



## Depression, hypertension, and comorbidity: Disentangling their specific effect on disability and cognitive impairment in older subjects

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### ARTICLE INFO

#### Article history:

Received 18 December 2009

Received in revised form 29 March 2010

Accepted 30 March 2010

Available online 22 April 2010

#### Keywords:

Depression in the elderly

Hypertension

Comorbidity

Disability in the elderly

Cognitive impairment

### ABSTRACT

We aimed to demonstrate that depression and hypertension are associated independently of each other with disability and cognitive impairment in older subjects and that such an association is not attributable to number and severity of comorbidities. An observational study was performed on elderly patients admitted to the Hospital Network of the Italian National Research Center on Aging (INRCA) from January 2005 to December 2006. Depression was defined according to 15-item geriatric depression scale (GDS) score; physical disability according to activities of daily living (ADL) and instrumental activities of daily living (IADL) scores; cognitive impairment on the mini-mental state examination (MMSE) test; the number and severity of comorbidities by means of physician-administered cumulative illness rating scale (CIRS). Among 6180 older subjects (age =  $79.3 \pm 5.8$  years; 47% men), 48.3% were normotensive, 21.8% normotensive depressed, 21.7% hypertensive, and 8.2% hypertensive and depressed. Both depression and hypertension remained significantly associated with functional disability and cognitive impairment. When controlling for age, gender, the number and severity of comorbidities, hypertension was associated with a significantly higher likelihood of having functional disability or cognitive impairment only in the presence of depression (odds ratio = OR = 2.02, 95% confidence interval = 95%CI = 1.60–2.54,  $p < 0.001$  for functional disability; OR = 2.21, 95%CI = 1.79–2.74,  $p < 0.001$  for cognitive impairment) as compared to normotensive controls without depression. We conclude that depression per se or co-occurrence of hypertension and depression is associated with higher functional disability and cognitive impairment in older subjects. This effect is not attributable to the number or to the severity of comorbidities.

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### 1. Introduction

Depression is a very common condition in the elderly, affecting 1–2% of the over 65 years population (Horwath et al., 1992), 14% of community-dwelling, and 32% of residential care-dwelling subjects (Anstey et al., 2007). Detection of depression in older subjects is more difficult because symptoms are often masked as physical complaints. Given the higher rate of depressive disorders in older subjects living in institution than in those living at home, it is expected that the prevalence of depressive symptoms is much higher in subjects with chronic disease (Niti et al., 2007). In other terms, depression maybe secondary to an increased number of

disease (higher comorbidity) rather than representing an independent contributor to physical disability and cognitive impairment. In addition, depressive symptoms complicate the course of treatment of chronic disease. For instance, it has been observed that older subjects complaining depressive symptoms are more prone to smoke, to be obese, to decrease physical activity (Penninx et al., 2000; Pratt et al., 2007). Indeed, depressive symptoms represent a risk factor for cardiovascular disease in older subjects and a significant prognostic factor in subjects who already developed cardiovascular disease (Frasure-Smith and Lépérance, 2006; Lichtman et al., 2008; Scuteri, 2008).

Hypertension is another common condition in older subjects, representing the most common morbid condition after osteoarthritis (Psaty et al., 2001). Hypertension represents a major risk factor for cardiovascular disease, the major source of morbidity and disability among the over 65 population (ISTAT, 2005). It has

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also been associated to an increased risk of incident depression (Luchsinger et al., 2008). A European study reported that hypertensive older subjects showed a 37–46% increased likelihood of developing depression as compared to normotensive age-matched group (Lobo-Escolar et al., 2008).

In such a context, the aims of the present study were to investigate: (a) whether depression and hypertension are associated with physical disability and cognitive impairment in older subjects; (b) whether the effects of depression and/or hypertension on disability are not attributable to comorbidity (the more illnesses the more disabled and, thus, the more depressed).

## 2. Subjects and methods

The present study uses data from a collaborative observational study aimed at surveying general health status of elderly patients admitted to the Hospital Network of the INRCA in seven Italian cities (Ancona, Fermo, Appignano, Casatenovo, Cosenza, Cagliari, and Rome). Our series consisted of 6180 patients aged 70 years or more, admitted consecutively in participating hospitals from January 2005 to December 2006. The study was approved by the Internal Ethical Committee.

### 2.1. Definition of hypertension

Based upon hospital discharge records, subjects were defined hypertensive if reporting any of the following ICD-9 code: 401 (essential hypertension), 402 (hypertensive cardiopathy), 403 (hypertensive nephropathy), and 404 (hypertensive cardiorenephropathy).

### 2.2. Assessment of depression

The GDS is widely used in geriatric clinical and research settings to screen elderly adults for the presence of clinically significant depressive symptoms. It is a self-rating scale. Items are summed and higher scores indicate a greater number of depressive symptoms. For the purpose of the present study the 15-item version of GDS (Sheik and Yesavage, 1986) was used. Conventionally, score  $\leq 6$  indicates the absence of clinically significant depression, whereas a score  $> 6$  indicates the presence of depressive symptoms and high likelihood of some form of depressive disorder. The GDS does not contain items concerning somatic complaints very often present in non-depressed geriatric patients with physical illnesses (Burke et al., 1989).

### 2.3. Cognitive and functional ability

The MMSE was adopted to assess global cognitive function (Folstein et al., 1975). MMSE assesses orientation to place and time, short-term memory, episodic long-term memory, subtraction, ability to construct a sentence, and oral language ability. The maximum score is 30. Decreased scores are associated with dementia (Folstein et al., 1975).

Personal independency was assessed by the ADL (maximum score 6) (Katz and Akpom, 1976) and IADL (maximum score 8) (Lawton and Brody, 1969). For both scales, the higher the score, the higher the personal independency.

### 2.4. Assessment of number and severity of comorbidity

The CIRS was applied to assess the number and the severity of illness. CIRS consists of 14 categories, each one exploring impairment in a specific organ or system, with a 0–4 grading scale (the higher the grading the more severe the illness). The severity index (ISV14) (Parmelee et al., 1995) is the mean of the

scores of the first 13 categories, excluding psychiatric disease. The comorbidity index (CM2) was calculated as the number of categories with a score of 2 or greater, including psychiatric disease (Parmelee et al., 1995).

### 2.5. Analytic approach and statistical analysis

The main “outcomes” of our study were cognitive and physical disability, as ascertained on the basis of MMSE, ADL, and IADL performance scores. Patients were considered cognitively impaired when MMSE score was less than 21 (Scuteri et al., 2005). In the absence of a consensus on its definition, physical disability was defined as loss of 3 or more ADL or loss of 4 or more IADL.

Other variables considered in the analyses were age, gender, CIRS comorbidity and severity scores, and diagnosis of hypertension. Patients were initially divided in two groups according to their GDS score ( $\leq 6$  and  $> 6$ ). Age, gender, comorbidity, cognitive status, physical performance, and prevalence of hypertension in the two groups were compared using Student's *t*-test for independent sample for continuous variables and  $\chi^2$ -test for categorical ones. Multiple logistic regression models were used to obtain a deconfounded estimate of the association between depression and/or hypertension, and outcomes. Three separate logistic regression analyses were performed for ADL  $\leq 3$ , IADL  $\leq 4$ , and MMSE  $< 21$ , respectively. For each of them, separate models were run adjusting for age and sex (Model 1) or for age, sex, number and severity of comorbidity (Model 2). Results are presented as adjusted OR with 95%CI.

Statistical analysis was performed with SPSS ver14.0 (SPSS Inc., Chicago, IL, USA) and the significance was accepted if the null hypothesis was rejected at the  $p < 0.05$  level.

## 3. Results

Our study population consisted of 6180 older subjects of mean age  $79.3 \pm 5.8$  years (ranging 70–103; 2904 or 47% M and 3276 or 53% F). Normotensive subjects represented 70.1% of the population. Prevalence of depression was 30.0% with a significantly higher occurrence in women than in men (36.9% vs. 22.1%, respectively,  $p < 0.001$ ).

As summarized in Table 1, older subjects with depression were on average 0.8 year older, with higher number (CIRS-CM2) and severity (CIRS-ISV14) of comorbidities, and decreased cognitive performance (on average 2.6 points of MMSE score lower) than the control subjects. Disability was significantly higher in depressed than in non-depressed subjects.

Depression was more common with hypertension and almost as twofold more prevalent in subjects with cognitive impairment (40% vs. 21.2%,  $p < 0.01$ ). Impairment in 3 or more ADL was twofold more common in depressed than in control subjects (31.4% vs. 15.1%,  $p < 0.0001$ ); similarly, subjects with impairment in 4+ IADL activities were more frequent among depressed than non-depressed subjects (57.5% vs. 34.7%,  $p < 0.001$ ).

### 3.1. Effects of depression and hypertension on disability and cognitive impairment: the role of comorbidities

The relationship between hypertension, depression, and physical or mental disability maybe attributable to the higher number of comorbidities in depressed older subjects. In other terms, a higher number of illnesses implies higher disability and this latter trigger depression. Indeed, in our population we also observed that depression was associated with higher number and severity of comorbidities (Table 2). Similarly, comorbidity was associated with functional disability (ADL disability: OR = 1.11, 95%CI = 1.04–1.19,  $p < 0.001$  for the number of comorbidities; OR = 2.32,

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