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Mild cognitive Impairment: Risk of Dementia according to Subtypes

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Mild cognitive impairment (MCI) has 3 clinical subtypes: amnestic (aMCI), multiple domains (mdMCI) and non-amnestic single domain (na-SD-MCI) whose evolutive possibility to dementia has not been profoundly studied. Objective: This paper aims to determine the conversion to dementia of the different subtypes of MCI and determine risk factors associated to conversion to dementia.

Methods: A total of 127 patients diagnosed with MCI (age=70.21; SD=13.17) were evaluated with a neuropsychological and neuropsychiatric battery. They were classified into 3 groups: amnestic MCI (n=20), multiple-domain MCI (n=98), non-amnestic MCI (n=9). Seventeen normal subjects (age=74.59; SD=10.63) were included.

Results: Of those included, 27.1% developed Alzheimer's type dementia [average time for conversion to Alzheimer's dementia (AD) 11.12 months (SD=0.183)]. None of the controls developed dementia. Thirty-five percent (n=7) of amnestic MCI converted to AD: 20% (n=4) at 6 months and 15% (n=3) at 12 months); 11.1% (n=1) of the non-amnestic single domain MCI converted to AD at 6 months. It was found that 31.6% (n=31) of multiple domain MCI rotated to AD: 15.3% (n=15) at 6 months and 16.3% (n=16) at 12 months. Age ($p<0.05$, $\beta=1.03$) increased the likelihood of rotation to AD. Multi-domain MCI subtype was the most frequent. However, the conversion to dementia in amnestic subtype was the highest, age and retirement being the variables that increased the likelihood of conversion to Dementia.

Key words: Mild cognitive impairment, Risk factors, Alzheimer's dementia

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Deterioro cognitivo leve: riesgo de demencia según subtipos

El deterioro cognitivo leve (DCL) presenta 3 subtipos clínicos: amnésico (DCLa), múltiples dominios (DCLmd) y dominio único no amnésico (DCLduna), cuya evolutividad a demencia no ha sido extensamente estudiada. El objetivo de este trabajo es evaluar la conversión a demencia de los diferentes subtipos de DCL y determinar los factores de riesgo asociados a la misma.

Métodos: Se reclutaron 127 pacientes con Deterioro Cognitivo Leve (edad 70,21; DS 13,17) fueron evaluados con una batería neuropsicológica y neuropsiquiátrica y clasificados en 3 grupos: DCLa (n=20), DCLmd (n=98) y DCLduna (n=9). Diecisiete controles normales (edad 74,59; DE 10,63) fueron incluidos.

Resultados: El 27,1% de los pacientes con DCL desarrolló demencia tipo Alzheimer (promedio 11,12 meses, DE=0,183). Ninguno de los controles convirtió a demencia. El 35% (n=7) del grupo con DCLa convirtió a Demencia: un 20% (n=4) a 6 meses y un 15% (n=3) a 12 meses; 11,1% (n=1) del grupo con DCLduna convirtió a demencia en 6 meses. El 31,6% (n=31) de DCLmd rotó a demencia: el 15,3% (n=15) en 6 meses y un 16,3% (n=16) al año. La edad ($p<0,05$, $\beta=1,03$) aumentó la probabilidad de conversión a demencia. El grupo de DCLmd fue el más frecuente, sin embargo fue mayor la conversión a demencia en el DCLa, siendo la edad y la jubilación las variables que aumentaron la probabilidad de conversión.

Palabras clave: Deterioro cognitivo leve, Factores de riesgo, Demencia tipo Alzheimer

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Dementia represents one of the greatest worldwide problems of public health because of the exponential growth of the disease with advancing age. Mild cognitive impairment (MCI) groups the subjects who have cognitive impairments without dementia but with high risk of developing it and currently represents the focus of study of many clinical investigations and pharmacological interventions.[1,2] The work group of the National Institute on Aging and Association of Alzheimer[3] developed new diagnostic criteria for mild cognitive impairment in order to identify the predemential symptomatic phase of Alzheimer's disease (AD). They incorporated the use of biomarkers in images and cerebral spinal fluid. That is how the concept of MCI due to AD was created, by the presence of positive biomarkers in association to the clinical syndrome. For those cases in which it is difficult to use biomarkers, the clinical and neuropsychological evaluation should be essential to establish a diagnosis.[3] In order to identify the subject having the greatest risk of evolving to Alzheimer, MCI has been classified from the neuropsychological point of view into 3 subtypes: amnestic (aMCI), multiple domains (mdMCI) and non-amnestic single domain (na-SD-MCI), whose evolution capacity to dementia has been profoundly studied.[4]

This study has aimed to evaluate conversion to dementia of the different subtypes of MCI and to determine the risk factors associated to it.

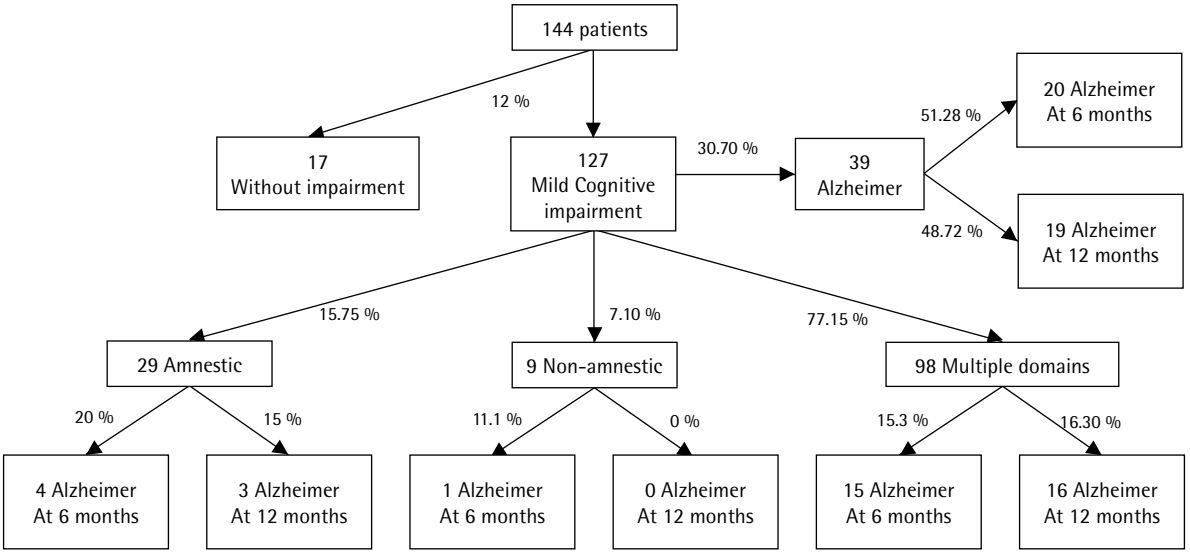
MATERIAL AND METHODS

This is a longitudinal type study of a cohort of patients who attended the Memory Research Laboratory of the Neurology Department of the Hospital Abel Zubizarreta. The patients were mostly referred by their medical practitioners due to having some type of cognitive disorder. The participants came from the autonomous city of Buenos Aires, Argentina. The data were collected prospectively and retrospectively between 2008 and 2010. The patients were enrolled during the first year of the study and followed-up longitudinally during 2009 and 2010.

Subjects "at risk of dementia" were selected, using the Petersen 2004[5] criteria. The absence of comorbidity that could explain the cognitive impairments (probably MCI) was taken into account.[6] Therefore, patients with cerebrovascular disease or another neurological or major psychiatric disorder according to DSM IV criteria[7] were excluded.

A total of 144 adult outpatients were recruited: 127 patients with MCI (age=70.21; SD=13.17) and controls (age=74.59; SD=10.63) (Figure 1). The group of patients with mild cognitive impairment (n=127) was divided into 3 sub-populations:

Amnestic mild cognitive impairment - (a-MCI) (those having low performance only on memory test >1.5 standard deviations below the mean according to age and education



Beginning with mild cognitive impairment, the percentage indicate the rate of conversion to dementia at 6 and 12 months

Figure 1 | *Flow chart of the patients*

level). Delayed recall and recognition were used as memory test, N= 20.

Mild Cognitive Impairment with involvement of multiple domains (mdDCL) (those with low performance in several cognitive domains: e.g. attention, memory, language, executive functions and visuospatial ability >1.5 standard deviations below the mean according to age and level of education). Delayed recall and recognition were used as memory test. The *Trail Making Test A* was used as attention test, the *Trail Making Test B* as executive test, the Boston naming test as language test and the clock test as visuospatial test, N= 98.

Non-amnestic single domain mild cognitive impairment (na-SD-MCI) (those with low performance in any area or non-amnestic cognitive domain >1.5 standard deviations below the mean according to age and education level), N=9. (Figure 1).

The patients who were enrolled in the study had undergone at least two cognitive evaluations (at 6 and 12 months).

A neuropsychological, neuropsychiatric and neurological evaluation was performed in the population studied. The DSM IV criteria[7] were used for the diagnosis of dementia and the probable or possible criteria of NINCDS ADRDA[8] were used for Alzheimer's type dementia.

All the clinical work was subject to the ICH Rules of Good Clinical Practices and to the final version of the declaration of Helsinski.[9]

First of all, a descriptive analysis was made of the sample in mild and normal cognitive impairment. For categoric variables, distribution of frequencies was established and expressed as percentages. For continuous variables, the mean was determined with its corresponding standard deviation. To compare the distribution of the variables being studied according to whether the subjects had an initial diagnosis of mild cognitive impairment or were controls, the Chi square test was used for the comparison of proportions in the case of nominal, ordinal or dichotomic variables. For continuous variables, the mean between groups was compared using the Student's T test. The proportion of subjects "who converted" to dementia was determined. Furthermore, the time from the diagnosis to conversion was estimated. Patients with mild cognitive impairment were classified into 3 subtypes: amnestic MCI, multiple domain MCIs and single domain non-amnestic MCI in accordance with the lowest cognitive performance. To do so, the score for each test for each individual was established and compared according to the mean and standard deviation for age and education level and z scores were established.

Given the cohort characteristics of follow-up of the study subjects, the Kaplan-Meier methodology was used to calculate the survival likelihood of the sample subjects in a determined time period.

Those factors associated to the likelihood of conversions were estimated. To do so, the bivariate survival function between the conversion was initially analyzed and each one of the prognostic variables was expressed as *Hazard Ratio* with their 95% confidence interval. To establish independent associations between the likelihood of conversion and the variables studied, those showing a significant association with the dependent variable in the previous analysis were chosen and they were included in a multivariate regression model. The relation between the rate of conversion and time was modeled as well as the possible relation with different variables recorded for each subject by a proportional risks model or Cox model, whose formulation was defined in relation to the distribution of the variables on goodness of fit of the model. The final intension was to obtain the most parsimonious model and the one that would best explain the survival variation. The possible interactions existing were determined and the data were expressed as *Hazard Ratio* with their 95% confidence interval.

RESULTS

The population of 144 subjects was divided into two:1) MCI and 2) controls (Figure 1). There were followed up longitudinally at one year.

No statistically significant differences were observed in their sociodemographic characteristics ($p>0.05$), or in their medical and family backgrounds considered ($p>0.05$). (Tables 1-4).

The control group had statistically significant differences with the MCI group regarding the neuropsychological profile ($p<0.05$), except for the direct digit span and presence of intrusions (Table 5).

When the neuropsychological tests of the different subtypes of MCI were compared, statistically significant differences were found between the a-MCI subgroup versus the md-MCI subgroup regarding Serial Recall, Naming, Phonological Fluency, Reverse Span, *TrailMaking A*, *TrailMaking B* and Clock Test. Significant differences were also found between aMCI and mdMCI vs na-SD-MCI in clue recognition. The subgroup of patients with multiple domain MCI had the greatest percentage of significant differences in the neuropsychological tests when compared with the controls (Table 6).

The patients with mild cognitive impairment and the controls did not show significant differences in the neuropsychiatric symptoms observed with the Neuropsychiatric Inventory (NPI) ($p>0.05$). However,

TablE 1 **Demographic characteristics of the population (Normal and MCI)**

	Normal	MCI	Sig. (between normal and MCI)
N	17	127	
Age	ξ = 74.59 S.D.= 10.63	ξ = 70.21 S.D.= 13.17	0.191
Gender	Male = 47.1% (n=8) Female = 52.9% (n=9)	Male = 44.1% (n=56) Female = 55.9% (n=71)	0.508
Years of Education	ξ = 12.53 S.D.= 3.08	ξ = 10.58 S.D.= 5.85	0.181
Occupational Activity	Retired = 50% (n=8) Active = 50% (n=8)	Retired = 66.7% (n=84) Active = 33.3% (n=42)	0.150
Laterality	Right handed = 100%	Right handed = 96.1% (n=122) Left handed = 3.9% (n=5)	0.529
Civil Status	Married = 70.6% (n=12) Single = 29.4% (n=5)	Married = 69.6% (n=87) Single = 30.4% (n=38)	0.589

Table 2 **Demographic Data of the Mild Cognitive Impairment subgroups**

Demographic data	aMCI	na-SD-MCI	mdMCI	Controls	p
Age	73.75 (±7)	68.11(± 10.3)	69.68(±14.2)	74.59(±10.6)	NS
Schooling	11.35 (± 3)	11.89(±3.7)	10.31(6.4)	12.53(3)	NS

aMCI: Amnestic Mild Cognitive Impairment
na-SD-MCI: Non-amnestic single domain Mild Cognitive Impairment
mdMCI: Multiple Domain Mild Cognitive Impairment
NS: Not significant

Table 3 **Medical and familial backgrounds of the populations (Normal and MCI)**

	Normal	MCI	sig. (between normal and MCI)
Hypertension	35.3% (n=6)	28.5% (n=35)	0.373
Diabetes	0 %	2.4% (n=3)	0.684
Cardiologic	5.9% (n=1)	5.5% (n=7)	0.644
Dyslipidemics	17.6% (n=3)	17.3% (n=22)	0.599
Smoking	0%	4.7% (n=6)	0.464
Family backgrounds of dementia	30% (n=3)	40.9% (n=36)	0.379
Extrapyramidalism	0%	1.6% (n=2)	0.777
Archaic Reflexes	0%	0%	-

regarding level of depression evaluated by the Beck Depression Inventory, greater depression was found in patients with NCI compared to the control group at baseline ($p<0.05$)[10-19] (Table 7).

Table 4 Neuropsychological battery of the population (Normal and MCI)

	Normal	MCI	Sig. (between normal and MCI)
MUSE	ξ = 28.76 S.D.= 1.52	ξ = 26.12 S.D.= 3.93	0.007
CDR Total	ξ =0.29 S.D.= 0.25	ξ = 0.57 S.D.= 0.46	0.026
Span direct	ξ = 5.56 S.D.= 0.89	ξ = 5.11 S.D.= 1.17	0.140
Span Indirect	ξ= 4.56 S.D.= 0.829	ξ = 3.37 S.D.= 1.30	0.001
Clock Test	ξ = 6.88 S.D.= 0.332	ξ = 5.51 S.D.= 2.21	0.012
Serial Learning	ξ = 8.29 S.D.= 2.02	ξ = 6.50 S.D.= 2.04	0.001
Serial Recall	ξ = 6.94 S.D.= 2.193	ξ = 4.25 S.D.= 2.78	0.000
Clues	ξ = 9.53 S.D.= 2.29	ξ = 7.29 S.D.= 3.33	0.008
Recognition	ξ = 11.41 S.D.= 0.939	ξ = 9.75 S.D.= 2.73	0.014
Intrusions	ξ = 0 S.D.= 0	ξ = 0.31 S.D.= 1.35	0.367
Naming	ξ = 53.12 S.D.= 4.01	ξ = 42.97 S.D.= 10.29	0.000
Semantic Fluency	ξ = 19.41 S.D.= 4.48	ξ = 13.91 S.D.= 4.48	0.000
Phonological fluency	ξ = 16.18 S.D.= 4.78	ξ = 10.80 S.D.= 4.92	0.000
Verbal Intellectual Coefficient	ξ = 118.33 S.D.= 9.53	ξ = 96.28 S.D.= 16.87	0.000
Intellectual Performance Coefficient	ξ = 110.33 S.D.= 15.182	ξ = 91.77 S.D.= 15.42	0.001
Global Intellectual Coefficient	ξ = 115.56 S.D.= 12.82	ξ = 93.68 S.D.= 15.68	0.000
TMTA	ξ = 48.94 S.D.= 18.34	ξ = 85.39 S.D.= 53.75	0.004
TMTB	ξ = 138.24 S.D.= 85.65	ξ = 250.37 S.D.= 149.51	0.003

Significant differences were not found in the neuropsychiatric tests among the different subgroups with Mild Cognitive Deterioration (Table 8).

The *Kaplan Meier* curves were calculated to estimate the likelihood of conversion to dementia over time. When the mild cognitive impairment and normal samples were analyzed (n=144), it was verified that 27.1% converted to Alzheimer type dementia, 13.90% (n=20) at 6 months and the rest, that is 13.20% (n=19) at one year. The mean time of conversion to Alzheimer was 11.12 months (SD=0.183). None of the normal group converted to ATD ($p<0.01$). (Figures 2 and 3).

When the *Kaplan Meier* curve was calculated with normal subjects, differentiating the patients with MCI (n=127) into amnestics, non-amnestics and multiple domains, statistically significance differences ($p<0.05$) were observed in the percentage of conversion to Alzheimer type dementia (ATD) among the different groups. None of the normal controls converted to ATD (n=17). A total of 35% (n=7) of the amnestic MCI converted to ATD (-20% (n=4) at

Table 5 Neurological tests of the MCI subgroups

Neuropsychological Tests	aMCI	na-SD-MCI	mdMCI	p < 0.05
MMSE	27.2(1.7)	28.4(1.3)	25.7 (4.2)	
Serial Learning	7.1 (1.7)	7.8 (1.6)	6.2(2.1)	
Serial Recall	4.6 (2.3)	7.5 (1)	3.8 (2.7)	na-SD-MCI vs mdMCI
Recall con clues	7.5 (-2.5)	11.2 (1.3)	6.8 (3.8)	(aMCI + mdMCI) vs na-SD-MCI
Recognition	10.7(1.5)	11.7(0.4)	9.3(±2.9)	
Naming	50.6 (5.3)	48.4 (5.6)	40.9 (10.5)	aMCI vs mdMCI
Semantic Fluency	15.2 (2.9)	15.7(4.6)	13.4 (4.6)	
Phonological Fluency	13.8 (3.8)	14.1(5.3)	9.8 (4.7)	aMCI vs mdMCI
Span Direct	5.8 (1.3)	4.7 (1.0)	5 (1.1)	
Span Reverse	4.2 (1.1)	3.7 (0.7)	3.1 (1.3)	aMCI vs mdMCI
Trail Making A	46.2 (10.6)	70.7 (27.7)	97.3 (56)	aMCI vs mdMCI
Trail Making B	119 (36)	188 (139)	286 (148)	aMCI vs mdMCI
Clock	6.8 (0.5)	6.7 (0.4)	5.1 (2.3)	aMCI vs mdMCI

aMCI: Amnestic Mild Cognitive Impairment
na-SD-MCI: Non-amnestic single domain Mild Cognitive Impairment
mdMCI: Multiple Domain Mild Cognitive Impairment

Table 6 Neuropsychiatric Battery in the Populations (Normal and MCI)

	Normal	MCI	Sig. (between normal and MCI)
Delusions	20% (n=2)	13.7% (n=14)	0.947
Hallucination	0%	10.7% (n=11)	0.504
Agitation	30% (n=3)	30.1% (n=31)	0.425
Depression	18.2% (n=2)	58.3% (n=60)	0.081
Anxiety	18.2% (n=2)	38.8% (n=40)	0.145
Euphoria	9.1% (n=1)	13.6% (n=14)	0.543
Apathy	9.1% (n=1)	36.9% (n=38)	0.113
Disinhibition	0%	13.7% (n=14)	0.340
Irritability	45.5% (n=5)	41.6% (n=42)	0.597
Beck	ξ = 4.75 S.D. = 3.84	ξ = 10.252 S.D. = 7.98	0.021

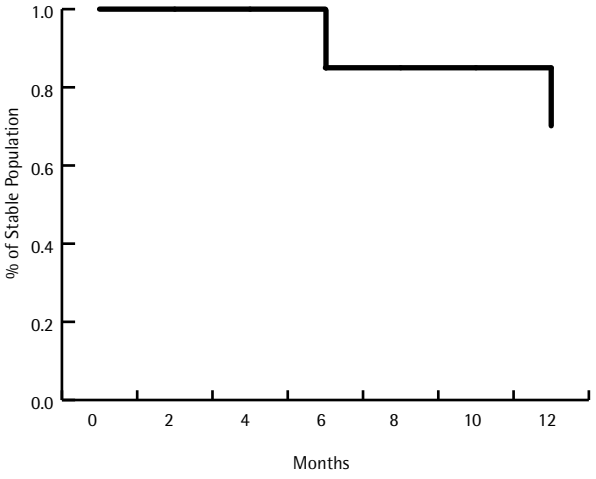
MCI: mild cognitive impairment; S.D.: Standard deviation, n= number of subjects,
Sig= significant= p<0.05 or p<0.01; %: percentage of cases that presents the symptoms,
MMSE: Mini Mental State Examination, CDR: Clinical Dementia Rating Scale

6 months and 15% (n=3) at 12 months and 11.1% (n=1) of the non-amnestic MCI evolved to ATD at 6 months. Of those with multiple domains, 31.6% (n=31) passed to ATD, 15.3% (n=15) at 6 months and 16.3% (n=16) at 12 months.

Table 7 Neuropsychiatric Tests of the subgroups of MCI

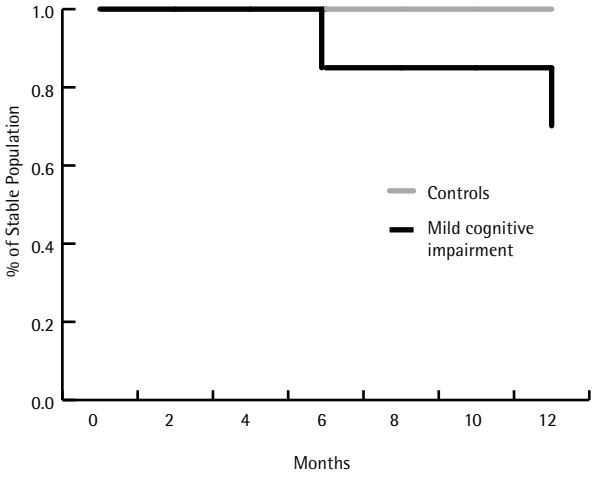
Neuropsychiatric Tests	aMCI	na-SD-MCI	mdMCI	p < 0.05
Delusions	0.44 (1)	0 (0)	0.39 (9.3)	ns
Hallucination	0.1 (0.3)	0 (0)	0.3 (1.4)	ns
Agitation	1.2 (2.4)	0.5 (1.5)	0.9 (2.2)	ns
Depression	1.6 (1.9)	2.1 (2.6)	2.1 (3.1)	ns
Anxiety	1.4 (2.2)	1.4 (2.5)	1.6 (2.8)	ns
Euphoria	0.2 (0.4)	0 (0)	0.4 (1.5)	ns
Apathy	0.8 (1.4)	1.4 (2.1)	1.7 (3.1)	ns
Disinhibition	0.1 (0.3)	0.8 (2.2)	0.5 (1.7)	ns
Irritability	0.6 (1.3)	1.4 (3.3)	1.7 (3.1)	ns
Beck	9.7 (6.5)	12.5 (0.5)	10.1 (0.3)	ns

aMCI: Amnestic Mild Cognitive Impairment
na-SD-MCI: Non-amnestic single domain Mild Cognitive Impairment
mdMCI: Multiple Domain Mild Cognitive Impairment



The curve shows the passage of the subjects at risk of evolving to dementia and it is expressed in the percentage of patients who remain stable over time. The time is expressed in months.

Figure 2 *Kaplan Meier Curve of the subjects at risk of conversion to dementia*



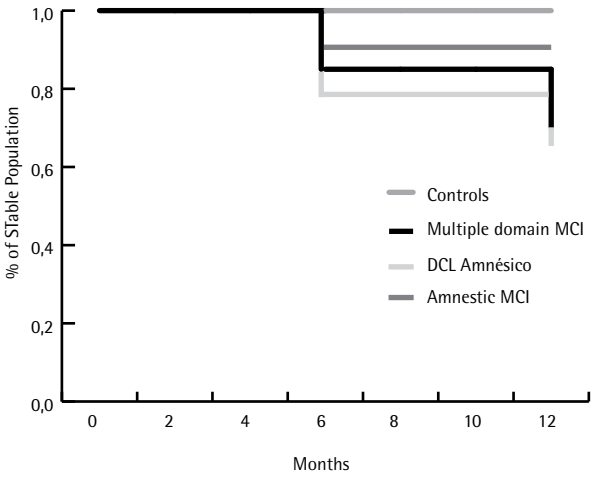
The curve shows the passage of the subjects at risk of evolving to dementia and it is expressed in percentage of patients who remain stable over time. The time is expressed in months

Figure 3 *Meier Kaplan Curve of conversion to dementia of the controls and MCI subjects*

Figure 4 shows the conversion of each one of the populations, that of amnestic MCI being the greatest.

Cox's regressions were calculated to verify the predictive capacity of some variables regarding passage or not to ATD. It was verified that age ($p<0.05$; $\beta=1.03$) increased the likelihood that Alzheimer's Type Dementia would occur earlier. Years of educations, family background, arterial hypertension, diabetes, cardiac background, dyslipidemia, smoking, the MMSE value and Beck's depression inventory were not significant predictors of conversion to Alzheimer's Type Dementia ($p>0.05$) (Table 3).

However, age was a significant predictor of conversion to Alzheimer ($p<0.05$; $\beta=1.03$).



The curve shows the passage of the subjects at risk of evolving to dementia and it is expressed in percentage of patients who remain stable over time. The time is expressed in months

Figure 3 | *Kaplan Meier Curve of conversion to dementia of the subtypes with MCI*

STUDY LIMITATIONS

The present study was conducted based on a cohort of patients evaluated in a Neuropsychology Department. The sample of patients with mild cognitive deterioration was divided into 3 groups and compared for their statistical analysis. It should be stressed that the number of cases in each group was not the same. The mdMCI has the largest number of cases, since in generally this was a population at risk of evolving to Alzheimer type and non-Alzheimer type dementia. Thus, a larger number of cases should be included to shed light on the statistically significant differences. However, the na-SD-MCI is more specific to a certain condition, as for example Primary Progressive Aphasia, so that it can be considered significant with a smaller number of patients. Consequently, as one of the groups has the majority of the cases, the statistical inferences should be considered with caution and the results should be interpreted within this context. It is not possible to extrapolate them to the general population or even to the hospital population in general.

DISCUSSION

Progress in scientific knowledge in the field of dementias, especially in Alzheimer's Disease, including clinical, neuropsychological and genetic aspects, development of specific biomarkers of the physiopathological process and the appearance of diagnostic criteria for the early phases of the disease as well as the mild cognitive deterioration due to AD[3,4] or prodromic AD[20] have constituted the bases for new investigations in order to detect this population at risk of dementia from the clinical point of view.

According to the literature, the population at risk of degenerative dementia (mild cognitive impairment, questionable dementia, Clinical Dementia Rating (CDR) 0.5, impairment with dementia, mild cognitive impairment due to AD, etc.) has a higher conversion rate to dementia than that of the general population. The progression level ranged from 10 to 25% per year.[6,21-28] In this study, with 127 patients followed up at one year, the mean conversion was 27.1% per year, similar to the study of Flicker et al. in the year 1991. This study also included 32 patients with an average age of 71 years followed up for two and a half years, with an annual conversion rate of 25%.[28] Other works on the MCI in the 1990's such as the Petersen et al. study in 1999, with 66 patients, reported a percentage of conversion to dementia of 12%/year.[29] In 1997, Bowen evaluated a cohort of 21 patients and observed an annual conversion rate of 12%.[30]

The mentioned studies, on the contrary to this one, included few MCI cases and these were not clinically typed by subtypes. However, their follow up was between one year (similar to this study) and three years on an average.

The longitudinal study of Espinosa A et al. in 2012 included 550 patients with MCI. It showed that the amnestic MCI subtype had a risk of conversion to dementia 8.5 times greater than the non-amnestic MCI subtype, which showed the slowest rate to conversion.[6] In our study, the patients who converted to dementia only did so to Alzheimer's type dementia according to the *DSM IV* and *NINCDS ADRDA* clinical criteria. This was in spite of the fact that most had vascular risk factors, none showed any clinical event consistent with CVA or progressed to vascular dementia. The vascular risk factors mentioned in the corresponding section, as arterial hypertension and cardiac backgrounds, were similar in all the populations studied. The average time in which the subjects converted to Alzheimer was 11.12 months (SD=0.183). None of the normal controls converted to dementia, the difference of likelihood of conversion between both groups being statistically significance. ($p<0.01$).

In this work, the MCI subjects did not have significant neuropsychiatric manifestations according to the Neuropsychiatric Inventory. As reported in the literature.[19-27] Demey et al. found irritability (55%), dysphoria (44%), apathy (37%) and anxiety (37%) in the population of MCI studied.[27] However, there were significant differences in comparison with the normal controls in the Beck depression inventory at the beginning of the study.

Regarding the prevalence of the different MCI subtypes, the most uncommon form was the single non-amnestic domain MCI. Only 1 patients out of 9 in this group converted

to dementia. Said case had very low performance on *TrailMaking Test* A and memory scores (delayed recall and recognition) and a low normal value in the first neuropsychological evaluation. At 6 months, the patient evolved clinically to dementia, showing an important decrease in performance on the memory tests. The 8 remaining subjects remained stable at 12 months (3 MCI with low naming measures by the *Boston* test, 3 MCI with very low performance on the attention tests (*TMT A*) and 2 MCI with low performance of the executive test performance (*TMT B*). The patients with low values on attention tests had forgetfulness complaints corroborated by the family member. They did not have backgrounds of attention disorder in childhood and the attention tests were more than 1.5 standard deviations below the mean for their age and education level. There were no mediating metabolic or endocrinological or psychiatric factors that could justify the attentional disorder.

The aphasic type MCI, scoring below 1.5 standard deviations of the mean according to age and education level in language performance. This condition per se implies risk of conversion to dementia and the presence of aphasia already represents the existence of pathology, that is, primary progressive aphasia. [31-33]

The MCI subtype with multiple domain involvement was the most frequent presentation form, followed by the amnestic subtype and finally by non-amnestic single domain.

Although MCI with multiple cognitive domain involvement was the most frequent, conversion to dementia was greater in the amnestic subtype (with the hippocampus type neuropsychological profile - low delayed recall and recognition) as is reported by different studies in the worldwide literature. It was not observed that the presence of intrusions was an important predictor of conversion to dementia as described in other studies.[21,34-43]

In 2012, Ward A et al. observed that the prevalence and incidence associated the MCI varied greatly in 42 publications in accordance with the definitions used to designate the subjects at risk of dementia. In this study, the prevalence of MCI was 3-42% and the amnestic form was 0.5 to 31.9%.[44]

Advanced age was the only variable that increased the likelihood that passage to Alzheimer type dementia would occur earlier.

The data presented stress the need in assistential medicine to recognize the existence of a "population at risk of degenerative dementia" and to extend the amnestic MCI criteria as the subtype of greater risk of evolving to dementia.

More long-term follow-up studies on the different subtypes of MCI are needed to corroborate these findings. However, at present, the evaluation of the subtype of MCI could be considered an important clinical biomarker with prognostic value, especially in those centers where the performance of the new diagnostic techniques, based on molecular studies, could be inaccessible.

On the other hand, adequate clinical identification of MCI with the association of biomarkers of beta amyloid deposition and/or neuronal damage as the functional neuroimaging could be an important challenge towards the future.[2]

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CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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