RESEARCH ARTICLE

In-hospital death according to dementia diagnosis in acutely ill elderly patients: the REPOSI study

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Objective: The aim of the study was to explore the association of dementia with in-hospital death in acutely ill medical patients.

Methods: Thirty-four internal medicine and 4 geriatric wards in Italy participated in the Registro Politerapie SIMI—REPOSI—study during 2008. One thousand three hundred and thirty two in-patients aged 65 years or older were enrolled. Logistic regression models were used to evaluate the association of dementia with in-hospital death. Socio-demographic characteristics, morbidity (single diseases and the Charlson Index), number of drugs, and adverse clinical events during hospitalization were considered as potential confounders.

Results: One hundred and seventeen participants were diagnosed as being affected by dementia. Patients with dementia were more likely to be women, older, to have cerebrovascular diseases, pneumonia, and a higher number of adverse clinical events during hospitalization. The percentage of patients affected by dementia who died during hospitalization was higher than that of patients without dementia (9.4 *versus* 4.9%). After multiadjustment, the diagnosis of dementia was associated with in-hospital death (OR = 2.1; 95% CI = 1.0–4.5). Having dementia and at least one adverse clinical event during hospitalization showed an additive effect on in-hospital mortality (OR = 20.7; 95% CI = 6.9–61.9).

Conclusions: Acutely ill elderly patients affected by dementia are more likely to die shortly after hospital admission. Having dementia and adverse clinical events during hospital stay increases the risk of death. Copyright © 2010 John Wiley & Sons, Ltd.

Introduction

It is estimated that currently around 24 million people have dementia in the world, with the number being projected to double every 20 years (Qiu *et al.*, 2007). Thus, increasing numbers of people will be hospitalized while suffering from dementia and many will end their lives in an acute care unit, despite dementia does not normally constitute the patient's main diagnosis at hospital admission.

Several studies have shown that patients with dementia are likely to have adverse hospital outcomes such as functional disability at discharge (Marengoni *et al.*, 2004), institutionalization (Zekry *et al.*, 2009) and longer length of hospital stay (Lang *et al.*, 2010). Moreover, few studies showed that dementia is

associated with both long- and short-term mortality after hospital admission (Sloan *et al*., 2004). Morrison and Siu (2000) found that the admission of a person with dementia and acute medical illness to hospital is a critical event associated with high 6-month mortality rates. Recently, Sampson *et al*. (2009) showed that dementia, highly prevalent in hospitalized elderly patients, is associated with markedly higher mortality. However, there is no agreement and few data on possible effects of the interaction between dementia, comorbid conditions, and clinical events during hospitalization on the outcome of older patients with dementia.

The aim of this study was to explore if older persons with dementia admitted to the acute hospitals have higher short-term mortality compared to their cognitively intact pairs, even after controlling for other key influences, including physical illnesses and adverse clinical events during hospitalization.

Methods

Data collection

The present study was held between January 2008 and December 2008 in 38 hospitals located in different regions of Italy, all participating in the Registro Politerapie SIMI (REPOSI) study, a collaborative effort between the Italian Society of Internal Medicine (SIMI) and the Mario Negri Institute of Pharmacological Research. The REPOSI study was designed with the purpose to create a network of internal medicine and geriatric wards in order to evaluate patients affected by multiple diseases and prescribed with polytherapy. Participation to the network was on a voluntary basis, but in the choice of the participating centers attention was put on their homogenous composition in terms of geographic distribution, size, and unselected admissions from the territory or the emergency room. The specific aims of the REPOSI study were: to describe prevalence of co-occurring multiple diseases and treatments in hospitalized elderly patients; to correlate clinical characteristics of the patients with type and number of diseases and treatments and to evaluate the main clinical outcomes at hospital discharge. The study included two phases; phase one was designed to create the network of internal medicine and geriatric wards; phase two was intended to activate a registry of patients included in the study. All the patients admitted to the wards participating in the study were consecutively recruited if they were 65 years old or older. Participation in the

study was voluntary and an informed consent was signed by all the patients. A sample of at least 40 patients consecutively admitted to each participating hospital during a period of 4 weeks, 3 months apart each from the other (one in February, one in June, one in September, and one in December 2008) was included in the study. A standardized web-based Case Report Form was filled in by the attending physicians, including socio-demographic factors, clinical parameters, diagnoses, and treatments at both hospital admission and discharge, clinical events during hospitalization and outcome. All the data recorded in the net were collected and checked by a central monitoring institution (the Mario Negri Institute for Pharmacological Research, Milan).

Data collection was in full compliance with the Italian law on personal data protection. Under the applicable legal principles on patients' registries, the study did not require the approval of Ethical Committees.

Sample

The initial study sample included 1411 subjects. Of these, 79 (5.6%) were excluded due to missing or incomplete data (25 had missing data on hospital outcome and 54 on socio-demographic and clinical characteristics due to errors in data input and recording). One thousand three hundred and thirty two individuals were ultimately available for these analyses. Patients who were not discharged home ($n = 111$) were excluded. Of these, six were terminally ill at hospital admission and transferred to end care of life structures; 44 were transferred to rehabilitation units or long-term facilities, and 61 were transferred to other hospital units for the onset of acute medical or surgical diseases during hospitalization. The proportion of patients affected by dementia and transferred did not significantly differ from the one of the whole sample (4.1 *versus* 8.3%, $p = 0.08$).

Assessment of diseases

Diseases examined in this study were diagnosed during hospitalization after careful clinical examination, clinical history, and laboratory and instrumental data collected by the attending physicians. Diagnoses were made using standardized criteria. The International Classification of Diseases—Ninth Revision (ICD-9) (WHO, 1987) was used for classifying all the diseases. The following ICD-9 codes were employed (corre-

sponding diseases are listed in alphabetical order); 280–285 (anemia); 300 (anxiety); 715 (arthritis); 427 (atrial fibrillation [AF]); 430–438 (cerebrovascular diseases [CVD]); 410–414 (coronary heart disease [CHD]); 490–496 (chronic obstructive pulmonary disease [COPD]); 585 (chronic renal failure [CRF]); 250 (diabetes); 272 (dyslipidemia); 574 (gallstones); 530–536 (gastric diseases); 428 (heart failure [HF]); 401–405 (hypertension); 560–569 (intestinal diseases); 571 (liver cirrhosis); 140–165, 170–175, and 179–208 (malignancy); 480–486 (pneumonia); 600 (prostate hypertrophy); 240–246 (thyroid diseases). The Charlson Index was employed to evaluate the coexistence and severity of multiple diseases [Charlson *et al.*, 1987]. Each condition is assigned with a score of 1, 2, 3, or 6 depending on the risk of dying associated with this condition. Then the scores are summed up and given a total score which predicts mortality (Charlson *et al.*, 1987).

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnostic criteria were used for the clinical diagnosis of dementia (APA, 1994). The ICD-9 codes used to indicate dementia diagnosis were 290 and 331.

Drugs were registered according to the Anatomical Therapeutic Chemical (ATC) classification system (WHO, 1990).

Adverse clinical events

Adverse clinical events were defined as any acute clinical problem that newly occurred during hospitalization (Bernardini *et al.*, 1993).

Statistical analysis

Socio-demographic and clinical characteristics of the sample by dementia diagnosis were described using univariate analysis (mean, or percentages). 95% confidence intervals (CI) were calculated for means and proportions. Logistic regression models were run to analyze the crude and adjusted association between dementia and in-hospital death. Covariates were dichotomized according to clinical judgement or mean values. The adjustment included age (years, 80+ *versus* <80), gender (females *versus* males), education (years of schooling), adverse clinical events during hospitalization (1+ *versus* 0 events), number of drugs (5+ *versus* 0–4), Charlson Index (score 3+ *versus* 0–2) (Model 1) or single diseases potentially related to death, (i.e., CVD, COPD, HF, AF, CHD,

pneumonia, malignancy, diabetes mellitus, liver cirrhosis, CRF, and anemia) (Model 2), length of hospital stay (number of days), vital parameters, such as systolic and diastolic blood pressure (mmHg), heart rate (beats per minute, bpm). Finally, the possible interrelation between dementia and adverse clinical events was explored by cross-classification of participants according to these two variables into four groups, considering the condition of no dementia/no adverse clinical event as the reference group. Descriptive and inference analyses used a cluster procedure to adjust standard errors for intergroup correlation. All the statistical calculations were performed with the software STATA 9th version (College Station, Texas, US).

Results

Of the 1221 patients included in the analyses, 54.1% were females. The mean age of the patients was 79.4 years. The most frequent diagnoses (including the primary reasons for hospitalization) were: hypertension (58.4%), diabetes mellitus (26.2%), CVD (26.2%), CHD (25.0%), AF (25.0%), and COPD (21.4%). The average number of prescribed drugs was 4.7. 36.4% of the patients had at least one adverse clinical event during the hospital stay (ranging from 0 to 9 events) (Table 1). The most frequent were urinary infection (12.0%), fever (6.0%), anemia (5.2%), pneumonia (5.0%), electrolyte disorders (4.5%), AF (4.3%), HF (3.0%), acute renal failure (2.7%). Sixteen patients had a diagnosis of delirium during the hospital stay (12 patients with dementia and four without dementia) and only one of those died ($p = 0.880$). One hundred and seventeen patients (9.6%) had dementia. 9.4% of patients with a diagnosis of dementia (10.6% of women and 4.3% of men with dementia) died during hospitalization *versus* 4.9% of patients without dementia. Causes of death in patients with dementia were: respiratory failure (62.5%), heart diseases (12.5%), acute neoplastic bleeding (12.5%), and septicemia (12.5%). In 37.5% of patients with dementia who died during hospitalization, the final cause of death was initiated by an adverse event occurred during hospitalization in comparison with 16.4% of those without dementia.

Table 1 shows patients' socio-demographic and clinical characteristics according to dementia diagnosis. Patients with dementia were more likely to be older and females; a higher proportion of them had at least one adverse clinical event during hospital stay. They were also more likely to be affected by CVD,

Table 1 Socio-demographic and clinical characteristics of the participants by dementia diagnosis. $N =$ Number. Data are given as means or proportions (95% confidence intervals) adjusted for participating centers

Characteristics		Dementia	
	All $N = 1221$	Yes $N = 117$	No $N = 1104$
Age, yrs, mean	79.4 (78.6−80.2)	83.9 (82.2−85.7)	78.9 (78.2−79.6)
Female, %	54.1 (50.2−58.1)	69.7 (58.8−80.5)	52.6 (48.9−56.2)
Education, yrs, mean	6.3 (5.8−6.9)	5.7 (4.8−6.6)	6.4 (5.8−6.9)
N of diseases, mean	3.6 (3.3−3.9)	3.7 (3.2−4.1)	3.6 (3.3−3.9)
Charlson Index score, mean	3.0 (2.7−3.4)	3.6 (2.9−4.3)	2.9 (2.7−3.3)
N of drugs, mean	4.7 (4.3−4.9)	5.0 (4.4−5.7)	4.6 (4.3−4.9)
Systolic blood pressure, mmHg, mean	134.8 (132.9−136.8)	132.9 (129.3−136.5)	135.0 (132.9−137.1)
Diastolic blood pressure, mmHg, mean	76.1 (75.2−76.9)	73.9 (71.3−76.7)	76.3 (75.4−77.1)
Heart rate, bpm, mean	81.2 (79.9−82.4)	80.0 (76.9−83.2)	81.3 (80.1−82.6)
N of adverse events, mean	0.6 (0.4−0.9)	1.0 (0.4−1.6)	0.6 (0.4−0.8)
Patients with at least one event, %	36.4 (29.0−43.7)	46.7 (32.6−60.8)	35.3 (28.2−42.4)
In-hospital deaths, %	5.4 (3.3−7.4)	9.4 (4.4−14.4)	4.9 (2.9−7.1)
Length of hospital stay, days, mean	11.2 (10.3−12.1)	11.6 (9.5−13.7)	11.2 (10.2−12.1)
Diseases, %:			
Hypertension	58.4 (53.6−63.2)	53.3 (46.2−60.3)	58.9 (53.9−63.9)
Diabetes mellitus	26.2 (22.4−30.0)	22.1 (13.1−31.2)	26.6 (22.8−30.5)
CVD	26.2 (21.5−30.8)	38.5 (28.5−48.4)	24.9 (20.4−29.4)
AF	25.0 (21.6−28.4)	26.2 (18.9−33.4))	24.9 (21.4−28.4)
CHD	25.0 (21.0−28.9)	24.6 (18.9−30.2)	25.0 (20.9−29.1)
COPD	21.4 (18.0−24.8)	20.4 (13.1−27.8)	21.5 (18.2−24.8)
Malignancy	20.3 (16.9−23.8)	12.3 (7.2−17.4)	21.1 (17.5−24.8)
Anemia	19.5 (15.8−23.1)	22.9 (16.0−29.8)	19.1 (15.3−23.0)
HF	17.8 (14.1−21.6)	16.4 (7.9−24.8)	17.9 (14.3−21.7)
Gastric diseases	16.4 (11.3−21.5)	12.3 (3.8−20.7)	16.8 (11.7−21.9)
CRF	14.8 (11.6−18.0)	14.7 (7.4−22.0)	14.8 (11.5−18.2)
Dyslipidemia	13.3 (9.6−16.9)	7.3 (3.7−11.0)	13.9 (9.9−17.8)
Intestinal diseases	10.7 (8.1−13.3)	12.3 (4.5−20.1)	10.5 (7.9−13.1)
Thyroid diseases	10.7(8.3−12.9)	15.5 (8.9−22.1)	10.1 (7.8−12.6)
Liver cirrhosis	9.5 (6.7−12.3)	6.5 (6.3−12.4)	9.7 (6.8−12.7)
Pneumonia	9.2 (7.0−11.4)	16.3 (9.3−23.4)	8.5 (6.2−10.8)
Anxiety	8.6 (6.5−10.6)	13.1 (7.6−18.6)	8.1 (6.1−10.2)
Prostate hypertrophy	8.2 (6.1−10.3)	8.1 (2.4−13.9)	8.2 (6.1−10.3)
Arthritis	7.4 (4.9−9.8)	12.2 (4.6−19.9)	6.8 (4.6−9.0)
Gallstones	6.8 (5.1−8.5)	5.7 (1.7−9.7)	6.9 (5.1−8.7)

CHD = coronary heart disease, AF = atrial fibrillation, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular disease, CRF = chronic renal failure, HF = heart failure.

pneumonia and less likely to be affected by malignancies (Table 1).

Table 2 shows the results of the logistic regression analysis aimed at identifying the association between dementia and in-hospital death. Model 1 was adjusted for age, gender, education, number of drugs, the Charlson Index, adverse clinical events, and vital parameters (blood pressure and heart rate). In Model 2, single diseases were included instead of the Charlson Index. Patients affected by dementia were twice more likely to die during hospitalization than those without such diagnosis. The other variables significantly associated with death were higher Charlson Index score and adverse clinical events (Model 1; Table 2). The strength of the association was not weakened when diseases potentially related to death were included in the model (Model 2; Table 2).

Finally, results from the logistic regression model testing a possible combined effect of dementia and adverse clinical events on in-hospital death showed that having dementia and at least one adverse event during hospitalization had an additive effect on mortality. In addition, the same model showed that having no dementia but at least one adverse event was also highly correlated with in-hospital death (Table 3).

Discussion

Findings from the REPOSI study showed that acutely ill elderly patients with dementia were more likely to die during hospitalization. The association between dementia and mortality remained significant after adjustment for several covariates, including other

Table 2 Odds ratio (OR) and 95% confidence intervals (CI) for in-hospital death due to dementia

	Model 1		Model 2	
	OR	95% CI	OR	95% CI
Dementia	2.14	1.02–4.49	2.64	1.16–6.00
Age, yrs (80+ versus <80)	1.55	0.74–3.26	1.57	0.88–2.81
Female versus male	0.77	0.42–1.43	0.65	0.35–1.20
Education, yrs	1.00	0.93–1.07	1.02	0.95–1.09
Charlson Index (score 3+ versus 0–2)	2.02	0.91–4.50	—	—
Drugs (5+ versus 0–4)	0.86	0.44–1.65	1.12	0.50–2.51
Adverse clinical events (1+ versus 0)	9.26	4.47–19.18	10.04	4.90–20.57
Length of hospital stay, days	1.00	0.97–1.02	1.00	0.97–1.02
AF	—	—	0.93	0.48–1.80
Anemia	—	—	0.50	0.27–0.93
CHD	—	—	0.82	0.45–1.49
COPD	—	—	0.65	0.30–1.40
CRF	—	—	1.74	0.78–3.89
CVD	—	—	0.70	0.34–1.40
Diabetes mellitus	—	—	0.59	0.31–1.11
HF	—	—	0.76	0.22–2.29
Liver cirrhosis	—	—	0.46	0.09–2.24
Malignancy	—	—	1.74	0.93–3.26
Pneumonia			1.16	0.53–2.50

Models adjusted for vital parameters (blood pressure and heart rate).

physical illnesses. Moreover, having dementia and adverse clinical events during hospitalization had an additive effect on in-hospital death.

One of the major consequences of the ongoing demographic changes is the increase in the occurrence of mental diseases (Marengoni et al., 2008). In fact, prevalence and incidence of mental conditions and especially dementia are highly age-correlated (Ferri et al., 2005). This will result in an increasing number of patients with dementia being hospitalized in acute care units, such as geriatric and internal medicine wards. Clinical management of the acute diseases in elderly people is challenging per se, but when the patients also suffer from dementia the process of clinical decision-making becomes even more difficult and the hospital outcome more uncertain.

Previous studies on the effect of dementia on hospital outcomes gave controversial results. Zekry et al. (2009) analyzed a sample of geriatric patients from acute and rehabilitation hospitals and they found that dementia was not predictive of in-hospital death, but only of discharge to a nursing home. On the contrary, Dinkel and Lebok (1997) compared hospital outcomes between German patients with dementia or not and they found that in-patients with a diagnosis of dementia had twice the possibility to die during hospitalization than those without dementia of the same age. The authors explain these results with the higher number of comorbid conditions of persons with dementia compared with those cognitively intact (Dinkel and Lebok, 1997). We found similar results regarding the association of dementia with death during acute hospitalization, but, in our study, patients with dementia had a similar number of comorbid conditions and Charlson Index score than those without dementia. Thus, it seems unlikely that the number and the severity of co-occurring conditions may explain the excess of mortality in the group of

Table 3 Odds ratio (OR) and 95% confidence intervals (CI) for in-hospital death due to the combined effect of dementia and adverse clinical events. N = Number

	All	N of deaths	OR	95% CI
No dementia and no events	720	10	1	—
No dementia and at least one event	384	45	10.80	4.87–24.08
Dementia and no events	64	3	4.25	1.00–19.16
Dementia and at least one event	53	8	20.74	6.94–61.96

Model adjusted for age, gender, education, number of drugs, the Charlson Index, length of hospital stay and vital parameters.

patients with dementia. Indeed, they were more likely to be affected by diseases highly related to mortality in geriatric patients, such as pneumonia and CVD, but after adjustment for these diseases, the strength of the association of dementia with mortality was not weakened. Thus, the reasons why these patients could be at high risk to die during acute diseases are still not clear. Some authors have shown that the acute care of patients affected by dementia could be suboptimal (Sloan *et al.*, 2004, Sampson *et al.*, 2006), whereas others have shown that patients with dementia receive the same procedures and care of those without such diagnosis (Morrison and Siu, 2000).

Our hypothesis is that the interaction between the acute hospital environment and people with dementia could be particularly problematic. In fact, in this study not only patients with dementia had a higher number of adverse events, but also the association of dementia with adverse clinical events during hospitalization was additive on the worse adverse outcome, in-hospital mortality. It is possible that persons with dementia have more difficulties to cope with acute stressors compared to those without cognitive impairment. On the other hand, adverse clinical events were strongly associated with mortality in patients without dementia as well. These findings raise the need of a continuous and accurate medical monitoring of the patients developing adverse events during hospitalization independently of the presence of dementia.

Major strengths of the REPOSI study are the multicenter design that involved 38 internal medicine and geriatric wards throughout Italy, resulting in a sample representative of the old hospitalized population of the country; and the inclusion of the patients during a period of 4 weeks (one per season) in order to balance the effect of seasons on acute diseases leading to hospitalization. However, a few limitations need to be mentioned. First, several problems can arise by using hospital data for research purposes, because hospital records are not designed for research purposes but rather for patient care and their diagnostic quality may vary depending on different hospitals, physicians, and clinical units. Moreover, hospital admissions are often selective on the basis of ward characteristics, severity of disease, associated medical conditions, and admissions policies that may vary from hospital to hospital. Second, cognitive impairment and dementia in medical in-patients can be missed by physicians (Harwood *et al.*, 1997). However, if dementia is underestimated, it is likely to undervalue the association of dementia with in-hospital death rather than produce a false positive result. Thus, the increased risk

> **Key Points**
> - Older patients affected by dementia are more likely to die during hospitalization for acute illnesses.
> - The association of dementia with adverse clinical events during hospitalization has an additive effect on in-hospital death.

of in-hospital mortality in patients with dementia could be higher than the one found in our study.

In conclusion, these findings reinforce the idea that one of the main goals for older persons with dementia should be to improve intermediate and community care in order to reduce emergency admissions.

Conflict of interest

No competing financial interests exist.

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Appendix: Collaborators and participating units

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