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ORIGINAL ARTICLE

Depressive symptoms and disability in acute patients with comorbidities in departments of internal medicine

Disturbi depressivi e disabilità in pazienti pluripatologici ricoverati in medicina interna

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KEYWORDS
Depression;
Comorbidity;
Disability.

Summary
Introduction: There are few data on the prevalence of depression among acute patients with comorbidities. The current study aimed to determine the prevalence of depressive symptoms in hospitalized patients admitted to Internal Medicine Units and the correlation between these symptoms and comorbidities and disability indexes.
Materials and methods: All consecutive patients admitted to 26 Internal Medicine Units of the Italian National Public Health System in Sicily, Italy, from September 2001 to March 2002 were screened. Within 24 hours of admission, patients were administered the Geriatric Depression Scale (GDS), Mini-Mental State Examination, Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL) and Charlson's Comorbidity Index.
Results: 1,947 subjects were included in the analyses. Of the patients, 509 (26.1%) showed depressive symptoms (indicated by GDS score $\geq$ 15). Depression was significantly associated (univariate analyses) with hypertension (OR 1.45; CI 95% 1.18-1.79), diabetes (OR 1.48, CI 95% 1.17-1.87), cerebrovascular disease (OR 1.50, CI 95% 1.08-2.07), cirrhosis (OR 1.49, CI 95% 1.01-2.19), ADL score (OR 0.72: CI 95% 0.63-0.82), and IADL score (OR 0.83; CI 95% 0.78-0.87), but not

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with Charlson's Comorbidity Index (OR 1.04; CI 95% 0.98-1.10). Multivariate analysis showed that independent predictive factors for depression were age (OR 1.02, CI 95% 1.01-1.02), female gender (OR 2.29, CI 95% 1.83 - 2.87), and IADL score (OR 0.86, CI 95% 0.81 - 0.93).
Conclusions: The data suggest that depressive symptoms are not linked to worse clinical conditions but are associated with the loss of autonomy in Instrumental Activities of Daily Living.

Introduction

It has been estimated that by the year 2020, the burden of depression will increase to 5.7% of the diseases, becoming the second leading cause of disability-adjusted life years lost [1]. In Europe, the annual cost of depression was estimated at Euro 118 billion in 2004 [2]. In Italy, the prevalence of the disease in the community and in primary care ranges from 8 to 11% [3,4]. A recent survey on hospitalized patients with chronic disease and previous studies on subjects with heart failure or other cardiovascular diseases suggest that depressive symptoms lead to worse clinical outcomes [5—11]. Symptoms of depression and anxiety also emerged as significant risk factors for the onset of type 2 diabetes [12]. Moreover, several studies showed a close link between depression and the risk of cardiovascular mortality [13—17]. Nevertheless, many results on this issue have been called into question [18,19], and the cause of increased risk of mortality is not fully understood [20]. The correlation between depression and comorbidities may be influenced by a proinflammatory state, but few data are available on this topic [21,22].

Screening for depression has been recognized as a useful tool for preventing persistent depression; however, it is not clear whether treatment improves clinical outcomes [23—27].

Despite these research findings, depression is underdiagnosed and undertreated by nonpsychiatric practitioners. In addition, few data are available about the prevalence of depression in acute patients with comorbidities hospitalized in departments of internal medicine [28].

The current study aimed to determine the prevalence of depressive symptoms among patients admitted into Internal Medicine Units and the correlation between these symptoms and comorbidities.

Materials and methods

The present analysis is part of an observational multicenter study (The DIMIS study - Depressione In Medicina Interna in Sicilia) that includes 26 Internal Medicine Units of The National Public Health System in Sicily, Italy. The study was conducted under the endorsement and scientific coordination of the Italian Federation of Internal Medicine (FADOI).

The primary goal of the DIMIS is to evaluate the prevalence of depression in acute patients hospitalized in departments of internal medicine and the association between depression, comorbidities, and health functional state.

From September 2001 to March 2002, all subjects $\geq$ 20 years old who were consecutively admitted to the hospital were screened. Patients were administered the Mini-Mental State Examination (MMSE), a complete clinical examination with a cognitive assessment. The scores for this examination range from 0 to 30 points. In order to exclude subjects with severe cognitive impairment, patients with a score $<$ 22 were not considered for the analyses [29,30].

Within 24 hours from admission, eligible patients completed the 30-item Geriatric Depression Scale (GDS), one of the most commonly used self-rating depression scales in geriatric populations [31]. The scale comprises 30 easy-to-use items, with answers in yes/no format, and it is designed to exclude the somatic symptoms of depression that are also observed in non-depressed elderly people [31,32]. A cut-off score of 11 on the GDS yields an 84% sensitivity rate and a 95% specificity rate for depression, whereas a cut-off score of 14 yields a slightly lower sensitivity rate of 80%, but a 100% specificity rate [32,33]. The GDS has been validated in geriatric medical outpatients, day-treatment patients, and younger subjects [34—38].

In the present study, the GDS was scored with two methods. In accordance with the above mentioned cut-off values [32,33], we first defined patients as ''not depressed'' (GDS $<$ 15) or ''depressed'' (GDS $\geq$ 15). Further, subjects were stratified using a ''screening score''. In accordance with the original classification of Brink and Yesavage, patients were defined as ''normal'' (GDS $<$ 10), ''screened for mild depression'' (GDS score between 10 and 19) or ''screened for severe depression'' (GDS score $\geq$ 20) [31,32].

The burden of cumulative comorbidities was calculated using the validated Charlson's method, a weighted index that takes into account the number and the severity of comorbid conditions [39]. An index of '0' has been associated with a 12% 1-year expected mortality rate, while scores of '1—2' / '3—4' and '5' have been associated with 1-year expected mortality rates of 26%, 52% and 59%, respectively [39].

The degree of disability was evaluated using the Katz's Activities of Daily Living (ADL) score and the Brody's Instrumental Activities of Daily Living (IADL) score [40,41]. ADL yields a score (ranging from 0 to 6) based on the personal care tasks of bathing and washing, dressing, feeding, getting in and out of bed, getting to and from the toilet, and continence management [40]. IADL yields a score (ranging from 0 to 8) based on domestic tasks such as shopping, laundry, vacuuming, cooking a main meal and handling personal affairs.

Data management and statistical analyses

In the present work, categorical variables are presented as percentages and continuous variables are presented as mean $\pm$ standard deviation (SD) or as median and interquartile range (IQR), when appropriate. The GDS score was analyzed using the non-parametric Mann-Whitney U test. The correlations between Charlson's score, MMSE, ADL, IADL, age and GDS score were analyzed using the Spearman's Rho index.

The primary study objective was to identify predictors for a prognostic model of depression (indicated by GDS $\geq$ 15). To accomplish this, a set of pre-specified covariates were investigated with univariate logistic regression models. In addition, variables deemed to be clinically relevant were subsequently tested in a multivariate analysis regardless of their univariate findings and using the conventional rule of thumb (no less than ten events for each covariate). Results were reported as odds ratios with 95% confidence intervals. The association between depression (indicated by GDS $\geq$ 15 or as ''screened score'') and other categorical variables (previous diagnosis of depression, use of drugs) was evaluated by Chi-Square test. A two-tailed p value $<$0.05 was considered statistically significant. All data were analyzed using SPSS software (version 12.1; SPSS, Inc., Chicago, Illinois).

Results

Of the 2,944 screened patients, 537 (18.2%) were excluded from the analysis because of severe cognitive impairment (MMSE $<$ 22), 224 (7.6%) declined the interview, 76 (2.6%) had incomplete data, and 264 (9.0%) did not have the GDS submitted within 24 hours of admission.

Table 1 Reasons for admission to hospital (n=1,947).

Reasons for admission	n	(%)
Diabetes Mellitus Impairment	192	(9.8)
Hypertensive Crisis	170	(8.7)
Heart Failure	127	(6.5)
Stroke or Transient Ischemic Attack	125	(6.4)
Pneumonia	105	(5.4)
Epigastrial Pain	86	(4.4)
Chronic Obstructive Pulmonary Disease	81	(4.2)
Angina Pectoris	70	(3.6)
Cirrhosis	69	(3.5)
Abdominal Pain	51	(2.6)
Cancer	47	(2.4)
Fever	47	(2.4)
Atrial Fibrillation	44	(2.3)
Anemia	43	(2.2)
Renal Chronic Failure	38	(1.9)
Chronic Liver Disease	33	(1.7)
Arthrosis	31	(1.6)
Syncope	19	(1.0)
Dyspepsia	17	(0.9)
Vertigo	16	(0.8)
Claudicatio	7	(0.4)
Headache	6	(0.3)
Others	523	(26.9)

Therefore, data from 1,947 (66.1%) patients were analyzed (mean age 59.8 $\pm$ 16 years, ranging from 20 to 90; 961 men (mean age 59.9 $\pm$ 16 years) and 986 women (mean age 59.7 $\pm$ 17 years)). The primary reasons for admission to the hospital are listed in Table 1.

The median value of the GDS was 9 (IQR 4 -15), and women displayed higher values than men (median 11, IQR 5 -17 vs median 7, IQR 3 -13, p$<$0.001). The overall prevalence of depression (indicated by a GDS $\geq$ 15) was 26.1% (n=509). Table 2 shows the prevalence of subjects with (GDS $\geq$ 15) or without depression according to demographic characteristics, concomitant diseases, cognitive assessment, and degree of disability. Using this cut-off, the prevalence of depression was significantly higher in women (33.5%, n=330) than in men (18.6%, n=179, unadjusted OR 2.20; CI 95% 1.78 $-$ 2.71). Depression was also high in patients with hypertension (OR 1.45; CI 95% 1.18-1.79), diabetes mellitus (OR 1.48, CI 95% 1.17-1.87), cerebrovascular disease (OR 1.50, CI 95% 1.08-2.07), and cirrhosis (OR 1.49, CI 95% 1.01-2.19). The median value of MMSE was significantly lower in patients with depression (28, IQR 26-30) than in patients without depression (30, IQR 27-30, unadjusted OR 0.92, CI 95% 0.88-0.96). Multivariate logistic regression analysis showed that the independent predictive factors for depression were age (adjusted OR 1.02, CI 95% 1.01-1.03), female gender (adjusted OR 2.17, CI 95% 1.62 - 2.91), and IADL (adjusted OR 0.86, CI 95% 0.79 - 0.93) (see Table 3).

Further, there was a mild but significant inverse correlation between GDS score and ADL (Spearman's Rho = -0.18, p$<$0.001), IADL (Spearman's Rho = -0.14; p$<$0.001), and MMSE (Spearman's Rho = -0.15; p$<$0.001) *(Figs. 1-3)* and a positive correlation between GDS score and Charlson's score (Spearman's Rho = 0.13, p$<$0.001) *(Fig. 4)*.

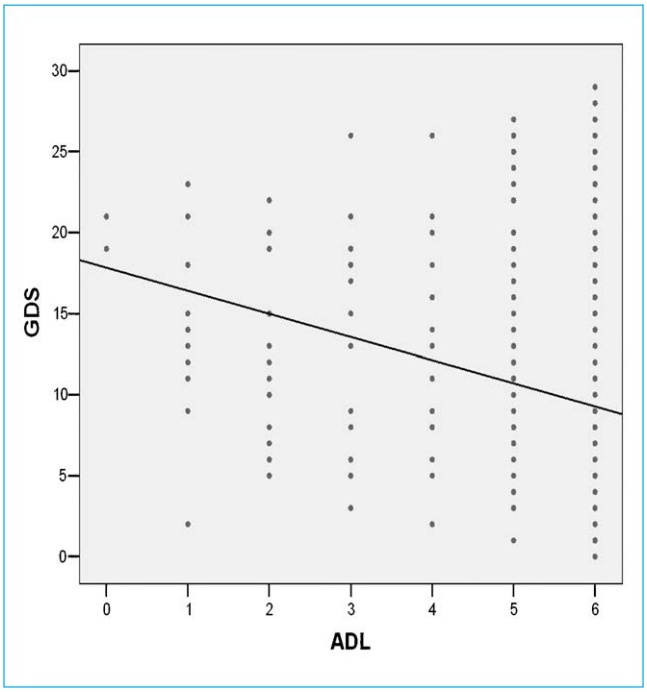

Figure 1 Correlation between Geriatric Depression Scale score and ADL score (Spearman's Rho = - 0.18; p$<$0.001).

Table 2 Prevalence of depression (GDS $\geq$ 15) according to comorbidities.

	Number of individuals (%) or mean $\pm$ SD* or median (IQR)[§]	Subjects not depressed, with GDS $<$ 15 (%)	Subjects depressed, with GDS $>$ 15 (%)	Unadjusted odds ratio (95% CI)	p value
Total study population	1947	1438 (73.9)	509 (26.1)	-	
Age *	59.8 $\pm$ 16	58.36 $\pm$ 17	64.0 $\pm$ 13	1.02 (1.01-1.03)	$<$ 0.001
Male	961 (49.4)	782 (81.4)	179 (18.6)	2.20 (1.78-2.71)	$<$0.001
Female	986 (50.6)	656 (66.5)	330 (33.5)		
Hypertension	671 (34.5)	463 (32.2)	208 (40.9)	1.45 (1.18-1.79)	$<$0.001
Diabetes mellitus	427 (21.9)	289 (20.1)	138 (27.1)	1.48 (1.17-1.87)	$<$0.001
Cerebrovascular disease	181 (9.3)	120 (8.3)	61 (12)	1.50 (1.08-2.07)	0.021
Cirrhosis	124 (6.4)	82 (5.7)	42 (8.3)	1.49 (1.01-2.19)	0.044
Heart Failure	166 (8.5)	118 (8.2)	48 (9.4)	1.16 (0.82-1.65)	0.396
Coronary Artery Disease	224 (11.5)	155 (10.8)	69 (13.6)	1.30 (0.85-1.75)	0.092
Chronic pulmonary disease	257 (13.2)	200 (13.9)	57 (11.2)	0.78 (0.57-1.07)	0.121
Connective tissue disease	29 (1.5)	20 (1.4)	9 (1.8)	1.28 (0.58-2.82)	0.547
Chronic renal disease	71 (3.6)	46 (3.2)	25 (4.9)	1.69 (1.01-2.82)	0.046
Ulcer disease	71 (3.6)	55 (3.8)	16 (3.1)	0.82 (0.46-1.43)	0.482
Hypothyroidism	22 (1.8)	13 (1.5)	9 (2.5)	1.77 (0.75-4.18)	0.19
Hyperthyroidism	19 (1.5)	13 (1.4)	6 (1.6)	1.45 (1.18-1.79)	$<$0.001
Cancer	102 (5.2)	80 (5.6)	22 (4.3)	0.96 (0.88-1.04)	0.28
Charlson's score[§]	1 (0-1)	0 (0-1)	1 (0-1)	1.04 (0.98-1.10)	0.21
ADL [§]	6 (6-6)	6 (6-6)	6 (6-6)	0.72 (0.63-0.82)	$<$0.001
IADL[§]	8 (5-8)	8 (6-8)	8 (4-8)	0.83 (0.78-0.87)	$<$0.001
MMSE [§]	29 (27-30)	30 (27-30)	28 (26-30)	0.92 (0.88-0.96)	$<$0.001

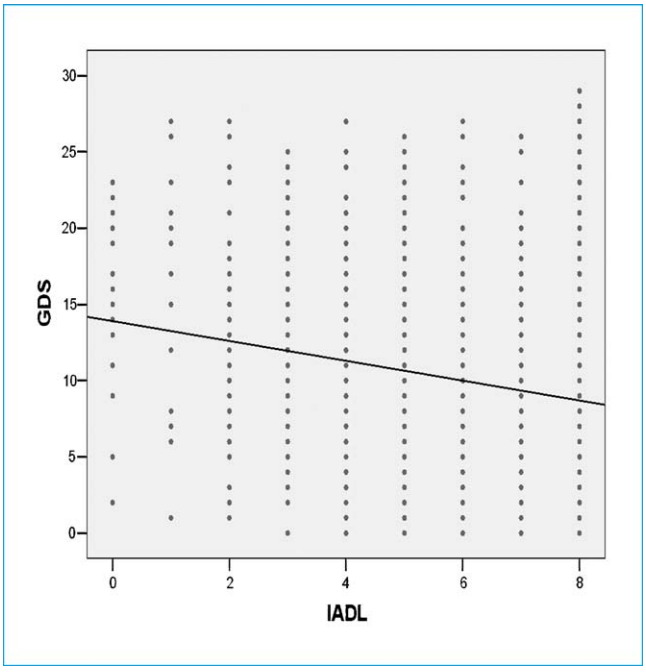

Figure 2 Correlation between Geriatric Depression Scale score and IADL score (Spearman's Rho = - 0.14; p$<$0.001).

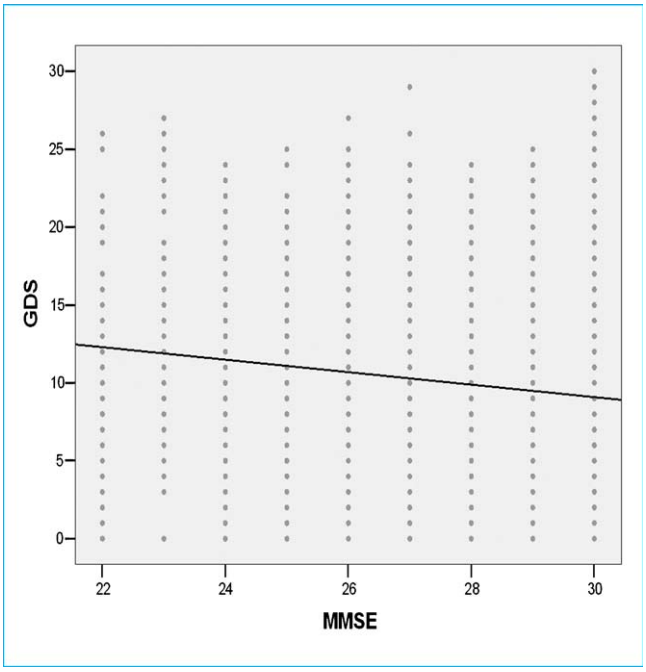

Figure 3 Correlation between Geriatric Depression Scale score and MMSE (Spearman's Rho = - 0.15; p$<$0.001).

Table 3 Multivariate logistic regression analysis (dependent variable is depression, indicated as GDS $\geq$ 15, predictive factors are variables deemed to be clinically relevant).

	Odd Ratio	CI 95%	p
Age	1.02	1.01 - 1.02	0.00
Gender (female)	2.29	1.83-2.87	0.00
Hypertension	1.13	0.89-1.43	0.33
Diabetes mellitus	1.86	0.98-3.52	0.06
Cerebropathy	1.89	0.90-3.95	0.09
Cirrhosis	5.62	0.92-34.34	0.06
Heart Failure	0.85	0.58-1.26	0.42
Coronary Artery Disease	1.02	0.72-1.44	0.91
Chronic pulmonary disease	1.17	0.60-2.28	0.65
Connective tissue disease	1.83	0.66-5.09	0.24
Chronic renal disease	3.17	0.87-11.58	0.08
Ulcer disease	1.36	0.59-3.12	0.48
Hypothyroidism	1.40	0.56-3.50	0.47
Hyperthyroidism	1.33	0.48-3.67	0.59
Cancer	1.40	0.77-2.53	0.27
ADL	0.87	0.74-1.04	0.12
IADL	0.86	0.81-0.93	0.00
MMSE	0.99	0.95-1.04	0.68
Charlson's score	0.65	0.36-1.18	0.16

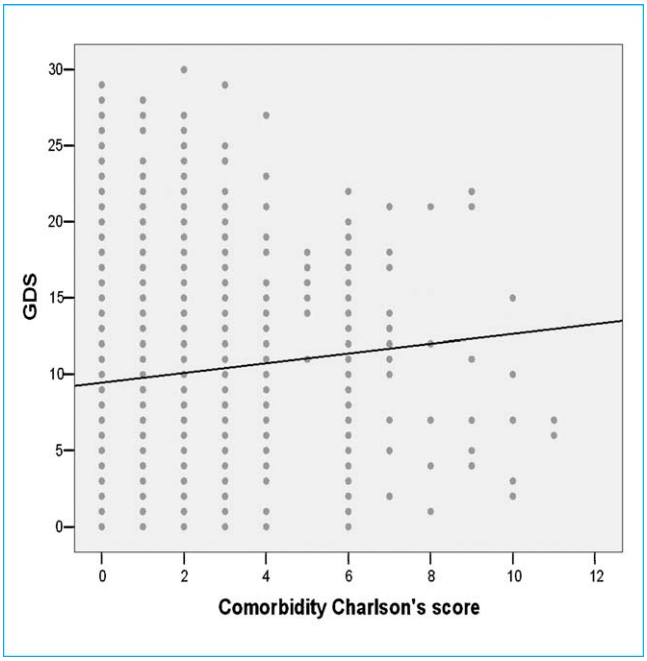

Figure 4 Correlation between Geriatric Depression Scale score and Charlson's score (Spearman's Rho = 0.13; p<0.001).

According to the original definition by Brink and Yesavage, 706 patients (36.3%) had a GDS score between 10 and 20 (defined as "screened for mild depression"), and 205 patients (10.5%) had a score equal to or greater than 20 (defined as "screened for severe depression"). In the overall study population, 188 patients (9.6%) reported a prior diagnosis of depression, 23 (1.1%) a diagnosis of major depression, and 55 (2.8%) generic "depressive symptoms". In the group of 509 patients with a GDS score $\geq$ 15, 113 subjects (22.2%) reported a prior diagnosis of depression (including all definitions) and 28 (5.5%) reported a prior diagnosis of anxiety. Fifteen subjects (2.9% of 509) reported a previous diagnosis of "depression major", 37 (7.3%) a generic "depression syndrome", and 70 (13.8%) were previously classified as having an "anxiety-depressive syndrome" (Table 4). Analyzing the group of patients screened for "severe depression" (205 subjects with GDS $\geq$ 20), 57 (27.8%) reported a prior diagnosis of depression (indicated with any definition).

Overall, 95 patients (4.8%) reported taking antidepressant drugs prior to hospital admission: 25 (1.3%) tricyclic antidepressants and 70 (3.6%) selective serotonin reuptake inhibitors (SSRI). Analyzing the group of depressed patients identified by GDS score $\geq$ 15, 59 patients (11.6%) used antidepressants: 19 tricyclic (3.7%), and 40 (7.9%) SSRI. Within the group of patients screened for "severe depression" (GDS $\geq$ 20), 24 (11.7%) used antidepressants: 9 tricyclic and 15 SSRI (Table 5). None of patients reported other types of treatment for depression (e.g., psychotherapy, psychoanalysis).

Table 4 Previous diagnosis of depression (any definition) and use of antidepressant at admission in respect to Geriatric Depression Scale.

	Number of individuals (%)	Subjects not depressed, with GDS < 15 N (%)	Subjects depressed, with GDS > 15 N (%)	p
Total study population	1947	1438 (73.9)	509 (26.1)	-
Depression Major	23 (1.2)	15 (0.6)	23 (2.9)	<0.001
Depressive syndrome	55 (2.8)	18 (1.3)	37 (7.3)	<0.001
Anxiety-depressive syndrome	119 (6.1)	49 (3.4)	70 (13.8)	<0.001
Depression (sum of all definitions)	188 (9.7)	75 (5.2)	113 (22.2)	<0.001
Use of Tryclicic	25 (1.3)	6 (0.4)	19 (3.7)	<0.001
Use of SSRI	70 (3.6)	30 (2.1)	40 (7.9)	<0.001

Table 5 Previous diagnosis of depression (any definition) and use of antidepressant at admission in respect to Geriatric Depression "Screening Score".

	Number of individuals (%)	Subjects with GDS $<$ 10	Subjects with GDS between 10 and 19	Subjects with GDS $\geq$ 20	p
Total study population	1947	1036 (53.2)	706 (36.3)	205 (10.5)	-
Depression Major	23 (1.2)	4 (0.4)	10 (1.4)	9 (4.4)	$<$0.001
Depressive syndrome	55 (2.8)	7 (0.7)	28 (4.0)	20 (9.8)	$<$ 0.001
Anxiety-depressive syndrome	119 (6.1)	26 (2.5)	61 (8.6)	32 (15.6)	$<$ 0.001
Depression (sum of all definitions)	188 (9.7)	37 (3.6)	94 (13.3)	57 (27.8)	$<$ 0.001
Use of Tryclicic	25 (1.3)	4 (0.4)	12 (1.7)	9 (4.4)	$<$ 0.001
Use of SSRI	70 (3.6)	11 (1.1)	44 (6.2)	15 (7.3)	$<$ 0.001

Discussion

In recent years, many issues have been raised on the significance of concomitant depression and comorbidities; however, few data are available on the rate and distribution of depression in large samples of unselected patients hospitalized in Internal Medicine wards.

The primary objectives of the current study were to evaluate the prevalence of depressive symptoms among medical inpatients and the association between these symptoms and the demographic, pathological and functional characteristics of the patients.

In the present survey, the GDS was used to classify patients as depressed or not depressed. This could be considered as a limitation of the study because DSM-IV criteria are typically utilized to diagnose clinical depression. However, the GDS has been used for large studies, and although it was developed for elderly patients, it has also been validated as a screening tool for depressive symptoms in younger subjects [36,37]. Previous studies in hospitalized patients indicated that GDS does not maintain its validity in populations with large numbers of cognitively impaired patients [42,43]. Therefore, the current survey excluded patients with a significant cognitive impairment (Mini-Mental State Examination $<$ 22). Further, in order to reduce the influence of hospitalization on the patient's mood and therefore on the GDS score, patients who did not complete the examination within 24 hours of admission to the hospital were excluded. Based on these perspectives, the GDS may be considered as a reliable test for the purposes of the study.

Based on previous literature [33,38], patients with a GDS score $\geq$ 15 were labeled as "depressed". By using this cut-off, we observed a prevalence of 26% of depressed patients. Moreover, on the basis of the original scoring by Brink and Yesavage [32], 46.8% of the subjects exhibited a GDS score $\geq$ 10 ("mild" or "severe depressives"). These data are consistent with previous studies that indicated a high prevalence of depression in patients with comorbidities. In particular, Freedland et al. observed that in a cohort of hospitalized patients affected with heart failure, 20% met the DSM-IV criteria for a current major depressive episode, 16% for a minor depressive episode, and 51% scored above the cut-off for depression on the Beck Depression Inventory [5].

The current findings suggest that the diagnosis of depression is largely underestimated. In the present sample, only 22.2% of subjects with a GDS score $\geq$15 were previously classified as depressed and only 11.6% were taking antidepressants prior to hospitalization. Analyzing the group of patients with a GDS score $\geq$ 20, the rate of patients with a previous diagnosis of depression remained low (27.8%) and only 11.7% reported prior treatment with antidepressants. As a consequence, approximately 90% of patients who were candidates to receive therapy for depression were not treated. These findings confirm other recent data that indicated an under use of antidepressants [44].

The current results indicate that elderly subjects, women, and patients with loss of autonomy have a significantly higher risk of depression. Although patients with hypertension, diabetes mellitus, cerebrovascular disease, or cirrhosis showed raised unadjusted odds ratio for depression, the multivariate analysis indicated that the independent risk factors for depression were age, gender (female) and IADL. Moreover, the study did not find a significant association between cancer and depression. The present data are consistent with other large surveys that showed high variability in the prevalence of depression in patients with cancer [45—47].

The study aimed to determine whether depression is related to the overall burden of comorbidity. To evaluate this issue, the Charlson's Comorbidity Index was used. The data indicate a mild correlation between Charlson's score and GDS score; however, this association was not confirmed in the multivariate analysis. This finding suggests that depression is not related to the severity of comorbidity (Charlson's score), but is more closely related to loss of autonomy and disability (IADL). This association has been suggested by other recent studies that indicated the role of severe functional impairment in determining post-stroke depression [48,49] and the correlation between depression and disability in a large sample of adults living in households [50].

Conclusions

In the present study, a high prevalence of depressive symptoms was found among patients hospitalized in Internal Medicine Units. Depressive symptoms were not independently related to the severity of concomitant diseases (Charlson's score), but were associated with the loss of autonomy for IADL. The data, showing a significant grade of under-diagnosis and under-treatment of depressive symptoms, suggest that physicians working in Internal Medicine Departments should take account of this condition and

consider introducing the mood evaluation into routine clinical practice. This approach may be justified as identifying and treating depression at early stages may have positive effects on clinical evolution and quality of life. Future studies are needed to further investigate the prognostic impact of concomitant depression and comorbidities and the role of specific treatments to improve patients' mood and clinical outcome.

Conflict of interest statement

The authors have no conflict of interest.

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