

POPULATIONS AT RISK

Characteristics of Nondisabled Older Patients Developing New Disability Associated with Medical Illnesses and Hospitalization

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OBJECTIVE: To identify demographic, clinical, and biological characteristics of older nondisabled patients who develop new disability in basic activities of daily living (BADL) during medical illnesses requiring hospitalization.

DESIGN: Longitudinal observational study.

SETTING: Geriatric and Internal Medicine acute care units.

PARTICIPANTS: Data are from 1,686 patients aged 65 and older who independent in BADL 2 weeks before hospital admission, enrolled in the 1998 survey of the Italian Group of Pharmacoepidemiology in the Elderly Study.

MEASUREMENTS: Study outcome was new BADL disability at time of hospital discharge. Sociodemographic, functional status, and clinical characteristics were collected at hospital admission; acute and chronic conditions were classified according to the International Classification of Disease, ninth revision; fasting blood samples were obtained and processed with standard methods.

RESULTS: At the time of hospital discharge 113 patients (6.7%) presented new BADL disability. Functional decline was strongly related to patients' age and preadmission instrumental activities of daily living status. In a multivariate analysis, older age, nursing home residency, low body mass index, elevated erythrocyte sedimentation rate, acute stroke, high level of comorbidity expressed as Cumulative Illness Rating Scale score, polypharmacotherapy, cognitive decline, and history of fall in the previous year were independent and significant predictors of BADL disability.

CONCLUSION: Several factors might contribute to loss of physical independence in hospitalized older persons. Preexisting conditions associated with the frailty syndrome, including physical and cognitive function,

comorbidity, body composition, and inflammatory markers, characterize patients at high risk of functional decline.

KEY WORDS: hospitalization; frailty; disability; functional status; aging.
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INTRODUCTION

Decline in physical function is common in older persons admitted to the hospital for medical events.^{1,2} Besides the disabling effect of the acute event, hospitalization itself might represent an additional stressor in terms of environmental hazard, reduced caloric intake, low physical activity or prolonged bed-rest, depressed mood, and social isolation.³ Moreover, acute illnesses and hospitalization often trigger functional decline in spite of adequate medical treatment of the acute disease. Decline in functional status during hospitalization has important consequences in terms of quality of life and health care utilization, as it has been associated with the risk of longer hospital stay, home care placement, and mortality.¹⁻⁵ Although some patients may quickly regain autonomy after hospital discharge,⁶ hospitalization has been associated with the risk of incident disability at 6 and 18 months, suggesting that the functional change associated with hospitalization might have important long-term consequences.⁷ Identification of patients at high risk of functional decline is of paramount importance for the prevention of this common negative outcome.

Previous studies have identified different risk factors for worsening functional status, including older age, sociodemographic characteristics, preexisting disability, cognitive decline, delirium, and comorbidity.⁸⁻¹⁰ Conversely, the role of biological characteristics and selected acute and chronic diseases has not been systematically evaluated. Moreover, most previous studies included patients who were already disabled before hospital admission, but predictors might be different in patients with different functional status.

The aim of this study was to evaluate the predictive value of sociodemographic characteristics, functional and cognitive status, acute and chronic conditions, global indicators of comorbidity, and several biomarkers in identifying patients,

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who were independent in basic activities of daily living (BADL), at high risk of developing new disability during hospitalization. We hypothesized that patients with the functional and clinical characteristics of the frailty phenotype would be more likely to experience functional decline associated to medical illnesses requiring hospitalization.

METHODS

Patients

The protocol of the Italian Group of Pharmacoepidemiology in the Elderly Study (GIFA) study has been described elsewhere.¹¹ Briefly, the GIFA is a multicenter periodical survey of hospitalized older patients, which started in 1988. All patients admitted to 81 clinical centers homogeneously distributed throughout Italy were enrolled and followed until discharge. For each participant, a questionnaire was completed at admission and updated daily by a study physician who received specific training. Data recorded included demographic characteristics; functional, cognitive, and mood assessment; medications use; admission and discharge diagnoses; and results of biochemical tests. In 1998, additional variables were included in the study protocol (for example, instrumental activities of daily living [IADL], Geriatric Depression Scale, and history of falls) and therefore we limited this specific project to patients enrolled during the 1998 survey.

In the 1998 survey, 3,746 patients were enrolled. Of them, 897 (23.9%) were younger than 65 years and were not considered for the analysis. Three hundred and five (8.1%) patients were then excluded because of missing data on functional status (184, 4.9%) or because they died during hospital stay (121, 3.2%). Of the remaining 2,544 (68%) patients, 1,686 (45%) were independent in BADL 2 weeks before hospitalization and represent our analytical sample.

Physical Function Evaluation

Functional status was evaluated by self-report information, including 5 BADL (personal hygiene, transferring from bed to chair, using the toilet, dressing, and eating) and 7 IADL (using the telephone, grocery shopping, preparing meals, doing housework, doing laundry, taking medications, managing money, and using transportation systems). Patients or proxy (15.8%) were interviewed at the time of hospital admission and hospital discharge. Patients were asked to report whether, 2 weeks before hospital admission, they could perform each activity independently. For every activity the level of dependency was coded as follows: independent, supervision, limited assistance, intensive assistance, and total dependency. The degree of dependence in performing the BADL was also assessed at time of hospital discharge. According to this information, the onset of new BADL disability was defined as being not fully independent in any of the 5 activities of daily living (ADL) considered.

Covariates

Demographic characteristics and history of fall in the previous year were collected from self-report information. Cognitive function was assessed at admission using the Hodkinson

Abbreviated Mental Test, a 10-item screening test for dementia. Cognitive impairment was defined as presence of 4 or more errors on the test.¹² For 75% of patients with cognitive impairment, ADL status was collected using proxy interview; for the remaining 88 patients with cognitive impairments (25%), the subgroup with less severe cognitive decline (4.7 average number of errors at the Hodkinson Abbreviated Mental Test), information were collected from the patient. The presence of significant depressive symptoms was defined by a score of 5 or higher at the short form (15 items) of the Geriatric Depression Scale (GDS).¹³ Body mass index (BMI) was computed using measured height and weight (kg/m^2). Values below 18.5 were considered underweight, between 18.5 and 24.9 normoweight, between 25 and 29.9 overweight, and values greater than 30 were considered as obesity.¹⁴ All diseases diagnosed by the trained physicians at discharge were classified according to the International Classification of Disease, ninth revision.¹⁵ Six acute clinical conditions (acute coronary syndrome, congestive heart failure, pneumonia, stroke, chronic obstructive pulmonary disease [COPD] exacerbation, and infections) and seven chronic clinical conditions (coronary heart disease, cerebrovascular disease, diabetes, hypertension, cancer, COPD, and Parkinson) were considered. To estimate the global burden of diseases and severity of comorbidity, the Cumulative Illness Rating Scale (CIRS) and the total number of drugs prescribed during hospital stay were considered and analyzed as potential risk factors.¹⁶ Among selected medications, the use of anxiolytics, antipsychotics, and antidepressants was considered as a potential risk factor for functional decline.

All routine laboratory tests were determined the morning after the first day after admission after an overnight 12-hour fast. Assays were performed in the central laboratory of each clinical center using standard enzymatic methods.

Statistical Analysis

Study participants were followed up until hospital discharge. Characteristics hypothesized to be associated with functional decline over hospitalization are listed in Table 2. For statistical analysis, continuous variables were recoded into categorical variables, according to predefined criteria when such criteria were available (BMI, albumin, cholesterol, erythrocyte sedimentation rate, number of drugs, Hodkinson Abbreviated Mental Test score, and GDS score) or tertiles of distribution (glucose, creatinine, and CIRS). A missing category was added to all variables with 1 or more missing values: BMI (13.8%), albumin (17.4%), cholesterol (11.5%), and erythrocyte sedimentation rate (9.7%). Logistic regression models were used to assess the association between potential risk factors for functional decline and the likelihood of having new BADL disability at hospital discharge. To control for the effect of age and preadmission functional status, odds ratios and 95% confidence interval (CI) were adjusted for age and IADL status. Although strongly affected by cognitive function, IADL impairment usually represents an early step in the disablement process of older persons and may convey important information for the identification of nondisabled person at high risk of physical decline.¹⁷ Candidate variables to be included in the logistic model were selected on the basis of biological and clinical plausibility as risk factor for functional decline. To identify factors independently associated with the risk of new

Table 1. Selected General and Clinical Characteristics of Participant Included in the Study Sample (n = 1,686) and Participants Excluded (n = 305)

Characteristic	Included	Excluded	P value
Age, years; mean (standard deviation)	77.4 (7.2)	79.6 (7.9)	<.001
Women, n (%)	816 (48.4)	127 (41.6)	.023
Educational level, years; mean (standard deviation)	5.4 (3.6)	5.5 (3.6)	.789
Living alone, n (%)	348 (20.6)	55 (18.0)	.297
Admitted from nursing home, n (%)	42 (2.5)	13 (4.3)	.082
Smoking, n (%)			
Former	671 (39.8)	133 (43.6)	
Current	176 (10.4)	39 (12.8)	.119
BMI, kg/m ² ; mean (standard deviation)	25.7 (4.6)	24.5 (4.9)	.004
HAMT score mean (standard deviation)	8.2 (1.9)	5.6 (3.8)	<.001
GDS, mean (standard deviation)	4.9 (3.5)	4.4 (3.5)	.021
Number of drugs, mean (standard deviation)	8.2 (5.2)	9.5 (6.9)	<.001
CIRS score, mean (standard deviation)	8.4 (4.2)	10.3 (6.9)	<.001
Number of independent IADL 2 week before admission, mean (standard deviation)	4.9 (3.5)	4.5 (4.6)	.022
Discharge diagnostic category, n (%)			
Cardiovascular	709 (42.0)	114 (37.4)	.127
Cerebrovascular	146 (8.6)	28 (9.2)	.767
Neurological	115 (6.8)	12 (3.9)	.058
Pulmonary	118 (7.0)	23 (7.6)	.734
Gastrointestinal	132 (7.9)	18 (5.9)	.241
Cancer	67 (4.0)	30 (9.8)	<.001
Others	399 (23.6)	80 (26.2)	.335
Length of hospital stay, days; mean (standard deviation)	11.2 (6.3)	14.8 (32.1)	<.001

BMI = Body mass index, HAMT = Hodkinson Abbreviated Mental Test, GD = Geriatric Depression Scale, Total Cumulative Illness Rating Scale (CIRS)

BADL disability, a multivariable logistic model was then computed including all the variables that were associated with the outcome at an α level of 0.1. Afterward, to obtain a more parsimonious predictive model and to achieve a suitable ratio of the number of events to the number of covariates,¹⁸ unnecessary variables were removed using a backward stepwise technique (P for removal .1). To quantify multicollinearity, the variance inflation factor (VIF) was also computed. Finally, the multivariable logistic regression model was validated by means of bootstrapping technique. One thousand bootstrap simulations were performed, producing 95% CI for the variables retained in the most parsimonious model.

RESULTS

Table 1 shows selected demographic and clinical characteristics of the study participants. The mean age of the patients was 77.4 years, 48.4% were women and 2.5% were nursing home residents. Two weeks before hospital admission, 35.5% were independent in all IADL, whereas 21% of the patients had cognitive impairment at hospital admission. The mean length of hospital stay was 11.2 days and cardiovascular disease was the most common discharge diagnosis category (42%). Com-

pared to individuals included in the analysis, those excluded were older, more likely to be men, and had a greater level of comorbidity and cognitive impairment.

At hospital discharge 113 patients (6.7%) presented new BADL disability; of them, 85% experienced functional decline in 2 or more BADL. New BADL dependence was associated with longer hospital stay (mean difference +2.8 days, $P<.001$) and higher rate of discharge to a nursing home (8.9% vs 1.0, $P<.001$). Transferring and dressing were the two activities more frequently lost by the patients. The likelihood of functional decline was strongly related to patients' age and IADL functional status. For example, almost 1 out of 4 patients 85 years and older and dependent in 5 or more IADL developed new BADL disability over the study follow-up.

Logistic regression analysis, adjusted for age and IADL status before admission, was used to screen variables hypothesized to predict functional decline at discharge (Table 2). Nursing home residency, low BMI, low albumin level, cholesterol level, high erythrocyte sedimentation rate, cognitive decline, the number of drugs, the CIRS score, and history of fall in the previous year were all associated with the risk of new BADL disability at a significance level $<.1$. Among the single diseases considered, only stroke and pneumonia were associated with the onset of new disability. These variables, of the 35 tested initially, were entered into a multivariable logistic regression model (Table 3). Older age, low BMI, high erythrocyte sedimentation rate, diagnosis of stroke, high level of comorbidity (CIRS score), high number of medications, cognitive decline, history of fall in the previous year, and baseline IADL status were independent predictors of loss of one or more BADL. The results were virtually unchanged after removal of unnecessary variables (Table 3, most parsimonious model). Overall, the binomial logistic model explained a remarkable proportion of the variability (area under receiver operating characteristic curve=0.805). Variance inflation factors analysis suggested a low level of collinearity (average VIF for the final model=1.38). Finally, to validate the final logistic model 1,000 bootstrap simulations were performed. In terms of the variables found to be significant in the original analysis, only history of falls in the previous year had a 95% CI that was not statistically significant (0.91–2.91).

DISCUSSION

The objective of this study was to identify factors associated with the risk of new BADL disability in nondisabled older patients admitted to the hospital for medical problems. After testing a large number of potential predictors, older age, nursing home residency, low BMI, high erythrocyte sedimentation rate, cognitive decline, high level of comorbidity, and history of falls in the previous year were identified as independent predictors of new difficulty in at least one BADL at hospital discharge. This study demonstrates that medical, functional, and biological characteristics, usually linked with the frailty phenotype,¹⁹ are among the most important predictors of functional decline associated with hospitalization. Indeed among the specific diseases leading to hospital admission, only acute stroke was identified as a significant predictor. Results of this study are based on an in-depth multidimensional assessment including various sociodemographics and anthropometric, clinical, biochemical, and functional charac-

Table 2. Potential Risk Factors for New ADL Disability at Hospital Discharge

Variables	No. of patients	No. of events	Percent	OR (95% CI)*
Sociodemographics				
Age				
65–74	693	22	(3.2)	1 (Reference)
75–84	686	52	(7.6)	2.26 (1.35–3.80)†
≥84	307	39	(12.7)	3.49 (1.99–6.11)†
Women	816	63	(7.7)	0.86 (0.56–1.27)
Married	890	43	(4.8)	0.75 (0.50–1.15)
Living alone	348	24	(7.3)	1.02 (0.66–1.58)
Nursing Home resident	25	10	(40.0)	7.16 (3.00–17.1)
Education <5 yr	1,268	91	(7.2)	1.20 (0.72–2.00)
Biomarkers and BMI				
BMI				
<18.5	61	9	(14.8)	2.67 (1.18–6.03)†
18.5–24.9	600	32	(5.3)	1 (Reference)
25–29.9	563	18	(3.2)	0.65 (0.36–1.17)
≥30	229	8	(3.5)	0.72 (0.35–1.74)
Missing	233	46	(19.7)	4.04 (2.39–6.83)
Glucose (mg/dL)				
≤89	561	34	6.1	1 (Reference)
90–118	560	34	6.1	0.95 (0.57–1.56)
≥118	565	45	8.0	1.36 (0.85–2.17)
Creatinine (mg/dL)				
<0.9	552	34	(6.2)	1 (Reference)
≥0.9 ≤1.2	474	25	(5.3)	0.85 (0.49–1.45)
>1.2	660	54	(8.2)	1.29 (0.82–2.04)
Albumin				
<3.5 g/dL	366	33	(9.0)	1.66 (1.05–2.62)
Missing	294	25	(8.5)	1.17 (0.67–2.08)
Total cholesterol (mg/dL)				
<160	387	27	(7.0)	1 (Reference)
160–199	390	22	(5.6)	0.87 (0.48–1.57)
200–239	363	12	(3.3)	0.51 (0.25–1.02)†
≥240	164	8	(4.9)	0.80 (0.35–1.81)
Missing	382	44	(11.5)	1.42 (0.84–2.40)
Erythrocyte sedimentation rate				
≥40 mm/h	383	38	(9.9)	1.81 (1.18–2.78)†
Missing	185	11	(5.9)	1.13 (0.57–2.22)
Anemia	662	51	(7.7)	1.26 (0.85–1.88)
Comorbidities				
Acute conditions				
Acute coronary syndrome	62	4	(6.5)	1.06 (0.37–3.02)
Congestive heart failure	318	12	(3.8)	0.73 (0.46–1.14)
COPD	44	4	(9.1)	1.20 (0.41–3.48)
Pneumonia	46	8	(17.4)	2.88 (1.25–6.62)†
Stroke	38	14	(36.8)	9.05 (4.34–18.9)†
Infections	79	3	(3.8)	0.54 (0.17–1.77)
Chronic conditions				
Cancer	187	18	(6.6)	1.56 (0.91–2.68)
COPD	279	22	(7.9)	1.09 (0.66–1.80)
Cerebrovascular disease	214	24	(10.3)	1.42 (0.85–2.36)
Coronary heart disease	494	30	(6.1)	0.87 (0.56–1.35)
Diabetes	334	21	(6.3)	1.09 (0.66–1.80)
Hypertension	747	45	(6.0)	0.87 (0.59–1.30)
Parkinson	34	5	(14.7)	1.77 (0.64–4.85)
Total CIRS score				
0–6	592	27	(4.6)	1 (Reference)
7–9	507	41	(8.1)	1.77 (1.06–2.96)†
≥10	587	45	(7.7)	1.63 (0.98–2.71)†
Medications				
Anxiolytics	350	24	(6.9)	1.08 (0.67–1.73)
Antipsychotic	77	11	(15.1)	1.91 (0.94–3.86)†
Antidepressant	138	11	(8.1)	1.06 (0.54–2.07)
No. of drugs				
0–4	363	13	(3.6)	1 (Reference)
5–7	522	23	(4.4)	1.14 (0.56–2.30)
≥8	801	77	(9.6)	2.50 (1.35–4.64)†
Cognitive and affective status				
Cognitive decline (HAMT <7)	355	47	(13.2)	2.14 (1.41–3.26)†
Symptoms of depression (GDS ≥5)	603	32	(5.3)	0.94 (0.59–1.48)

(continued on next page)

Table 2. (continued)

Variables	No. of patients	No. of events	Percent	OR (95% CI)*
Functional status				
History of fall	199	26	(13.1)	1.83 (1.13–2.96)
Number of independent IADL				
7	798	41	(5.1)	1 (Reference)
6–3	628	31	(4.9)	0.86 (0.53–1.39)
2–0	260	41	(15.8)	2.59 (1.61–4.16)†

CI = Confidence interval, OR = odds ratio, COPD = chronic obstructive pulmonary disease, CIRS = Cumulative Illness Rating Scale, HAMT = Hodkinson Abbreviated Mental Test, GDS = Geriatric Depression Scale

*Adjusted for age and IADL preadmission functional status

† $P < .1$

teristics. From this point of view our results extend the information of previous studies focusing mainly on selected determinant of functional status in older patients.¹⁰ The findings of a number of characteristics independently predicting disability is consistent with the frequent clinical picture of multiple contributing causes of poor health outcome in the elderly. Moreover, our study focusing on patients without disability at baseline, a subgroup that received less attention

in previous studies, might provide new and additional insights on the pathological mechanism underlying functional decline associated with medical illness and hospitalization.

Functional Status

Several studies investigated the role of sociodemographic and clinical features as risk factors for functional decline during

Table 3. Multivariable Logistic Regression Analyses Predicting New BADL Disability at Hospital Discharge

Variables	Full model	P value	Most parsimonious model*	P value	Bootstrap estimation
	OR (95% CI)		OR (95% CI)		95% CI
Age					
65–74	1 (Reference)	–	1 (Reference)	–	
75–84	1.76 (1.01–3.07)	0.046	1.94 (1.12–3.34)	0.017	(1.06–3.36)
≥84	2.24 (1.21–4.16)	0.010	2.75 (1.52–4.97)	0.001	(1.44–4.76)
Nursing home resident	4.50 (1.68–12.1)	0.003	4.75 (1.80–12.6)	0.002	(1.15–13.3)
BMI					
<18.5	2.32 (0.93–5.78)	0.070	3.41 (1.49–7.81)	0.004	(1.04–7.27)
18.5–24.9	1 (Reference)		1 (Reference)		
25–29.9	0.63 (0.34–1.18)	0.152			
≥30	0.77 (0.34–1.75)	0.537			
Missing	4.11 (2.28–7.40)	<0.001	5.50 (3.36–8.99)	<0.001	(3.04–8.27)
Albumin					
<3.5 g/dL	1.39 (0.80–2.43)	0.245			
Total cholesterol (mg/dL)					
<160	1 (Reference)				
160–199	1.05 (0.55–2.00)	0.882			
200–239	0.70 (0.32–1.54)	0.374			
≥240	0.95 (0.38–2.42)	0.920			
Erythrocyte sedimentation rate					
≥40 mm/h	1.60 (0.98–2.62)	0.062	1.75 (1.11–2.75)	0.016	(1.02–2.73)
Pneumonia	1.65 (0.63–4.32)	0.304			
Stroke	6.72 (2.87–15.8)	<0.001	6.32 (2.75–14.5)	<0.001	(2.21–14.9)
Antipsychotic	1.92 (0.85–4.33)	0.117			
Number of medications					
0–4	1 (Reference)		1 (Reference)		
5–7	1.32 (0.62–2.83)	0.476			
≥8	2.06 (1.03–4.13)	0.041	1.95 (1.24–3.06)	0.004	(1.18–2.86)
Total CIRS score					
0–6	1 (Reference)		1 (Reference)		
7–9	2.00 (1.13–3.50)	0.018	2.06(1.17–3.60)	0.012	(1.21–3.52)
≥10	2.12 (1.16–3.91)	0.014	2.17(1.21–3.89)	0.010	(1.28–3.80)
Cognitive decline (HAMT <7)	1.75 (1.08–2.83)	0.023	2.01 (1.28–3.15)	0.012	(1.11–2.82)
History of fall	1.75 (1.01–3.04)	0.046	1.73 (1.01–2.94)	0.045	(0.91–2.91)
Number of independent IADL					
7	1 (Reference)				
6–3	0.92 (0.54–1.58)	0.758			
0–2	1.39 (0.80–2.46)	0.252			

For variables removed from the initial model, OR and 95% CI are not displayed in table. Variables included in the initial model are all the same variables included in the full model.

OR = odds ratio, CI = Confidence interval, CIRS = Cumulative Illness Rating Scale, HAMT = Hodkinson Abbreviated Mental Test

*Backward stepwise logistic regression model (P value for removal >0.1).

hospitalization. Despite considerable methodological differences in terms of patients' characteristics and study outcomes, age, functional status, and cognitive function were consistently reported as major predictors.¹⁰ In agreement with these findings, our study reinforces the role of older age, cognitive impairment, and prehospital functional status as risk factors for new BADL disability. With regard to functional status, we found that history of fall in the previous year was associated with the risk of disability independent of other clinical characteristics and baseline IADL status. The risk of fall increases with age and is strongly associated with functional limitation, comorbidity, frailty, and presence of subclinical neurological dysfunction,^{20,21} suggesting that among nondisabled older persons a recent history of fall might identify subjects at higher risk of functional decline.

BMI and Biomarkers

Low BMI but not overweight or obesity was associated with the risk of incident BADL disability. In the general population BMI is considered an indirect but clinically useful measure of adiposity. In the older population, however, because of the age-related anthropometric changes, the relationship of BMI with fat mass is less defined and low BMI is considered a better indicator of reduced lean mass.²² In older persons, low BMI has been associated with increased risk of all-cause mortality and involuntary weight loss has been proposed as diagnostic criteria for the frailty syndrome.^{19,23,24} Nevertheless, the relationship between low BMI and functional limitation or disability has gained less attention. Our finding suggests that older patients with low BMI might be at higher risk of functional decline as a consequence of reduced lean body mass and presence of sarcopenia.²⁵ We evaluated the potential role of several biological markers that have been suggested as biomarkers of frailty or risk factors for disability.^{26–28} Elevated erythrocyte sedimentation rate, an unspecific but sensitive marker of inflammation, was associated with a 75% increased risk of disability. Several acute and chronic conditions are associated with elevated erythrocyte sedimentation rate. However, in our analysis, the association between elevated erythrocyte sedimentation rate and risk of disability was independent of a number of potential confounders, including comorbidity and multiple diseases. Recent epidemiological studies have demonstrated that inflammatory markers are powerful risk factors for mortality and disability in older persons.^{29–31} Our study extends these previous findings to the clinical setting and reinforces the concept that older persons with low-grade inflammation have reduced functional reserve and are at high risk for multiple clinical outcomes.

Clinical Conditions and Comorbidity

This study confirms that comorbidity is associated with an increased risk of functional decline during hospitalization. Our findings, however, highlight the importance of evaluating the global burden and the severity of diseases because a higher value of the CIRS score was significantly and independently associated with the risk of new BADL disability. It has been demonstrated that nondisabled persons with poor objective tests of lower extremity function have a greater prevalence of

chronic diseases;³² it is likely therefore that patients with higher comorbidity, although not yet disabled, were characterized by lower level of functional reserve and homeostatic capacity. Moreover, a high number of medications used during hospitalization was independently associated with an increased risk of functional decline. Conversely, among the different single diseases evaluated, only acute stroke was significantly related with the risk of new disability. Globally taken, these results suggest that a disease-oriented approach might underestimate the risk of functional decline in the hospital setting.

Limitations

This study has important limitations. Functional status was not assessed at the time of hospital admission. It has been demonstrated that functional status of older patients can decline just before hospital admission and that some patients can regain functional independence between admission and discharge.² From this point of view our study design allowed only for a limited picture of patients' functional trajectory. We did not collect information on hospital characteristics and rehabilitation treatments that might influence functional trajectory of older patients. For selected variables there was a substantial rate of missing data. For cholesterol, albumin, and erythrocyte sedimentation rate, patients with missing data had a risk of functional decline that was similar and not statistically significant when compared with the reference category. Analysis performed after exclusion of subjects with missing data on these variables did not change the results (data not shown). Conversely, patients with missing BMI had a higher probability of functional decline. It is likely that these patients had mobility limitation at hospital admission. Exclusion of this subgroup of patient did not change the point estimate of most of the variables but substantially reduced the statistical power and the likelihood of finding significant associations. For this reason we decided to present the result of the analysis including all the patients considered in the study.

Conclusions

This study shows that, besides acute illnesses, several factors might contribute to the loss of physical independence often experienced by older patients during hospitalization. Pre-existing characteristics associated with the frailty syndrome, including physical and cognitive function, comorbidity, body composition, and inflammatory markers, are important predictors. We believe that these findings might have a twofold implication; understanding the characteristics of patients who develop new disability might help us in understanding the biological mechanism underlying the hospital-related loss of physical function. Furthermore, primary and secondary prevention of functional decline is a basic goal of geriatric care also in the acute setting. From a practical point of view, screening and early identification of patients at higher risk is the first step of this process. Our findings identified a set of simple characteristics, readily available to clinicians that might be helpful for a more efficient risk stratification leading to prompt implementation of preventive strategies and optimal planning of hospital and postdischarge care.

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REFERENCES

- Inouye SK, Wagner DR, Acampora D, et al. A predictive index for functional decline in hospitalized elderly medical patients. *J Gen Intern Med.* 1993;8:645-52.
- Covinsky KE, Palmer RM, Fortinsky RH, et al. Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: increased vulnerability with age. *J Am Geriatr Soc.* 2003;51:451-8.
- Gillick MR, Serrell NA, Gillick LS. Adverse consequences of hospitalization in the elderly. *Soc Sci Med.* 1982;16:1033-8.
- Fortinsky RH, Covinsky KE, Palmer RM, Landefeld CS. Effects of functional status changes before and during hospitalization on nursing home admission of older adults. *J Gerontol Ser A Biol Sci Med Sci.* 1999;54:M521-6.
- Brown CJ, Friedkin RJ, Inouye SK. Prevalence and outcomes of low mobility in hospitalized older patients. *J Am Geriatr Soc.* 2004;52:1263-70.
- Sager MA, Franke T, Inouye SK, et al. Functional outcomes of acute medical illness and hospitalization in older persons. *Arch Intern Med.* 1996;156:645-52.
- Boyd CM, Xue QL, Guralnik JM, Fried LP. Hospitalization and development of dependence in activities of daily living in a cohort of disabled older women: the Women's Health and Aging Study I. *J Gerontol Ser A Biol Sci Med Sci.* 2005;60:888-93.
- Sager MA, Rudberg MA, Jalaluddin M, et al. Hospital admission risk profile (HARP): identifying older patients at risk for functional decline following acute medical illness and hospitalization. *J Am Geriatr Soc.* 1996;44:251-7.
- Pedone C, Ercolani S, Catani M, et al. GIFA Study Group. Elderly patients with cognitive impairment have a high risk for functional decline during hospitalization: the GIFA Study. *J Gerontol Ser A Biol Sci Med Sci.* 2005;60:1576-80.
- McCusker J, Kakuma R, Abrahamowicz M. Predictors of functional decline in hospitalized elderly patients: a systematic review. *J Gerontol Ser A Biol Sci Med Sci.* 2002;57:M569-77.
- Carosella L, Pahor M, Pedone C, et al. Pharmacosurveillance in hospitalized patients in Italy. Study design of the 'Gruppo Italiano di Farmacovigilanza nell'Anziano' (GIFA). *Pharmacol Res.* 1999;40:287-95.
- Rocca WA, Bonaiuto S, Lippi A, et al. Validation of the Hodkinson abbreviated mental test as a screening instrument for dementia in an Italian population. *Neuroepidemiology.* 1992;11:288-95.
- Shah A, Phongsathorn V, Bielawska C, Katona C. Screening for depression among geriatric inpatients with short version of the Geriatric Depression Scale. *Int J Geriatr Psychiatry.* 1996;11:915-8.
- Physical status: the use and interpretation of anthropometry: report of a WHO expert committee. WHO Tech Rep Ser. 1995;854:1-452.
- International Classification of Disease, 9th revision. Clinical Modification, 2nd edn. Washington: Public Health Service-Health Care Financing Administration; 1980.
- Linn BS, Linn MW, Gurel L. Cumulative illness rating scale. *J Am Geriatr Soc.* 1968 1968;16(5):622-6.
- Thomas VS, Rockwood K, McDowell I. Multidimensionality in instrumental and basic activities of daily living. *J Clin Epidemiol.* 1998; 51:315-21.
- Harrell FE Jr. Regression Modeling Strategies with Applications to Linear Models, Logistic Regression, and Survival Analysis. In: Chatterjee S, Hadi AS, Price B, eds. *Regression Analysis by Example*, 3rd edn. New York, NY: Springer-Verlag New York; 2001.
- Fried LP, Tangen CM, Walston J, et al. Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol Ser A Biol Sci Med Sci.* 2001;56:M146-56.
- Ferrucci L, Bandinelli S, Cavazzini C, et al. Neurological examination findings to predict limitations in mobility and falls in older persons without a history of neurological disease. *Am J Med.* 2004;116:807-15.
- Lindenberger EC, Landefeld CS, Sands LP, et al. Unsteadiness reported by older hospitalized patients predicts functional decline. *J Am Geriatr Soc.* 2003;51:621-6.
- Seidell JC, Visscher TL. Body weight and weight change and their health implications for the elderly. *Eur J Clin Nutr.* 2000;54(suppl 3):S33-9.
- Landi F, Onder G, Gambassi G, et al. Body mass index and mortality among hospitalized patients. *Arch Intern Med.* 2000;160:2641-4.
- Volpato S, Romagnoni F, Soattin L, et al. Body mass index, body cell mass, and 4-year all-cause mortality risk in older nursing home resident. *J Am Geriatr Soc.* 2004;52:886-91.
- Roubenoff R. Sarcopenia: effects on body composition and function. *J Gerontol Ser A Biol Sci Med Sci.* 2003;58:1012-7.
- Volpato S, Leveille SG, Corti MC, et al. The value of serum albumin and high-density lipoprotein cholesterol in defining mortality risk in older persons with low serum cholesterol. *J Am Geriatr Soc.* 2001;49:1142-7.
- Shlipak MG, Stehman-Breen C, Fried LF, et al. The presence of frailty in elderly persons with chronic renal insufficiency. *Am J Kidney Dis.* 2004;43:861-7.
- Maraldi S, Volpato S, Cesari M, et al. Anemia and recovery from disability in activities of daily living in hospitalized older persons. *J Am Geriatr Soc.* 2006;54:632-6.
- Volpato S, Guralnik JM, Ferrucci L, et al. Cardiovascular disease, interleukin-6 and the risk of mortality in older women: the Women's Health and Aging Study. *Circulation.* 2001;103:947-53.
- Ferrucci L, Penninx BW, Volpato S, et al. Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. *J Am Geriatr Soc.* 2002;50:1947-54.
- Cesari M, Penninx BW, Pahor M, et al. Inflammatory markers and physical performance in older persons: the InCHIANTI study. *J Gerontol Ser A Biol Sci Med Sci.* 2004;59:242-8.
- Ferrucci L, Penninx BW, Leveille SG, et al. Characteristics of nondisabled older persons who perform poorly in objective tests of lower extremity function. *J Am Geriatr Soc.* 2000;48:1102-10.