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Prevalence and evolution of delirium in a community population of 70 years and older

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Introduction. There are many studies on delirium in clinical populations and nursing home patients but not in community populations. This study has aimed to know the prevalence of delirium in a community population and to know the survival rate during a five-year period.

Method. Case-control and survival study based on data from an epidemiological study to measure the prevalence and incidence of dementia in eight rural villages in Girona. According to the Diagnostic and Statistical Manual of Mental Disorders, delirium was identified for the prevalence study using the information obtained from the Cambridge Mental Disorders of the Elderly Examination. A hypothesis contrast method was used in order to compare all clinical features of the subjects according the presence or the absence of delirium. The Kaplan-Meier technique was used to estimate survival of the subjects, and a multivariate Cox regression analysis was done to know the effect of delirium on mortality over the five-year period.

Results. 1,460 subjects older than 69 participated in the study. A prevalence of 0.96% (95% confidence interval [CI]: 0.43-1.49) was detected (14 cases of delirium). Mean survival for subjects with delirium was 3.0 years (CI 95%: 1.9-4.1) and it was slightly lower than for healthy controls. The presence of delirium increased the risk of death in five years by 2.65.

Conclusion. The prevalence of delirium in community populations is low and most of the times it is superimposed on dementia. Patients with delirium have a higher risk of mortality at the end of a five-year period.

Key words:
Delirium. Dementia. Prevalence. Survival. Epidemiology. Risk factors.

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Prevalencia y evolución del delirium en una muestra comunitaria de 70 años y más

Introducción. Existen numerosos estudios sobre el delirium con muestras clínicas e institucionalizadas, pero son escasos con muestras comunitarias. El objetivo del estudio fue determinar la prevalencia de delirium en una muestra comunitaria y la supervivencia en un período de 5 años.

Método. Estudio de casos y controles y de supervivencia a partir de los datos de un estudio epidemiológico para determinar la prevalencia de demencia y su incidencia tras 5 años en ocho municipios de la provincia de Girona. Se aplicaron criterios DSM-IV para identificar los casos de delirium en el estudio de prevalencia a partir de la información recogida mediante el *Cambridge Mental Disorders of the Elderly Examination*. Se aplicaron técnicas de contraste de hipótesis para comparar las características de los participantes según la presencia o ausencia de delirium. Se utilizó la técnica de Kaplan-Meier para estimar la supervivencia de los participantes y un modelo de regresión multiariante de Cox para determinar el efecto del delirium sobre la mortalidad a los 5 años.

Resultados. Participaron 1.460 habitantes mayores de 69 años y se detectaron 14 casos de delirium que representaron una prevalencia del 0,96% (intervalo de confianza [IC] 95%: 0,43-1,49). La supervivencia media para los participantes con delirium fue de 3 años (IC 95%: 1,9-4,1) y fue significativamente inferior a la de los controles sanos. La presencia de delirium incrementó en 2,65 el riesgo de mortalidad a los 5 años.

Conclusiones. La prevalencia de delirium en muestras comunitarias es baja y la mayoría de los casos está superpuesto a una demencia. Los pacientes con delirium tienen un mayor riesgo de mortalidad a los 5 años.

Palabras clave:
Delirium. Demencia. Prevalencia. Supervivencia. Epidemiología. Factores de riesgo.

INTRODUCTION

Delirium, also known as acute brain failure, acute brain syndrome, organic brain syndrome, dysergastic reaction, en-

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cephalopathy, acute confusional episode and reversible or masked dementia, is a frequently reversible and transitory condition characterized by an acute or subacute and fluctuating onset[1]. Clinically, it is manifested by the presence of a large number of neuropsychiatric abnormalities, among which awareness and/or attention disorder in addition to other symptoms, such as cognitive and non-cognitive, predominate[2].

This is a very frequent disease in elderly hospitalized patients with a prevalence that ranges from 10% to 40%[3-6], 15% to 20% of whom already have it at the time of admission and 5% to 40% develop it during the hospitalization[4]. It should be stated, however, that the prevalence in community samples of delirium is much less and ranges from values under 0.5%7 to 1%[8] in patients without dementia and globally is found to be between 1% and 2%[9]. Its prevalence increases in patients with dementia[10] and approximately one fourth of the patients with Alzheimer type dementia had a delirium episode during their disease[11].

In spite of its low prevalence in community samples, the importance of delirium is determined by being treatable and potentially preventable. its development often begins a cascade of events that generally end up in a loss of independence, increase of morbidity and mortality risk and increase of health care costs which are mostly due to a longer hospital stay, although it also affects post-hospital costs[4,6,12]. It is so important that it has even been proposed as an indicator of the quality of the health care services[6].

Given that there are few population studies on the prevalence of delirium, this present study has aimed to determine its prevalence in the general population in those of 69 years of age and survival at 5 years based on the data of a population epidemiological study on the prevalence and incidence of dementia, called Girona study[13-15].

METHOD

Design

Case and control and survival study based on the data of an epidemiological study of prevalence and incidence of dementia whose design has been previously described[13-15]. Briefly, this is a double phase, door-to-door population epidemiological study whose purpose was to determine the prevalence of dementia and its incidence after 5 years in a rural zone formed by 8 municipal areas of the north east of the province of Girona that included a total population of 10,986 inhabitants[16].

Subjects

Based on the population data of the municipal census of the towns, 1,581 elderly inhabitants over 69 years were selected and 1,460 of them participated in the first phase of the prevalence study in the year 1990. A total of 335 individuals with suspicion of dementia as they scored below the cut-off of the Mini Mental State Examination (MMSE)[17] that we used as screening instrument were chosen for the second phase. Furthermore, 314 subjects with scores above the cut-off of the MMSE were chosen randomly for the second phase in order to determine the number of false negatives in the screening phase and to correct the estimation of the dementia prevalence. Twenty-four subjects who, due to sensorial deficits, could not be administered the MMSE in the first phase, also passed directly to the second phase.

All the participants of the second phase were contacted in 1995, this being 5 years after the prevalence study was performed to determine the incidence of dementia. For the present study, only the information on the life condition of the participants in 1995 was used. Figure 1 shows the algorithm of participation in the study.

Diagnosis of delirium and dementia

The diagnostic process was performed in the second phase of the prevalence study which aimed to verify or reject the suspicion of dementia established in the first phase. One neurologist and one clinical psychologist administered the Cambridge Mental Disorders of the Elderly Examination CAMDEX (CAMDEX) protocol18 in the home of each participant. The CAMDEX is formed by several sections that include: a standardized interview to the subject on his/her physical and mental condition, a structured interview to the family member or caregiver who knew the patient well about the disease background of the patient and the current clinical manifestations, a battery of neuropsychological examinations (Cambridge Cognitive Examination CAMCOG) and a simple physical examination that included the evaluation of the auditory and visual capacity, measurement of blood pressure and gait and osteotendinous and plantar reflexes. The administration of the CAMDEX protocol makes it possible to obtain the score from the Blessed Dementia Rating Scale (BDRS)[19], from the Hachiski scale (E-HA)[20] and from two scales from the protocol that evaluate depression, that is the E-DEP scale and the organicity scale (E-ORG). The CAMDEX protocol was adapted and validated in our setting[21].

The diagnosis of delirium and dementia was made according to the DSM-IV criteria[21] based on the clinical information gathered with the CAMDEX protocol. Delirium «case» was considered to be all the subjects who fulfilled delirium criteria independently of whether it was superimposed or not to dementia. Dementia «case» was considered to be all the subjects who fulfilled dementia criteria independently of the subtype of dementia.

Onset time of delirium and/or of dementia was established as time passed from the first manifestations of cognitive deterioration detected by the patient him or herself and his or her family members until time of diagnosis.

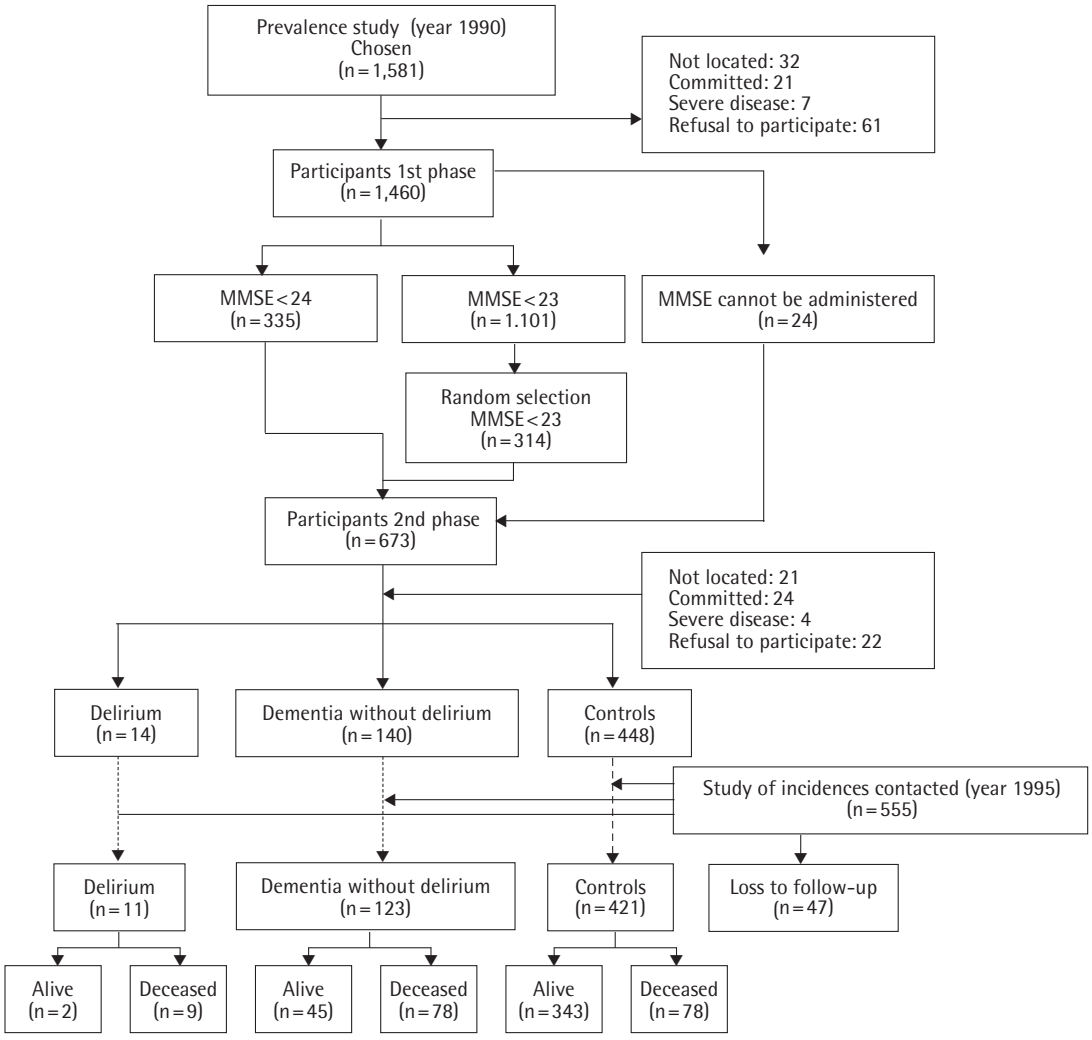

Figure 1 *Algorithm of participation of the Girona 1990-1995 study: cases with delirium.*

Statistical analysis

A descriptive analysis of the characteristics of the participants using central tendency and dispersion measures for the quantitative variables and absolute and relative frequency measures for the qualitative variables was performed. Prevalence of delirium was calculated as the relative frequency of cases in regards to the total of the sample and 95% confidence interval was calculated. In order to determine the presence of significant differences in the clinical manifestations between the groups of participants without delirium or dementia, parametric and non-parametric univariate hypothesis contrast techniques, considering the data distribution, were applied to the participants with delirium and those with dementia without delirium. Normality of the variables was compared with the Shapiro-Wilk test.

The Kaplan-Meier product limit method[23] was used to make the univariate estimate of survival and the log-rank test was used to compare the survival curves among the patients with delirium, those with dementia and the healthy controls. Survival time was defined as time passed between the date of diagnosis in the prevalence study and date of the follow-up study interview at 5 years or in case of death, date of death.

In order to determine the effect of delirium on mortality, the Cox proportional hazards model[24] was used to adjust a multivariate regression model, using the life condition of the patient at the end of the study as dependent variable. Diagnosis (0: healthy controls; 1: dementia without delirium; 2: delirium) was included as principal independent variable. Those variables with statistical significance in the univariate analysis and that had also demonstrated possible confounding effects such as gender (0: feminine; 1: masculine), age (age in years of patients when diagnosed of dementia or delirium), score on the E-ORG and CAMCOG, and time (in months) of cognitive deterioration duration were also included as covariables.

The results are expressed as absolute numbers and percentages, means, standard deviations and 95% confidence intervals (CI). A level of 0.05 statistical significance was considered in the hypothesis contrasts. Data processing and analysis were performed using the SPSS program, version 14.0 for Windows.

RESULTS

The sample was made up of 1460 participants with a mean of 76.9 years (SD: 5.49) of age, 60.1% (n: 877) of whom were women. Using the double phase detection process, 14 cases of delirium were detected, this representing a community prevalence of 0.96% (95% CI: 0.43-1.49). Among the patients with delirium, 85.7% of them (12/14) had a concomitant diagnosis of dementia. The delirium prevalence between the participants with dementia was 7.95% (95% CI: 3.30-12.59) and among the participants without dementia, it was 0.15% (95% CI: 0.02-0.55). The *odds ratio* of having delirium in patients with dementia was 19.20 (95% CI: 4.24-86.82).

In table 1, the clinical and sociodemographic characteristics of the participants according to those with diagnosis of dementia, delirium and healthy controls who participated in the second phase of the prevalence study (n = 602) are shown. Patients with delirium compared with those diagnosed of dementia without delirium were younger (Mann-Whitney U: 583.5; p = 0.013), had greater functional alteration (Mann-Whitney U: 623.5; p = 0.025) in spite of obtaining similar results in the CAMCOG (Mann-Whitney U: 825.5; p = 0.331) and obtained higher scores on the E-ORG (Mann-Whitney U: 567.5; p = 0.009). Regarding the healthy controls, those patients with delirium had lower level of schooling (Mann-Whitney U: 2066.5; p = 0.028), obtained lower scores on the CAMCOG (Mann-Whitney U: 480.0; p = 0.001) and higher scores on the E-ORG (Mann-Whitney U: 182.5; p = 0.001) and the E-HA (Mann-Whitney U: 741.0; p = 0.001) (table 1).

During the period between the prevalence study and the incidence study, 165 participants (27.4%) died, 9 (64.3%) of whom had delirium at the time of diagnosis, 78 (55.7%) with dementia and 78 (17.4%) healthy controls (χ^2: 88.45; gl: 2; p = 0.001). Mean survival of the patients with delirium was 3.00 years (95% CI: 1.94-4.06), that of the patients with dementia was 3.71 years (95% CI: 3.35-4.07) and that of the healthy controls 5.40 years (95% CI: 5.27-5.53). Statistically significant differences were observed in the survival between the three groups (log-rank: 130.44; gl: 2; p < 0.001).

The regression adjustment model was made after verifying that the mortality risk remained constant over time on the graphical representation. The final model was obtained using the backward exclusion method of the significant variables in the univariate analysis and after performing the tests to detect the possible interaction factors. The final model, with an adequate goodness of fit (p < 0.005), incorporated the female gender, age, score on E-ORG and diagnosis (control, dementia or delirium) as predictive variables of survival. Presence of delirium obtained a relative risk of mortality of 2.65 (95% CI: 1.18-5.96) and was the highest value among the variables forming the model. In table 2, the relative risks of each variable included in the model are presented and figure 2 shows the graphic representation of survival stratified by diagnosis.

Table 1 Comparison of clinical and sociodemographic characteristics of the participants according to the presence or absence of delirium and/or dementia

	Delirium (n = 14)	Dementia without (n = 140)	Control (n = 448)
Age, mean (SD)*	78.6 (5.6)	82.65±5.84	76.9±5.50
Female gender, n (%)	(57.1)	(79.3)	(65.6)
Years of schooling, mean (SD)**	2.2 (3.5)	1.5 (2.8)	4.2 (3.8)
CAMCOG, mean (SD)**	27.1 (21.7)	31.7 (16.0)	67.5 (17.7)
BDRS, mean (SD)***	17.6 (11.7)	10.4 (7.9)	1.3 (2.3)
E-DEP, mean (SD)	3.4 (3.2)	3.3 (3.2)	2.7 (3.0)
E-ORG, mean (SD)***	16.4 (7.2)	11.0 (6.8)	1.6 (2.4)
E-HA, mean (SD)****	6.6 (3.0)	4.9 (3.2)	2.1 (2.3)
Family psychiatric background, n (%)	(7.1)	(19.3)	(18.3)
Personal psychiatric background, n (%)	(0.0)	(19.3)	(15.4)
Family background of dementia, n (%)	(7.1)	(15.0)	(15.6)

* Delirium < dementia (p < 0.05). ** Delirium < control (p < 0.03). *** Delirium > dementia and control (p < 0.02). **** Delirium > control p < 0.02). CAMCOG: Cambridge Cognitive Examination; BDRS: Blessed Dementia Rating Scale; E-DEP: Depression Scale; E-ORG: Organicity Scale; E-HA: Hachinski Scale.

DISCUSSION

Our results corroborate the low prevalence of delirium in community geriatrics samples. Both the global prevalence of 0.96% and the 0.15% registered in subjects without dementia are found in the low range of the values provided up to now[7-9]. Furthermore, 7.28% of the delirium prevalence superimposed to dementia is also inferior to the 13% of other studies[8], although the differences in methodology and samples of other works must be pointed out. The diagnostic criteria used can partially explain the differences in the results between the epidemiological studies[25].

Table 2 Variables included in the COX multivariate regression model of survival at 5 years

	HR	95% CI	p
Age	1.10	1.07-1.13	0.001
Female gender	0.61	0.44-0.84	0.002
E-ORG	1.07	1.04-1.10	0.001
State			
Control	1.00*	–	–
Dementia	1.63	1.03-2.58	0.038
Delirium	2.65	1.18-5.96	0.018

*Reference group; E-ORG: Organicity Scale.

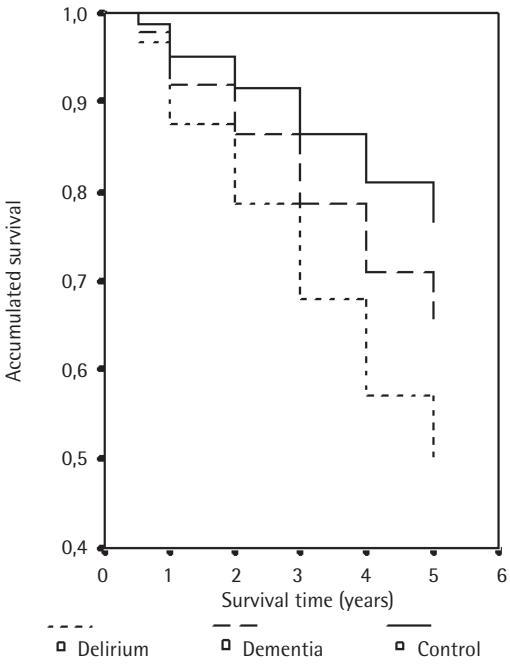

Figure 2 *Function of survival estimated according to diagnosis.*

In the same way as in hospital samples, there was also a greater rate of delirium in patients with dementia recorded in the community setting[10]. Our study supports these results and shows that there are 19.2 patients with delirium and associated dementia for each patient with delirium and without dementia. This strong epidemiological partial superposition between delirium and dementia, together with a decrease in brain metabolism, cholinergic deficit and increase in the inflammatory process have even suggested an overlapping of clinical, metabolic and cellular mechanisms between the two diseases. In fact, it has been suggested that delirium and dementia could represent different points over a continuum of the cognitive disorders more than different diseases[6].

It has been repeatedly observed that patients who have suffered a delirium during hospitalization have a greater risk of mortality[26-28] and that the greater the severity of the delirium, above all in regards to cognitive deterioration, the greater the risk[29]. Delirium superimposed to dementia has greater clinical severity[4] and seems to maintain the risk of mortality[30]. Our work, as in other studies, demonstrates that delirium continues to be a factor that increases mortality risk in maintained in community samples and that it is similar to that recorded in patient with dementia without delirium[7].

In spite of the scarce evidence on the efficacy in delirium for both classical as well as new generation antipsychotics[31], both have been recommended[3,34,35], even though they provoke an increase in mortality in patients with dementia[36-38]. Thus, the increase of mortality of delirium may not be due to delirium per se but rather to the treatment that is usually prescribed in these patients. However, it should be mentioned that the hypoactive subtype of delirium is relatively elevated[40-41]. This probably determines the low detection rate of patients with delirium1 and requires specific therapeutic implications different from the hyperactive or mixed variants[42]. In these cases, it is likely that the prescription of antipsychotics is lower. Evolutive studies according to the delirium subtype throw more light on the role of antipsychotics in the increase of mortality experienced by these patients.

It should be indicated, however, that the previous arguments may have an inverse reading. The increase of mortality of patients with dementia who have received antipsychotic treatment[36-39] is probably not due to the drugs but to the presence of delirium, the cause of the prescription of the antipsychotics[3,34-35].

While the delirium superimposed to dementia tends to have a better prognosis[28], it behaves with greater severity than dementia. Delirium has an influence in the patients with dementia, causing a dramatic worsening of the cognitive deterioration and faster progression of the functional loss[6]. Our results support the statement that delirium entails greater severity of dementia since, with equality of cognitive function, patients with delirium have greater functional alteration.

One third of the patients with delirium superimposed to dementia of our study are erroneously labeled as dementia since this diagnosis was not corroborated in the follow-up. It is likely that the long-term persistence of the delirium symptoms[28,44] may be an element that affects the diagnostic error. On the other hand, Lewy body dementia that includes fluctuations in cognition and visual hallucinations as nuclear symptoms not only illustrates the overlapping between dementia and delirium, but may also be another reason why

some patients are badly diagnosed of dementia. However, it must be pointed out that this error does not significantly affect the epidemiological studies of dementia due to the low prevalence of delirium in community samples.

The epidemiological studies show that suffering delirium increases the risk of developing a dementia condition[45], although this may also identify a subgroup of subjects vulnerable to cognitive deterioration or patients with initial manifestations of a dementia condition that had not been detected prior to the delirium[6]. The low number of subjects with delirium without dementia recorded in our study prevents us by providing data in this regards.

Certain medical conditions may be factors that act as predisposing and/or precipitating ones of delirium46. This makes it possible to explain the higher scores we observed in the E-ORG in patients with delirium of our study. A tendency to obtain higher scores in the E-HA could determine that part of these medical conditions are vascular type ones.

Different aspects that limit the results obtained should be kept in mind. In the first place, it should be stated that this is a secondary analysis based on the data of an epidemiological study of dementia and that the sample size was not determined based on the estimated prevalence of delirium but rather on that of dementia, which is much higher. Thus, a reduced number of delirium cases has been obtained, this limiting the potency of the statistical contrasts. In the second place, the study does not contemplate the presence of other chronic diseases such as chronic obstructive pulmonary disease, that could introduce a bias into the results of the measurements that are competitive factors of mortality. Among the strong points of the study, it could be stated that although the CAMDEX offers a diagnosis of delirium based on its own criteria, the extensive information gathered by the CAMDEX protocol made it possible to make the diagnosis of delirium based on the DSM-IV criteria and to be able to compare our results with other studies.

As conclusion, we point out that our study makes it possible to corroborate the low prevalence of delirium recorded in community samples, affirm the close association recorded between delirium and dementia, observe that the increase of mortality risk associated to the delirium detected in hospital studies can also be transferred to our communities, verify that survival from delirium is lower than in that of dementia and that there is the risk that an elevated number of patients with delirium in the epidemiological studies may be erroneously labeled with dementia.

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