults. **Methods:** This was an observational, cross-sectional, and retrospective study. Older adults hospitalized in the Cardiology department between June 2019 and January 2020 were included in the study. PIPs were determined using the Beers and Screening Tool of Older Person's Prescriptions (STOPP)/Screening Tool to Alert doctors to Right appropriate, indicated Treatment (START) criteria. A review of clinical records was carried out to identify principal ADRs to analyze their relationship using Chi-square, Mann-Whitney U test, and odds ratio on statistical software Statistical Package for the Social Sciences v22. **Results:** Five hundred and eighty-four patients were included in the study; 56% male, with a median age of 76 years. The prevalence of PIPs and ADRs was 46% and 64%, respectively. The PIPs demonstrated an odds ratio: 2.45 confidence interval (1.71-3.45),  $p = 0.0001$  for ADRs. The prescription tools showed an adequate diagnostic value for ADRs with the following characteristics: Beers Criteria (sensitivity: 37%, specificity: 81%) and STOPP Criteria (sensitivity: 29%, specificity: 84%). **Conclusions:** PIPs were related to ADRs during the hospitalization, showing that the Beers Criteria and STOPP Criteria are adequate diagnostic value tools. **Originality:** First study in a Mexican population was to evaluate the relationship between PIPs and ADRs in hospitalized older patients.

**Keywords:** Beers criteria. STOPP/START criteria. Drugs. Adverse drug reaction.

## Relación entre reacciones adversas a medicamentos con prescripción potencialmente inapropiada en adultos mayores hospitalizados

### Resumen

**Objetivo:** Analizar la relación entre reacciones adversas a medicamentos con la prescripción potencialmente inapropiada en adultos mayores hospitalizados. **Método:** Estudio observacional, transversal y retrospectivo, se incluyeron adultos mayores hospitalizados en el departamento de Cardiología del periodo de junio 2019 a enero 2020. Se determinaron la prescripción potencialmente inapropiada durante las primeras 24 horas de estancia hospitalaria, mediante los criterios de Beers y Criterios STOPP/START. Se realizó una revisión de expedientes clínicos buscando las principales reacciones adversas a medicamentos, para posteriormente analizar su relación utilizando Chi cuadrada, U de Mann Whitney y odds ratio con el programa estadístico SPSS v22. **Resultados:** Se incluyeron 584 pacientes; 56% hombres, con mediana de edad de 76 años. La prevalencia para la prescripción potencialmente inapropiada fue de 46%, y para reacciones adversas a medicamentos de 64%. La prescripción potencialmente inapropiada demostró un OR: 2.45; CI (1.71-3.45),  $p = 0.0001$  a reacciones adversas a medicamentos. Las herramientas de prescripción presentaron un adecuado valor diagnóstico para determinar prescripción potencialmente inapropiada con las

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siguientes características: Criterios de Beers (sensibilidad: 37%, especificidad: 81%), y Criterios STOPP (sensibilidad: 29%, especificidad: 84%). **Conclusiones:** La prescripción potencialmente inapropiada se relacionaron a reacciones adversas a medicamentos durante el internamiento de pacientes mayores, demostrando que los Criterios de Beers y Criterios STOPP son herramientas con un adecuado valor diagnóstico. **Originalidad:** Primer estudio en población mexicana que evalúa la relación entre prescripción potencialmente inapropiada y prescripción potencialmente inapropiada en pacientes mayores hospitalizados.

**Palabras clave:** Criterios de Beers. Criterios STOPP/START. Medicamentos. RAM.

## INTRODUCTION

Older adults receive a greater number of prescriptions and are more exposed to the development of adverse drug reaction (ADR), defined by the World Health Organization as any unwanted response to a drug at doses used for prophylaxis, diagnosis, and treatment<sup>1</sup>. Older adults present physiological compositional changes, such as increased percentage of body fat, decreased total body water, and decreased renal clearance, which leads to an accumulation of metabolites, making the development of adverse effects more likely<sup>2</sup>.

Tools have been designed to improve drug prescription. Explicit criteria are agreed upon in consensus with an accepted standard and can be applied with minimal clinical interpretation<sup>3</sup>. The first explicit criteria were the Beers Criteria, published by the American Geriatrics Society in 1991. Likewise, the Screening Tool of Older Person's Prescriptions (STOPP)/Screening Tool to Alert doctors to Right appropriate, indicated Treatment (START) criteria were published in 2008 by Gallagher and colleagues in Ireland and later endorsed by the European Society of Geriatrics, the most novel contribution of which was the inclusion of a list that sought to detect the lack of use of potentially indicated drugs (START Criteria). A cohort in Ireland using the STOPP Criteria observed a 42% prevalence of potentially inappropriate prescription (PIP) and determined that those who present 2 or more PIP have twice the risk of presenting ADR<sup>4</sup>. Concluding that the number of drugs is not as relevant as the number of PIP<sup>5</sup>.

ADR has been reported in approximately 30% at the time of hospital admission in older adults, between 15% and 65% of ADR are preventable by avoiding inappropriate prescription<sup>6</sup>. The average incidence of ADR in the hospitalized geriatric population is reported to be between 14% and 88%, it has been described that patients with heart disease are the ones who mostly receive prescriptions<sup>7</sup>. Few studies have evaluated the consequences of inappropriate prescriptions in hospitalized older patients. The study in a cardiology department, the first one on the

Mexican population of this nature, sought to find an association between ADR and PIP by evaluating the value of reasoned prescription tools, comparing their effectiveness, and relating them to unwanted outcomes in hospitalized older adults.

The primary endpoint of the study was to analyze the relationship between ADR and PIP in hospitalized older adults with heart disease. The secondary endpoints were to determine the prevalence and types of ADR and the sociodemographic and clinical characteristics associated with PIP and ADR, to evaluate the parameters of the Comprehensive Geriatric Assessment (CGA) that are related to the development of ADR, and to compare the different tools of Inappropriate Prescription (Beers Criteria and STOPP/START Criteria) with the development of ADR.

## MATERIALS AND METHODS

### Study design

This was an observational, cross-sectional, analytical, and retrospective study. Considered no greater than minimal risk. The study was approved by the local Research Ethics Committee and the Hospital Health Research Committee for data collection and use for research purposes, maintaining the anonymity of the research subjects. Registration number: R-2020-1902-020.

### Participants

A total of 584 study subjects were included: adults over 69 years old, without gender preference, who were hospitalized in the cardiology department of a 3<sup>rd</sup> level hospital in northeastern Mexico, and who underwent CGA for the first time by the Geriatric department. Patients with incomplete medical records were excluded for the purposes of this study as well as for subsequent hospitalizations during the study period. Patients with a diagnosis at admission that overlapped with those used to determine ADR were eliminated (see in variables).

## Variables

A review of the clinical records was carried out, covering only the documents made during the hospitalization of its first assessment by the geriatric department. Data recollection was performed by transcribing what was reported in the clinical records: evolution notes, laboratory reports, nursing notes, and clinical nutrition notes. Sociodemographic, clinical, and paraclinical variables, and geriatric syndromes reported on CGA were collected.

## Comprehensive Geriatric Assessment

During the first 24 h of hospitalization, patients over 69 years of age undergo CGA by the geriatric department composed by geriatric specialists and residents in training in this area. Geriatric syndromes were identified using various tools: polypharmacy was defined by the prescription of five or more drugs; in-hospital and chronic functional decline was determined with a score on the Barthel Index for Activities of Daily Living<sup>8</sup>  $\leq 60$  points; probable sarcopenia was defined using the Strength, Assistance in walking, Rise from chair, Climb stairs, Falls (SARC-F) scale<sup>9</sup> with a value greater than or equal to 4 points; frailty syndrome was reported in the CGA with the Fatigue, Resistance, Aerobic, Illnesses, Lost of weight (FRAIL)<sup>10</sup>, Ensrud<sup>11</sup>, or Edmonton scale<sup>12</sup>; immobility syndrome; cognitive impairment was clinically assessed and was reported as present or absent; previous episode of delirium was determined at this point and malnutrition syndrome was defined using the Mini-Nutritional Assessment<sup>13</sup> with a score  $\leq 17$  points. All of this was carried out by the geriatric first contact evaluator through the medical interview.

## PIP

The Beers Criteria v2019<sup>14</sup> and STOPP/START Criteria v2015<sup>15</sup> were applied to the list of hospital medications reported in the CGA.

## ADR

The presence of one or more of the following ADR were detected intrahospitally secondary to previous PIP, such complications included: hypokalemia ( $< 3.0$  mEq/L), hyperkalemia ( $> 5.5$  mEq/L), hyponatremia ( $< 130$  mEq/L), hypernatremia ( $> 150$  mEq/L), hypocalcemia ( $< 8.5$  mEq/L), hypercalcemia ( $> 10.2$

mEq/L), QT interval prolongation (male:  $> 450$  ms; female:  $> 480$  ms), bradycardia (cardiac frequency  $< 60$  bpm plus low cardiac output symptoms  $< 40$  bpm asymptomatic), sangrado (from any site), thromboembolism, hyperglycemia ( $> 200$  mg/dL), hypoglycemia ( $< 70$  mg/dL), delirium, falls, anemia, thrombocytopenia ( $< 150\,000$  cells/ $m^3$ ), diarrhea, constipation ( $> 72$  h), dyspepsia, acute kidney injury (AKI) (glomerular filtration rate  $< 50\%$ , serum creatinine elevation 2 times its basal level or urinary index  $< 0.5$  mL/kg/h), urticaria and/or angioedema, and other complication.

## Statistical analysis

The quantitative variables were in accordance with the distribution curve non-symmetric, determined by the Kolmogorov–Smirnov test and were reported with the measured central tendency (median) and dispersion (minimum and maximum ranges), and the Mann–Whitney U test was used. The qualitative variables are shown as frequency percentages for the inferential statistics, and the Chi-square test was used. The prevalence ratio, 95% confidence interval, and level of statistical significance  $p < 0.05$  were determined. Odds ratios were measured and sensitivity and specificity were calculated for each reasoned prescription tool. Data were analyzed using Statistical Package for the Social Sciences v22.

## RESULTS

### Demographic characteristics

From November 2019 to June 2020, 785 CGA were performed by the Geriatrics Department; 201 subjects who did not meet the selection criteria to be considered in the study were excluded, resulting in a total of 584 patients. About 56% were male, with a median age of 76 years, a median hospital stays of 5 days, and 80% were admitted urgently. The characteristics of hospitalization, procedures performed during the hospital stay, and comorbidities on admission were determined (Table 1). The admission diagnoses are shown by frequency in figure 1. Geriatric syndromes reported in CGA were evaluated (Table 2).

### Sub analysis in subjects with PIP

Using the Beers criteria, a prevalence of 31% was determined for the STOPP criteria 25% and for the



**Table 1.** Population characteristics and comorbidities, differences between patients with and without PIP

Characteristics	Total, n = 584 (%)	PIP, n = 266 (%)	No PIP, n = 318 (%)
Male	326 (56)	152 (57)	174 (53)
Female	258 (44)	114 (43)	144 (56)
Age <sup>†</sup>	76 (70-97)	76 (70-97)	76 (70-97)
Body mass index <sup>†</sup>	26.65 (16.5-46.8)	27 (16.5-41.3)	26.6 (18-46.8)
Days of hospitalization <sup>†</sup>	5 (1-55)	5 (1-34)	5 (2-55)
Years of schooling <sup>†</sup>	6 (0-22)	6 (0-22)	6 (0-22)
Coronary angiography	287 (49)	137 (52)	150 (47)
Bypass surgery or valve replacement	65 (11)	38 (14)*	27 (8)
IV contrast-media	297 (51)	143 (54)	154 (48)
<b>Comorbidities</b>			
Arterial hypertension	442 (76)	205 (77)	237 (75)
Diabetes mellitus type 2	276 (47)	134 (50)	142 (45)
Chronic coronary syndrome	194 (33)	98 (37)	96 (30)
Prostatic hyperplasia	83 (14)	61 (23)*	22 (7)
Cardiac arrhythmia (any type)	82 (14)	44 (17)	38 (12)
Dyslipidemia	80 (14)	42 (16)	38 (12)
Congestive heart failure	64 (11)	39 (15)*	25 (8)
Chronic kidney disease	51 (9)	32 (12)*	19 (6)
Cerebrovascular disease	30 (5)	16 (6)	14 (4)
Malignant neoplasm (any type)	29 (5)	16 (6)	13 (4)
Hypothyroidism	28 (5)	15 (6)	13 (4)
Major depression disorder	27 (5)	21 (8)*	6 (2)
Osteoporosis	15 (3)	13 (5)*	2 (1)
Chronic obstructive pulmonary disease	14 (2)	12 (5)*	2 (1)
Peripheral venous insufficiency	10 (2)	3 (1)	7 (2)
Major neurocognitive disorder	10 (2)	7 (3)	3 (1)

\*p ≤ 0.005.

<sup>†</sup>Median (Minimum range- maximum range).

IV: intravenous; PIP: potentially inappropriate prescription.

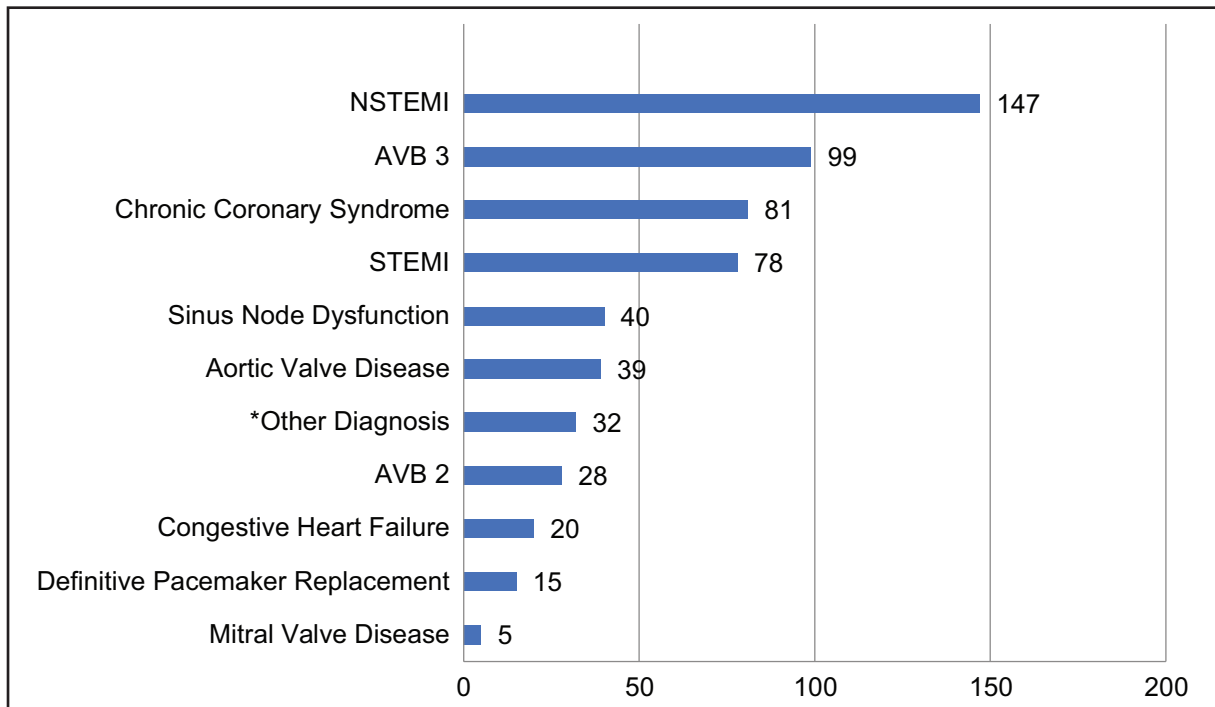
START criteria 18%. A comparative sub-analysis of the study variables was performed between those with at least one PIP and those who did not present any criteria. It was observed that those who underwent myocardial revascularization surgery or aortic valve replacement had an odds ratio (OR): 1.80; confidence interval (CI): (1.07-3.03), p = 0.027 to receive any medication considered as PIP. The comorbidities that were significantly associated with PIP were as follows: prostatic hyperplasia OR: 4.0; CI: (2.38-6.72), p = 0.0001; congestive heart failure OR: 2.01; CI: (1.18-3.42), p = 0.009; chronic kidney disease OR: 2.15; CI: (1.19-3.89), p = 0.01; major depressive disorder OR: 4.46; CI: (1.77-11.21), p = 0.001; osteoporosis OR: 8.12; CI: (1.82-36.3), p = 0.001; and chronic obstructive pulmonary disease OR: 7.47 CI: (1.66-33.66), p = 0.002 (Table 1). In relation to geriatric syndromes were significantly associated to PIP polypharmacy OR: 2.18; CI: (1.48- 3.22), p = 0.0001 and chronic functional decline OR: 2.12; 95% CI: (1.04-4.29), p = 0.034 (Table 2).

### Study end points

Using the Beers criteria and STOPP/START criteria, the prevalence of PIP was 46%, whereas the prevalence of any in-hospital complication related to ADR was 64%. The presence of PIP confers an OR: 2.45; CI: (1.71-3.45), p = 0.0001 for ARD. In the analysis for each prescription tool, the Beers criteria and STOPP criteria demonstrated a significant association, but not the START criteria (Table 3). Diagnosis value calculation was performed for the Beers criteria, a sensitivity of 37% and specificity of 81%; for the STOPP criteria, a sensitivity of 29% and a specificity of 84% were observed.

In-hospital complications related to ADR were determined (Table 4); PIP was significantly associated with AKI OR: 1.58; CI: (1.09-2.84), p = 0.015; hyperglycemia OR: 1.81; CI: (1.2-2.72), p = 0.004; hospital-acquired delirium OR: 1.79; CI: (1.09-2.93), p = 0.02, and over-anticoagulation OR: 2.21; CI: (2.02-2.42), p = 0.028.





**Figure 1.** Admission diagnoses. Other diagnosis: Other non-aortic or non-mitral valve diseases, Tachyarrhythmias and Pericardial pathology, Infectious endocarditis. AVB 3: 3<sup>rd</sup> degree Atrioventricular Block; AVB 2: 2<sup>nd</sup> degree Atrioventricular Block; STEMI: ST-segment elevation Acute Coronary Syndrome; NSTEMI: Non-ST-segment elevation Acute Coronary Syndrome.

**Table 2.** Geriatric syndromes reported on CGA, differences between patients with and without PIP

Geriatric syndromes	Total, n = 584 (%)	PIP, n = 266 (%)	No PIP, n = 318 (%)
Polypharmacy (5 or more drugs)	430 (74)	217 (82)*	213 (67)
Number of drugs <sup>†</sup>	6 (0-13)	7 (0-13)	6 (0-12)
In-hospital functional decline	263 (45)	122 (46)	141 (44)
Probable sarcopenia	165 (28)	80 (30)	85 (27)
Frailty syndrome	148 (25)	77 (29)	71 (22)
Immobility syndrome	109 (19)	46 (17)	63 (20)
Cognitive impairment	74 (13)	23 (9)*	51 (16)
Previous delirium episode	39 (7)	23 (9)	16 (5)
Chronic functional decline	35 (6)	22 (8)*	13 (4)
Malnutrition	28 (5)	14 (5)	14 (4)

\*p ≤ 0.005.  
<sup>†</sup>Median (Minimum range- maximum range).  
 CGA: comprehensive geriatric assessment; PIP: potentially inappropriate prescription.

In the analysis of reported geriatrics, it was found that there is a risk for development of ADR with previous delirium OR: 2.25; CI: (1.01-4.98), p = 0.041; in-hospital functional decline OR: 1.43; CI: (1.01-2.01), p = 0.043; and probable sarcopenia OR: 1.51; CI: (1.02-2.22), p = 0.39 (Table 5).

## DISCUSSION

In this study, it was shown that there is a relationship between PIP using explicit prescription tools, Beers criteria and STOPP/START criteria, and the development of in-hospital complications related to

**Table 3.** Odds ratio for the presence of ADR and PIP criteria

Criteria	ADR		p	OR 95% (CI)
	Yes	No		
	n (%)	n (%)		
PIP	200 (75)	66 (25)	0.0001	2.45 (1.71-3.45)
Beers criteria	140 (78)	39 (22)	0.0001	2.57 (1.71-3.86)
STOPP criteria	111 (77)	33 (23)	0.0001	2.22 (1.44-3.43)
START criteria	76 (71)	31 (29)	0.112	1.45 (0.92-2.29)

ADR: adverse drug reaction; OR: odds ratio; PIP: potentially inappropriate prescription; STOPP: screening tool of older person's prescriptions; START: screening tool to alert doctors to right appropriate, indicated treatment.  
Statistical significance  $p \leq 0.05$ .

ADR. A high prevalence of PIP was found, like that reported in the literature in hospitalized older adult patients<sup>16,17</sup>. With respect to ADR, a higher prevalence was found than that reported in the literature in community dwelling, a study carried out in a hospital reported a similar prevalence<sup>18</sup>. Not all in-hospital complications could be related to the effects of medications; there were population differences between the subjects with and without PIP. It should be noted that 11% of subjects studied underwent some surgical procedure, which may be related to the development of complications during hospitalization, being reported in recent studies with a prevalence between 8% and 23%<sup>19</sup>. The Beers and STOPP criteria are tools with good diagnostic value for predicting the development of ADR. In a Latin American study carried out in older adults, it was observed that the drugs that were most associated with the development of ADR were cardiovascular drugs (43%), followed by psychotropic drugs (18%)<sup>20</sup>.

The most prevalent in-hospital complication related to ADR was AKI; despite the fact that the use of intravenous contrast medium is not part in the explicit criteria of reasoned prescription, in the sample of this study, it was observed that 51% underwent some diagnostic-therapeutic procedure with contrast-media, 49% underwent coronary angiography; it is inferred that the high prevalence of AKI could be associated with Contrast-Media-Induced AKI, being a point to consider in the future assessments the use of contrast media as a risk factor for the development ADR, this finding has been reported in the literature with an incidence in 10% in general population<sup>21</sup>; in the SILVER-AMI study, carried out in people older than 75 years, an incidence in 19% was reported with a significant increase in mortality<sup>22</sup>.

A previous episode of delirium was associated with a greater risk for ADR, a meta-analysis shows an association between an episode of delirium with a long-term cognitive impairment, inferring the existence of brain vulnerability in these patients that predisposes to unwanted outcomes<sup>23</sup>. In this study, an association between ADR and in-hospital functional decline was reported, with a prevalence higher than that estimated in a meta-analysis conducted in older people, and it was observed that this geriatric syndrome was associated with a progression to functional dependence and a longer in-hospital stay<sup>24</sup>. Finally, the probable sarcopenia, reported on CGA, the prevalence observed in this study was lower than that reported in a meta-analysis in hospitalized older adults patients, as well as an association between sarcopenia with functional decline and malnutrition<sup>25</sup>. In the literature, reference has been made to the association between scales for depression and functionality with in-hospital complications with weak correlations<sup>26</sup>, therefore, it is considered an area of opportunity to continue studying the relation between geriatric syndromes detected through CGA in older patients hospitalized with unfavorable outcomes. Neither was found a relation with ADR with frailty syndrome, cognitive impairment, multimorbidity,<sup>27</sup> or mortality<sup>28</sup> which were reported in other studies<sup>29</sup>.

The strengths of this study were obtaining a representative sample larger than estimated; the application of different reasoned prescription tools; and the capture of clinical characteristics and geriatric syndromes of patients, which are characterized by a detailed description of the social, functional, cognitive, nutritional, and clinical situations. The limitations that were found were the evaluation in a single

**Table 4.** In-hospital complications related to ADR developed during the hospitalization period, differences between subjects with and without PIP

Complications	Total, n = 584 (%) PIP, n = 266 (%) No PIP, n = 318 (%)		
Adverse drug reaction	376 (64)	200 (75)*	176 (55)
Acute kidney injury	154 (26)	83 (31)*	71 (22)
Hyperglycemia > 180 mg/dL	117 (20)	67 (25) *	50 (16)
Hypocalcemia < 8.5 mEq/L	110 (19)	53 (20)	57 (18)
Thrombocytopenia < 150 000 cells/mm <sup>3</sup>	109 (19)	49 (18)	60 (19)
Hemoglobin decrease > 2 g/dL	78 (13)	39 (15)	39 (12)
Acquiring hospital delirium	74 (13)	43 (16)*	31 (10)
Constipation > 72 h	54 (9)	27 (10)	27 (8)
Bradycardia < 60 bpm plus symptoms or < 40 bpm	28 (5)	15 (6)	13 (4)
Hemorrhage	28 (5)	13 (5)	15 (5)
QT prolongation male > 450 ms; female > 480 ms	27 (5)	8 (3)	19 (6)
Hyperkalemia > 5.5 mEq/L	23 (4)	10 (4)	13 (4)
Hypoglycemia < 70 mg/dL	23 (4)	12 (5)	11 (3)
Death	19 (3)	9 (3)	10 (3)
Hyponatremia < 130 mEq/L	17 (3)	7 (3)	10 (3)
Infection (pulmonary, soft tissue, urinary)	17 (3)	7 (3)	10 (3)
Hypokalemia < 3.0 mEq/L	10 (2)	7 (3)	4 (1)
Hypernatremia > 150 mEq/L	10 (2)	5 (2)	5 (2)
Thromboembolism	7 (1)	5 (2)	2 (1)
Lower hypotension 90/60 mmHg	7 (1)	4 (2)	3 (1)
Dyspepsia	6 (1)	1 (0)	5 (2)
Hypomagnesemia < 1.5 mEq/L	6 (1)	3 (1)	3 (1)
Diarrhea	5 (1)	2 (1)	3 (1)
Over anticoagulation	4 (1)	4 (2)*	0 (0)

\*p ≤ 0.005.

ADR: adverse drug reaction; PIP: potentially inappropriate prescription.

**Table 5.** Odds ratio for the presence of ADR and geriatric syndromes reported on GCA

Geriatrics syndromes	ADR		p	OR 95% (CI)
	Yes	No		
	n (%)	n (%)		
Cognitive impairment	47 (64)	27 (37)	0.867	0.95 (0.58-1.59)
Previous delirium episode	31 (80)	8 (21)	0.041	2.25 (1.01-4.98)
Chronic functional decline	24 (69)	11 (31)	0.59	1.22 (0.59-2.55)
In-hospital functional decline	181 (69)	82 (31)	0.043	1.43 (1.01-2.01)
Frailty syndrome	104 (70)	44 (30)	0.089	1.42 (0.95-2.12)
Malnutrition	17 (61)	11 (39)	0.678	0.85 (0.39-1.85)
Immobility syndrome	77 (71)	32 (29)	0.13	1.42 (0.90-2.23)
Probable sarcopenia	117 (71)	48 (29)	0.039	1.51 (1.02-2.22)
Polypharmacy	285 (66)	145 (34)	0.11	1.36 (0.93-1.99)

ADR: adverse drug reaction; CGA: comprehensive geriatric assessment; OR: odds ratio.

Statistical significance p ≤ 0.05.

center, the homogeneity of the admission diagnoses, and the need to require a greater number of medications because the optimal medical treatment for coronary disease, valvular pathology, or heart failure requires it. Similarly, at the time of making a comparison between the population with some criteria for PIP and those who did not, clinical differences were found in medical history, cardiac surgery during hospitalization, exposure to contrast media, and some geriatric syndromes. Although they were related to PIP, they did not reflect an association with ADR development.

This study did not demonstrate that PIP was related to longer hospital stay and increased in-hospital mortality, as reported in the literature. Because it is retrospective, causality cannot be inferred between the study variables. Therefore, it is necessary to use the findings already described for the development of a surveillance tool for prescriptions with a high risk of developing ADR to implement pharmacovigilance and prevention programs for in-hospital complications in the older person. Although the Beers Criteria and STOPP/START Criteria have adequate diagnostic value, their application in daily clinical practice represents a challenge in its execution because of its extension.

## CONCLUSIONS

PIP was associated with a higher risk for the development of ADR in hospitalized older adults patients, and the Beers criteria and the STOPP criteria, but not the START criteria, are reasoned prescription tools that can be used in practice. Adequate clinical diagnostic value. There are also considerations, such as surgical procedures and geriatric syndromes, such as a history of delirium, acute functional depression, and probable sarcopenia, which are related to the development of ADR. The presence of PPI has greater clinical relevance than the number of medications, which reflects the importance of a reasoned prescription of medications based on scientific evidence and contemplating the characteristics of older persons that could increase the risk of developing ADR. With the results of this study, we will seek to create a tool for pharmacovigilance and prevent adverse effects with the intention of reducing the incidence of in-hospital complications in hospitalized older patients, opening the possibility of continuing this line of research and conducting a clinical trial.

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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 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.

**Right to privacy and informed consent.** Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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# Quality of life in elderly adults with infarct code in cardiac rehabilitation

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## Abstract

**Introduction:** Ischemic heart disease, the leading cause of death in this age group, increases dependency and disability. Cardiac rehabilitation reduces hospital readmissions, morbidity, and mortality and improves function and quality of life (QoL). Few studies on older Mexicans have analyzed the impact of cardiac rehabilitation on the perception of QoL. **Objectives:** The aim is to compare the initial and final measurements of QoL of cardiac rehabilitation therapy in older adults using the infarct code program. **Materials and methods:** This is an analytical cross-sectional study. Patients  $\geq 60$  years of the Infarct Code program who completed Cardiac Rehabilitation during 2018-2021, with initial and final measurements of the Velasco del Barrio instrument, were included. Demographic variables, comorbidities, and physical improvement were also documented. The analyses were performed using descriptive and inferential statistical methods. **Results:** A total of 143 patients were included in this study, 80% of male, with a median age of 67 years. Arterial hypertension (71%) and diabetes mellitus (52%) were the primary comorbidities. The initial metabolic equivalent of task was  $5 \pm 1.7$  versus the final  $7.3 \pm 2$ . Regarding the instrument applied, 18% had an excellent QoL, 78% were good, and 3.5% were intermediate. Finally, 75% had an excellent QoL, and 25% had a good QoL, with statistical significance. **Conclusions:** Older patients who completed the cardiac rehabilitation program had improved QoL in all dimensions.

**Keywords:** Older adults. Cardiac rehabilitation. Quality of life.

## Calidad de vida en adultos mayores de código infarto en rehabilitación cardíaca

### Resumen

**Introducción:** La cardiopatía isquémica principal causa de muerte en adultos mayores, incrementa la dependencia y discapacidad. Este grupo etario tiene limitado acceso a rehabilitación cardíaca después de un infarto, aun conociendo el beneficio en la disminución de mortalidad, morbilidad y reingresos hospitalarios, también existe mejoría sobre la función y calidad de vida. En México existen estudios limitados en personas mayores infartadas, que analicen el impacto de la rehabilitación cardíaca en la percepción de la calidad de vida. **Objetivo:** Comparar la calidad de vida inicial y final de terapia de rehabilitación cardíaca en adultos mayores del programa de Código Infarto. **Material y Métodos:** Estudio transversal analítico, donde se incluyó pacientes  $\geq 60$  años del programa Código Infarto, que terminaron Rehabilitación Cardíaca durante 2018-2021, con medición inicial y final del instrumento de Velasco del Barrio que mide la percepción de la calidad de vida. Se documentaron variables demográficas, de comorbilidad, y mejoría física. El análisis se realizó con estadística descriptiva e inferencial. **Resultados:** Un total de 143 pacientes, con edad promedio de 67 años, 80% eran hombres. En cuanto a comorbilidad: 71% tenían hipertensión arterial, 52% diabetes mellitus. Los Equivalentes Metabólicos de Tareas iniciales fueron  $5 \pm 1.7$  vs las finales  $7.3 \pm 2$ . Los resultados obtenidos del cuestionario de Velasco del Barrio al inicio fue de 18% considerándose una calidad de vida excelente, 78% buena y 3.5% intermedia.

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Al finalizar 75% tuvo excelente calidad de vida y 25% buena, con significancia estadística. **Conclusiones:** Los pacientes mayores que concluyeron el programa de rehabilitación cardiaca mejoraron calidad de vida en todas sus dimensiones.

**Palabras clave:** Adulto mayor. Rehabilitación cardiaca. Calidad de vida.

## INTRODUCTION

This study identified three points: First, the high prevalence of ischemic heart disease in older adults; second, deconditioning and functional dejection that it causes; and third, few opportunities for older adults to receive certain interventions. According to the World Health Organization, 17 million people worldwide die of cardiovascular disease (CVD) annually. In people  $\geq 75$  years old, it remains the main cause of death and disability<sup>1-3</sup>.

In Mexico, they affect 26% of the population, with a total cost of \$6.1 billion dollars, accounting for 4% of all health spending<sup>4</sup>.

The health sector strategy for the timely reperfusion treatment of acute coronary syndrome (ACS) is the "Infarct Code," which consists of training hospital centers for diagnosis, treatment, and early referral to a specialized center to perform urgent angioplasty<sup>5</sup>.

Cardiac rehabilitation (CR) is a comprehensive lifestyle program that promotes physical activity, education, diet, risk reduction, and adherence. In older adults, it has also been associated with improvement in cognition, frailty, sarcopenia, depression, gait and balance, improvement in the metabolic profile and control of cardiovascular risk factors, quality of life (QoL), and functional capacity and mortality<sup>3,6-11</sup>.

CR is composed of three phases: Phase I, from hospital admission to discharge; Phase II, from discharge to 6 weeks after the CVD; and Phase III, from week 6 to 3 months after the event<sup>7</sup>. Phase II includes supervised physical training, psychological actions, and advice on nutrition, etc<sup>12</sup>. Older adults represent a special challenge for medicine and CR, because they have more comorbidities, polypharmacy, cognitive problems, functional, nutritional, and psychosocial impairment that reduce their ability to exercise, and they depend on other people for transport to the hospital<sup>13</sup>.

In addition, they are less likely to be referred to CR programs, especially if they are women and are generally excluded from trials, even though most ischemic heart disease (IHD) patients are over 65 years of age<sup>7</sup>.

One study compared the CR results in 133 women with a mean age of 63 years. The CR program improved women's general health perceptions, mental health, vitality, and social functioning in women<sup>14</sup>.

In 2015, Jacob et al. evaluated 11,862 patients aged  $\geq 65$  years with CR after acute myocardial infarction (AMI). They found that for each increase of five sessions, there was a 13% decrease in the outcomes of death, adverse cardiac events, and readmission<sup>15</sup>.

The World Health Organization defines QoL as an individual's perception of their position in life, in the cultural context and value system in which they live, and in relation to their goals, expectations, standards, and concerns<sup>16</sup>.

The usefulness of assessing QoL in patients with CR lies in its potential as a predictor of treatment response and as an aid in decision-making regarding treatment and care planning. This makes it an important measure of the effectiveness of RC programs<sup>1</sup>.

The Spanish Questionnaire for QoL developed by Velasco et al. In 1993, it was one of the most used tests in CR, designed for Spanish-speaking patients with AMI, and consists of 40 items grouped into 9 dimensions: Health, sleep/rest, emotional behavior, future projects, mobility, social relations, the behavior of alert, and leisure/work; each item is rated on a scale from 1 to 5, obtaining a worse perception of QoL with a higher score<sup>17,18</sup>.

The perceived deficit is ordered from excellent = 0-50 points, good = 51-100 points, intermediate = 101-150 points, and bad = 151-200 points<sup>16</sup>. It has high validity ( $r = 0.81$ ), using the QoL questionnaire for myocardial infarction as the gold standard, with a reproducibility of 0.75 and a reliability of 0.90<sup>17</sup>.

Braga et al., in 2021, performed a retrospective analysis of 731 70-year-old coronary patients who attended CR. The responses of the patients aged  $\geq 65$  and  $< 65$  years were compared. The analysis showed an increase in physical capacity measured by the metabolic equivalent of task (METs)  $7.6 \pm 1.8$  versus  $9.3 \pm 1.8$  ( $p < 0.001$ ). Older patients also improved the Short Form Health Survey (SF-36), a Health-related QoL evaluation instrument<sup>19</sup>.

A 2018 case-control study included 1,141 patients of all ages with a diagnosis of AMI from the "Infarct Code" program with the aim of evaluating QoL measured with the Velasco Del Barrio questionnaire. Both groups showed improvement in QoL<sup>20</sup>.

Due to the above mentioned in the CR studies, the evidence of the improvement in functionality and QoL

and the fact that older Mexican adults have not been systematically included as the main interest group of these care with ischemic heart disease is that considered it prudent to compare the QoL at the beginning and at the end of cardiac rehabilitation therapy in adults over 60 years of age with “Infarct Code” in a 3<sup>rd</sup> level hospital in northeastern Mexico.

## **MATERIALS AND METHODS**

### ***Study design***

The present study was an analytical cross-sectional study conducted at a 3<sup>rd</sup> level hospital in northeastern Mexico. Considered no greater than minimal risk. The study was approved by the local research ethics committee and hospital health research committee for data collection and use for research purposes, maintaining the anonymity of the research subjects. Registration number R-2020-1902-045.

### ***Participants***

A total of 143 study participants were included: Adults over 60 years of age, without gender preference, with ischemic heart disease from the “Infarct Code” program who completed the CR program from 2018 to 2021 and who had the initial and final measurement of the validated post-AMI QoL by Velasco del Barrio.

### ***Variables***

Clinical records were reviewed, and the information available in the clinical records of patients from 2018 to 2021 was analyzed.

The following variables were documented:

- Demographic variables: Age, sex, and body mass index.
- Cardiovascular risk factors: Smoking, dyslipidemia, high blood pressure, diabetes mellitus.
- Characteristics of AMI: Artery responsible for coronary angiography, infarct area according to electrocardiographic data, and presence of multivessel disease.
- Physical conditioning parameters: MET is the measure used to calculate the energy cost of physical exercise regardless of weight, where 1 MET is equivalent to 1 kcal/kg/h. METs at the beginning and end of cardiac rehabilitation therapy were measured, and the difference between them.

- QoL based on the Spanish QoL by Velasco et al. initial and final cardiac rehabilitation therapy. The interpretation of results from the de score will be divided into excellent, good, intermediate, and bad.

### ***Statistical analyses***

The quantitative variables were in accordance with the distribution curve determined by the Kolmogorov–Smirnov test and were reported with the measured central tendency (median) and dispersion (minimum and maximum ranges) using the Paired Student’s t-test Statistical was used. Qualitative variables are shown as frequency percentages for inferential statistics, and the Chi-square test was used. The prevalence ratio, 95% confidence interval, and level of statistical significance ( $p < 0.05$ ) were determined. Data were analyzed using SPSS v22.

## **RESULTS**

### ***Demographic characteristics***

Between January 2018 and December 2021, 252 participants who met the selection criteria were included in the study. The mean age of our study population was  $67 \pm 6$  years, and 80% of the patients were men. 52% had type 2 diabetes mellitus and 71% had systemic arterial hypertension. The most affected artery was the anterior descending artery (48%) followed by the right coronary artery (32%) (Table 1).

The mean initial METs was  $5 \pm 1.7$  and the final METs was  $7.3 \pm 2$ , with a mean gain of  $2.3 \pm 1.3$  total METs.

### ***Study endpoints***

When starting the CR program, 18% of the patients reported having an excellent QoL, 78% good QoL, and 4% intermediate QoL, according to the Velasco del Barrio questionnaire. At the end of this program, 75% of the patients reported having excellent QoL, while 25% said they had good QoL.

The total integrated score of all the evaluated areas had an initial mean of  $61 \pm 14$  and a final mean of  $49 \pm 9$  ( $p = 0.001$ ) (Table 2).

### ***Subanalysis in groups by age and sex***

In table 3, the population was divided into groups by age: Group 1 corresponds to patients aged 60-69 years

**Table 1.** Sociodemographic characteristics of the population

Variable	n	Percentage
<b>Total population (n = 143)</b>		
Age ( mean ± SD)	67 ± 6	
Female	28	20
Male	115	80
Risk for malnutrition	26	18
Regular	51	36
Overweight	36	25
Obesity	30	21
Smoking	86	60
Dyslipidemia	36	25
Diabetes mellitus type 2	75	52
Arterial hypertension	101	71
Decrease FEVI	23	18
Slightly reduced FEVI	61	47
Conserved FEVI	46	35

Elaboration: own source.  
FEVI: left ventricular ejection fraction.

**Table 3.** Quality of life by age groups

Age groups	n (143)	Perception of quality of life		p*
		Excellent, n (%)	Good, n (%)	
60-69 years old	100	76 (76)	24 (24)	0.622
≥ 70 years old	43	31 (72)	12 (28)	

Elaboration: own source.  
\*Chi-square test p ≤ 0.05.

**Table 4.** Quality of life by gender (n = 143)

Groups by Gender	n (143)	Perception of quality of life		p*
		Excellent, n (%)	Good, n (%)	
Females	28	19 (68)	9 (32)	0.343
Males	115	88 (77)	27 (23)	

Elaboration: own source.  
\*Chi-square test p ≤ 0.05.

**Table 2.** Differences between the areas evaluated in the quality-of-life questionnaire\*

Evaluated dimensions	Evaluated questionnaires (n = 143)		p†
	Score Mean ± SD		
	Initial	Final	
Health	13 ± 4	10 ± 2	0.001
Sleep and rest	4 ± 1	3 ± 1	0.001
Psychoaffective	4 ± 1	3 ± 1	0.001
Future	4 ± 1	3 ± 0.5	0.001
Mobility	8 ± 3	6 ± 2	0.001
Social relations	10 ± 3	8 ± 2	0.001
Cognition	3 ± 2	3 ± 1	0.001
Communication	3 ± 2	3 ± 0.9	0.001
Work and free time	8 ± 3	6 ± 2	0.001
Total score	61 ± 14	49 ± 9	0.001

Elaboration: own source.  
\*Velasco JA. Rev Esp Cardiol. 1993; 46 (9):552-8<sup>17</sup>.  
†Paired Student's t-test p ≤ 0.05.

As shown in table 4, the population was divided into two groups according to sex; it was found that there was no significant difference in the QoL reported at the end of the CR between the two groups (p = 0.343).

## DISCUSSION

In this study, it was shown that nearly 20% of the patients who attend the CR are older adults, like those previously reported by Young et al. and Chen et al., who reported attendance between 15-30%, and 13-34%, respectively<sup>7,11</sup>.

In our hospital, the referral rates to this type of program for geriatric patients are low, despite knowing that CR has a level of evidence (I-a) as secondary prevention in ACS<sup>7</sup>.

The most prevalent comorbidities were hypertension and diabetes, with cardiovascular risk factors: 60% were current or previous smokers, and 21% had a body mass index classified as obesity, which contrasts with what was found in the study "Cardiac Rehabilitation after an ACS: The Impact in Elderly Patients" published in 2015, where the main comorbidity found was dyslipidemia and hypertension in second place, and they also reported a lower

and Group 2 corresponds to those over 70 years of age; there was no statistically significant difference in QoL reported at the end of the program for CR between both groups, with a p-value of 0.622.

percentage of smokers and obese patients 34% and 17%, respectively<sup>21</sup>.

In our population, there was evidence of an improvement in physical capacity evaluated by METs, with a mean gain of  $2.3 \pm 1.3$ , similar to those found in a study carried out at our institution "Impact of the Functional Capacity of a Conventional Cardiac Rehabilitation Program Vs. Distributive in Infarct Code Patients" in 2019, where a METs gain of 2.19-2.71 was observed depending on the CR program used in young patients<sup>22</sup>.

Older adult patients diagnosed with ACS who completed the CR program reported improvement in QoL in all areas evaluated by the Velasco del Barrio scale<sup>17</sup>, with statistical significance pre- and post-CR, similar to that reported in other studies, despite the use of different rating scales<sup>13,23-26</sup>.

At the end of the CR program, both women and men had an improvement in the gain of METs and in the QoL score, which is consistent with the findings of Beckie et al., where women showed improvements in exercise capacity of up to 30% and significant improvements in total QoL after finishing CR, with no significant difference versus men<sup>14</sup>. Certainly, greater referral and participation of older adult patients in CR are needed to fully harness the therapeutic and secondary prevention potential of such programs<sup>19</sup>.

Increased awareness of physicians, nurses, patients, and their families about the benefits of secondary prevention programs such as CR will provide a basis for achieving a higher referral rate and assist in the implementation of such programs<sup>19</sup>.

An excellent alternative to supervised CR could be home CR, which aims to bridge the gap between patients who are interested in participating but are constrained by logistics.

The expansion of digital health (telehealth, telemedicine, mHealth, and remote patient monitoring), Internet access, and cellular technologies provide the opportunity to improve patient care and improve health outcomes, and it is hoped that they can be used to address contemporary challenges in older adults<sup>26,27</sup>.

The findings of this study support the fact that the public health objective is not only to increase life expectancy but also to preserve functionality, well-being, and confidence among older adults with CVD, so that a majority live well and enjoy preserved independence with a good QoL.

The limitations of this research are that it was retrospective, the sample selection was convenient, a selection bias could not be excluded, and most of

our population was men; however, this reflects the application of the program in real life. In addition, this observational study lacked a control group. A cutoff of 60 years was used because it has been used in most studies and is often the cutoff chosen in many countries to define older people for different social and insurance purposes, such as Medicare. Therefore, the results cannot be generalized to national or international patients with CR or to women.

Our proposals include conducting educational programs for medical staff, patients, and family members so that they are aware of the benefits of cardiac rehabilitation therapy, thus eliminating doubts and/or myths, and encouraging referral and care for both women and men. Addresses possible social and economic limitations that may cause non-attendance at therapy. Development of person-centered multicomponent cardiac rehabilitation programs to enhance the benefits of therapy. Carry out new research that includes older patients with geriatric syndromes, especially frailty and functional dependence. QoL scales focus on the concept of intrinsic capacity, which better defines the characteristics and needs of older adults.

## CONCLUSIONS

CR is an important secondary prevention strategy in patients with coronary artery disease, regardless of age.

One in five patients over 70 years of age participated in our hospital's cardiac rehabilitation program.

The probability of referral to CR for older patients was low, while the probability of abandonment was higher than that for young patients. The most frequent location of AMI was the anterior wall, followed by the inferior wall, where 86.7% had a significant lesion in only one vessel.

Older persons showed an improvement in physical capacity, as measured by METs.

Geriatric patients diagnosed with ACS who completed the cardiac rehabilitation program showed improvement in QoL in all areas evaluated using the Velasco del Barrio scale (health, sleep/rest, emotional behavior, future projects, mobility, social relationships, alert behavior, and leisure/work), with statistical significance before and after CR.

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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.** Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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## Nephrotic syndrome secondary to Sjögren syndrome in an older adult: a clinical case analysis

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### Abstract

We report an 80-year-old woman who was admitted to our geriatric unit with progressive symptoms of proteinuria, edema, and fatigue. The clinical presentation was caused by a nephrotic syndrome (NS) due to membranoproliferative glomerulonephritis secondary to Sjögren's syndrome. Treatment with immunosuppressive drugs was initiated, which resulted in significant improvement in the patient's clinical symptoms and laboratory findings. The case highlights the importance of an appropriate diagnostic approach to NS in older adults, and the need for prompt management to prevent further kidney damage and improve older patient clinical outcomes.

**Keywords:** Nephrotic syndrome. Nephrogeriatrics. Membranoproliferative glomerulonephritis. Sjögren syndrome.

### Síndrome nefrótico secundario a síndrome de Sjögren en un adulto mayor: análisis de caso clínico

### Resumen

Presentamos el caso de una mujer de 80 años que ingresó en nuestra unidad geriátrica por un cuadro progresivo de proteinuria, edema y fatiga. La presentación clínica fue causada por un síndrome nefrótico debido a una glomerulonefritis membranoproliferativa secundaria al síndrome de Sjögren. Se inició tratamiento con inmunosupresión, que resultó en una mejoría significativa de los síntomas clínicos y los hallazgos de laboratorio de la paciente. Este caso destaca la importancia de un enfoque diagnóstico adecuado del síndrome nefrótico en adultos mayores y la necesidad de un tratamiento oportuno para prevenir mayor daño renal y mejorar los desenlaces clínicos de los pacientes mayores.

**Palabras clave:** Síndrome nefrótico. Nefrogeriatria. Glomerulonefritis membranoproliferativa. Síndrome de Sjögren.

### INTRODUCTION

Nephrotic syndrome (NS) in older patients is a common clinical conundrum. Membranoproliferative glomerulonephritis (MPGN) is rarely found to cause the nephrotic state in such patients. Determining with reasonable certainty whether the NS is primary (idiopathic) or due to an underlying disease such as neoplasia or an autoimmune etiology can be a daunting clinical challenge. Through the presentation of an

illustrative case and a focused review of the relevant literature, the approach to evaluation of such patients is analyzed and a potential contemporary pathway for acquiring the correct diagnosis is offered.

### CASE PRESENTATION

An 80-year-old woman, with a medical history of hypertension, inactive rheumatoid arthritis (RA),

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osteoporosis, chronic obstructive pulmonary disease, mild cognitive impairment, and secondary Sjögren's syndrome (SS), was admitted due to a progressive onset of peripheral and facial edema and proteinuria, associated to uncontrolled hypertension, and intermittent episodes of delirium. Prior medications included methotrexate, omeprazole, atorvastatin, folic acid, calcitriol, sertraline, spironolactone, telmisartan, nifedipine, metoprolol, and bumetanide. There was no family history of renal disease, diabetes, or cancer. She had no drug allergies.

She was well until approximately 3 months prior when she noticed ankle swelling followed by 18 kg weight gain accompanied by easy fatigability. In addition, family members reported documenting systolic blood pressures (BP) up to 200 mmHg during this period, despite the use of antihypertensive and diuretic treatments. Furthermore, she developed progressive dependence in instrumental and basic activities of daily living (Katz 3/6, Lawton 4/8), mobility impairment and falls syndrome in the past 2 weeks. Previously, she was totally independent and had no problems with mobility.

Physical examination showed a BP of 176/100 mmHg and a pulse of 69 bpm (regular). The patient weighed 67 kg. The optic fundi were unremarkable. Lymphadenopathy was absent. 3+ bilateral edema up to the upper thigh, diminished breath sounds, drowsiness, and low O<sub>2</sub> saturation (80%) that required 1L/min supplementary O<sub>2</sub>. Initial laboratory data showed hemoglobin 10.4 g/dL, hematocrit 30.3%, WBC count was 9.8/mm<sup>3</sup>, platelet count 171,000/mm<sup>3</sup>, and MCV 92.9 fl. Serum creatinine 1.39 mg/dL (using chronic kidney disease-epidemiology collaboration [CKD-EPI] estimated glomerular filtration rate [eGFR] was 38 mL/min/1.73 m<sup>2</sup>). Serum sodium was 119 mmol/L, serum albumin 2.06 g/dL, serum total cholesterol 201 mg/dL, serum calcium 7.11 mg/dL, and normal serum uric acid. Normal A1C (5.8%), serum bilirubin, alkaline phosphatase, fasting blood glucose, phosphate, and globulins were all within normal limits and atrial natriuretic peptide was 900 pg/mL. Dipstick urinalysis revealed 3+ proteinuria without blood and 24-h urine protein >5 g/day with IPC 5.2 g/g. A stool sample was negative for occult blood. As well as an unremarkable ekg. Chest CT reported bilateral pleural effusion with segmental atelectasis, intra-abdominal free fluid, and diffuse soft-tissue edema. Renal ultrasound revealed chronic renal damage. A central venous catheter line was placed without complications and IV furosemide was started together with antiproteinuric treatments until negative balances were obtained.

On the 3<sup>rd</sup> day of hospitalization, a gradual decrease of all cell lines was observed, documenting: grade II

anemia (8.9 d/dL), severe neutropenia (total neutrophils  $210 \times 10^3/\mu\text{L}$ ), and moderate thrombocytopenia ( $62 \times 10^3/\mu\text{L}$ ). Blood smear showed decreased platelets, anisocytosis 1+, macrocytes 1+, ovalocytes, and dacrocytes. Hemolysis profile with normal LDH (176 U/L), normal haptoglobin (121 mg/dL), elevated D-dimer (11,379 ng/mL FEU), and a negative direct Coombs test. Normal Vitamin B12 (448 pg/mL) and normal folic acid (> 46 ng/mL) was reported. An evaluation by the Hematology team was requested, and a concomitant myelodysplastic syndrome was suspected.

## DIFFERENTIAL DIAGNOSIS

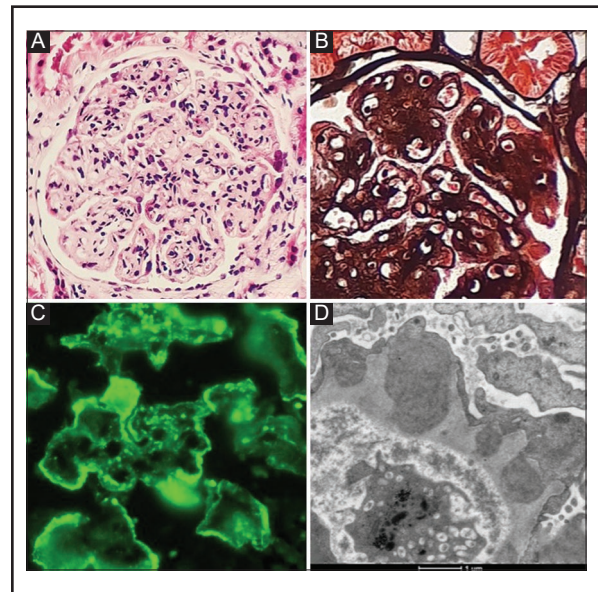
NS is a clinical syndrome defined by proteinuria (3 g or more of proteins per 24 h or, on a single spot urine sample, the presence of 2 g of protein per gram of urinary creatinine), hypoalbuminemia (< 30 g/L), with resulting hyperlipidemia, edema, and various complications<sup>1</sup>. Once the diagnosis of NS was confirmed in this patient, the etiological approach was initiated.

Among patients aged > 65 years presenting with NS, the most common causes identified by kidney biopsy are membranous nephropathy (MN), minimal change disease (MCD), and amyloidosis (AML) with approximately 60% of all cases accounted for by these three lesions<sup>1</sup>. Less common lesions among older patients undergoing a biopsy for diagnosis of NS are focal-segmentary glomerulonephritis (FSGS), MPGN, and diabetic nephropathy (DN)<sup>1,2</sup>. A membranoproliferative (MP) pattern can be seen in association with a monoclonal deposition disease<sup>3</sup>, which is more common in older adults than younger patients, and it is commonly associated with cryoglobulinemia, HCV infection, and autoimmune diseases (AD). DN is less commonly encountered, largely because patients with diabetes and NS seldom undergo renal biopsy unless "atypical" features are present such as onset of NS < 5 years from discovery of diabetes, rapid progression of renal impairment, or absence of proliferative retinopathy and other microvascular complications of diabetes. Although crescentic GN (e.g., that due to antineutrophil cytoplasmic or anti-glomerular basement membrane autoantibodies [Ab]) is relatively common in the older adult, it seldom presents with isolated NS. MCD is encountered in approximately 12%-15% and MN is encountered in approximately 30%-40% of renal biopsies in older adult participants with isolated NS<sup>4</sup>. Both MN and MCD can be a primary idiopathic glomerular disease or secondary

to any number of conditions such as neoplasia, drugs, or infection<sup>5,6</sup>. Approximately 10-12% of renal biopsies in older patients believed to have primary idiopathic NS on clinical grounds will reveal AML<sup>6</sup>. AML in the older adult is most often of the primary variety, although secondary and hereditary AML have also been described in such participants. Performance of a kidney biopsy is essential to delineate the various causes of NS in this age group and will greatly aid in focusing the diagnostic evaluation in a cost-effective manner and in planning appropriate treatment. Many experienced clinicians recommend deferring additional laboratory or imaging procedures until the histopathologic diagnosis of NS has been made by renal biopsy<sup>5-7</sup>.

## DIAGNOSTIC EVALUATION

After adequate control of hypertension was reached, a percutaneous kidney biopsy was performed without complications. The biopsy reported an immune complex-mediated MP pattern glomerulonephritis, with 20% interstitial fibrosis, 10% tubular atrophy and arteriosclerosis. Immunofluorescence showed 3+ IgG, C3 and Lambda, 1+ C1q, kappa chains and 2+ lineal albumin deposits (Fig. 1). When the renal biopsy shows a pattern of MPGN with immunoglobulin deposits, it would be indicated to rule out the association with an infectious process, autoimmune disease, or the presence of monoclonal gammopathy or other immunoplasmyc processes. The battery of tests to be performed includes microbiological, immunological studies, and electrophoresis and immunofixation tests, which are summarized in (Table 1). Therefore, the following additional laboratory tests were performed to continue the evaluation: antiphospholipid syndrome profile was normal (anti-cardiolipin Ab, anti- $\beta$ 2GP1 and lupus anticoagulant were negative). Anti-nuclear IgG Ab were also requested with fine speckled pattern 1:320, negative anti-ds DNA IgG (6.4 IU/mL), positive anti-Ro/SSA (12.2 IU/mL), negative anti-La/SSB (5.0 IU/mL), negative antiSm (5.9 IU/mL) and anti-RNP Ab. Serum C3 was 96 mg/dL and serum C4 was 22 mg/dL (both normal), rheumatoid factor was elevated (> 240 IU/mL) as well as TSH (13 mIU/L) (probably due to cross-reaction), serum immunoglobulins (Ig) reported normal IgA (120 mg/dL), normal IgM (107 mg/dL), and decreased IgG (572 mg/dL). Negative viral tests for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). Cryoglobulins were not detected (0%)



**Figure 1.** **A:** glomerulus with membranoproliferative pattern, accentuation of the lobular aspect, caused by mesangial proliferation and thickening of the glomerular basement membrane (H and E  $\times$ 200). **B:** double contours of the glomerular basement membrane (Jones methenamine silver  $\times$ 400). **C:** deposits with pseudolin-ear granular pattern in capillary loops and mesangium (direct immunofluorescence, IgG  $\times$ 400); **D:** capillary loops with subepithelial and subendothelial electron-dense deposits, with glomerular basement membrane spicules (electron microscopy  $\times$ 6800).

and elevated kappa and lambda light chains with no monoclonal pattern were not identified in serum nor in urine samples. These findings led to suspect of either a primary idiopathic GN versus an underlying secondary cause, such as AD. Because of the patient's age and medical history, along with active AD, the latter being the most probable etiology.

The relationship between AD and the development of GNMP has been widely described, although it should be mentioned that its presentation is infrequent in older adults. Such involvement is considered predominant in women who suffer from any of these entities for long periods of time, as in our patient. The AD described in association with GNMP are systemic lupus erythematosus (SLE), most frequently, and occasionally, SS, RA, and collagen diseases. While there are limitations to current diagnostic classifications to distinguish various connective tissue diseases, the patient did not have the clinical criteria for SLE or clinical or serologic evidence of another associated new onset AD. Furthermore, a relationship has been recognized between monoclonal gammopathies and

**Table 1.** Suggested stepwise approach to the evaluation of nephrotic syndrome in older adults

Step 1: Initial studies	Complete history (hx) and physical examination (family hx, med use, infection hx, and assessment of systemic manifestations)
	Urinalysis (+ urine sediment)
	24-h urine protein (> 3.5 g/d) or spot urine protein/creatinine ratio (> 3.0) and serum albumin < 3.4 g/dL
	Serum creatinine concentration and calculate estimated GFR
	Serum biochemical profile, fasting lipids, and a complete blood count
	A1c and examine the retina with dilated pupils (if patient has diabetes)
	Serum-free light chains and perform a serum and urine immunofixation test for monoclonal proteins.
	Consider an abdominal fat pad biopsy/aspiration if amyloidosis is suspected
	Assess renal size and configuration by abdominal US
	Step 2: Perform kidney biopsy (If no contraindication)
Congo red stain, if appropriate	
Step 3: Targeted evaluation	HVB surface antigen and HCV Ab
	Antinuclear Ab and anti-DNA Ab (particularly if features of SLE are noted on biopsy)
	Serum C3 and C4 complement, anti-PLA2R Ab (Western blot or alternative if available)
	Immunofluorescence for IgG subclass deposition and PLA2R deposits (if available)
	If IgG4+ and anti-PLA2R + (serum and/or glomerular deposits), consider primary idiopathic MN and manage accordingly
	If IgG1-3 dominant and IgG4 weak or absent, consider of an underlying neoplasia.
Step 4: Evaluate for malignancy	Conduct a CT scan of the chest, especially if smoking history
	Check stool for occult blood and arrange for colonoscopy (if not)
	In women, (breast examination and mammography) and in men, (rectal examination and PSA) (if not)
	Consider abdominal CT scan to evaluate for subdiaphragmatic neoplastic processes (i.e., renal cell carcinoma, lymphoma, etc.)

NS: nephrotic syndrome; MN: membranous nephropathy; anti-PLA2R: antiphospholipase A2-receptor; Ab: Antibody; CT: computed tomography; PSA: prostate-specific antigen; HBV: hepatitis B virus; HCV: hepatitis C virus.

the development of MPGN, within which monoclonal gammopathy of uncertain significance is the most associated entity, followed by multiple myeloma, low-grade B-cell lymphoma, and chronic lymphocytic leukemia, which were ruled out in our patient.

This disease is rare in older patients. Most of the described cases present MN, and a few cases focal proliferative GN. The pathogenesis of immune complex-mediated MPGN results from the deposition of immune complexes in glomeruli due to persistent antigenemia, leading to the formation of immune complexes of antigenic Ab. Another pathophysiological mechanism consists of dysregulation of the alternative complement pathway due to mutations

or autoAb against complement regulatory proteins and generates the deposition of these products in the mesangium and subendothelial region triggering glomerular inflammation and leading to MPGN<sup>8</sup>.

Patients with active MPGN with no significant chronic changes on biopsy, associated with an AD should receive treatment for their underlying disorder as appropriate, which usually involves the use of immunosuppression in addition to conservative therapy<sup>8,9</sup>. Therefore, in consensus with the rheumatology and nephrology teams, in addition to considering the patient's previous functionality as well as the geriatric prognostic scales calculated, it was decided to initiate an anti-CD20 monoclonal Ab as the main treatment

(Rituximab). The first dose was applied without adverse reactions and the patient was discharged afterward. In addition, given the persistence of severe neutropenia, it was decided to initiate a single dose of granulocyte colony-stimulating factor, with improvement of neutropenia. Platelet counts normalized as well, only with persistence of Grade II anemia. Our hematology team decided to differ bone marrow aspirate and suggested surveillance and follow-up.

She was evaluated in the Geriatric and Nephrology Clinic, 4 and 8 weeks later, respectively. The following laboratories were documented: hemoglobin 12.3 g/dL, hematocrit 37.4%, white blood cell count 4.5/mm<sup>3</sup>, platelet count 262,000/mm<sup>3</sup>, and mean corpuscular volume 94 fl. A well response to rituximab was documented. Her BP is now 120/80 mmHg and weighs 50 kg. Her current 24 h-urine protein is at 1.9 g/d, serum creatinine is 0.79 mg/dL, and her serum albumin level has risen to 3.2 g/dL. After a complete comprehensive geriatric assessment, she had regained functionality and independence (Katz 6/6, Lawton 5/8), improved mobility and no longer had falls. No new geriatric syndromes were documented.

## DISCUSSION

In summary, we report the case of an 80-year-old woman who was admitted to our geriatric unit with a progressive onset of proteinuria, edema, and fatigue. The clinical presentation was caused by a severe NS secondary to MPGN.

NS is the most common glomerular pathology in older adults<sup>10-12</sup>; the most common forms of primary glomerulopathies include FSGS and MN; while DN, AML, and malignant neoplasms are most common causes of secondary glomerulopathies<sup>12,13</sup>. In our case, we concluded a diagnosis of NS secondary to a MPGN of the secondary form, according to its microscopic features and after secondary causes of NS were excluded satisfactorily such as: AML, viral infections (HIV, HCV, and HBV), malignant neoplasms such as monoclonal gammopathy, cryoglobulinemia, thymoma, myelodysplastic syndromes, or Hodgkin's lymphoma<sup>13-15</sup>, and other new AD such as SLE. A suggested stepwise approach to evaluation of an older adult with NS is outlined in table 1.

Something relevant to discuss in this patient is the role of relatively preserved renal function; since it is known that eGFR formulas based on creatinine in patients with NS have limitations, especially the CKD-EPI formula, since these could overestimate

eGFR because of elevated proteinuria and hypoalbuminemia, which have been described as factors that increase tubular creatinine secretion<sup>15</sup>. eGFR, in addition to uncontrolled hypertension and the presence of crescents, segmental sclerosis, interstitial fibrosis and tubular atrophy in the renal biopsy have been found to be poor prognostic factor in these patients<sup>16,17</sup>.

The prognosis for patients with MPGN was previously considered unfavorable<sup>17,18</sup>, but the advent of new immunological treatments directed at the underlying causes has brought about a change in the prognosis. Good prognostic factors have been described, predicting a benign course in patients with MPGN, which include proteinuria in non-nephrotic ranges (< 3.5 g/day), normal serum creatinine, absence of hematuria, and normal BP<sup>16</sup>. Thus, it is challenging in this case, as there are both favorable and unfavorable prognostic factors, adding to the complexity of the clinical situation. In addition, it is crucial to always include the geriatric comprehensive assessment and prognosis when making decisions and choosing treatment.

Targeted therapy for MPGN includes drugs such as rituximab, cyclophosphamide, steroids, or calcineurin inhibitors (CI). The evidence supporting immunosuppressive therapy for patients with MPGN, specifically those with NS and preserved renal function is very limited in older adults. However, if renal biopsy shows evidence of ongoing active GN, cyclophosphamide and rituximab are reasonable treatment options<sup>19,20</sup>. In our case, rituximab was considered the best therapeutic strategy, although it is especially considered in cases where the NS is resistant to steroids and CI.

Rare entities with wide heterogeneity in their clinical presentation such as NS are a medical challenge to identify and treat in a timely manner to avoid fatal outcomes and irreversible complications. This article highlights the importance of an appropriate diagnostic approach to NS in older adults.

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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 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.

**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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