THE GERONTOLOGICAL SOCIETY OF AMERICA®

OXFORD

Research Article

The Severity of Acute Illness and Functional Trajectories in Hospitalized Older Medical Patients

Filippo Luca Fimognari,[1] Andrea Pierantozzi,[2] Walter De Alfieri,[3] Bernardo Salani,[4] Stefano Maria Zuccaro,[5] Andrea Arone,[1] Giacomo Palleschi,[6] and Lorenzo Palleschi[7]

[1]Unit of Geriatrics, Azienda Ospedaliera di Cosenza, Cosenza, Italy. [2]Department of Laboratory Medicine, Università Tor Vergata, Roma, Italy. [3]Unit of Geriatrics, Ospedale di Casteldelpiano, Azienda USL 9, Grosseto, Italy. [4]Geriatric Agency Unit, Azienda Ospedaliera-Universitaria Careggi, Firenze, Italy. [5]Unit of Geriatrics, Ospedale Israelitico, Roma, Italy. [6]Casa di Cura Villa Fulvia, Roma, Italy. [7]Unit of Geriatrics, Azienda Ospedaliera S. Giovanni-Addolorata, Roma, Italy.

Address correspondence to Filippo Luca Fimognari, MD, Unità Operativa Complessa di Geriatria, Azienda Ospedaliera di Cosenza, Ospedale dell' Annunziata, Via Felice Migliori, 87100 Cosenza, Italy. E-mail: filippo.fimognari@virgilio.it

Abstract

Background: Acute diseases and hospitalization are associated with functional deterioration in older persons. Although most of the functional decline occurs before hospitalization in response to the acute diseases, the role played by comorbidity in the functional trajectories around hospitalization is unclear.

Methods: Observational prospective study of 696 elderly individuals hospitalized in two Italian general medicine wards. Functional status of the elderly patients at 2 weeks before hospitalization (baseline), at hospital admission, and at discharge was measured by the Barthel Index. Comorbidity was measured at admission by the Geriatric Index of Comorbidity (GIC), a tool mostly based on illness severity. The association of GIC with changes in functional status before hospitalization (between baseline and admission), during hospitalization (between admission and discharge), and in the overall period between baseline and discharge was assessed by logistic regression analyses. Hospitalization-associated disability (HAD) was defined as a functional decline between baseline and discharge.

Results: Illness severity (GIC 3–4 vs 1–2: odds ratio [OR] 2.2, 95% CI [confidence interval] 1.5–3.3, $p < .0001$) and older age significantly predicted prehospital functional decline (between baseline and admission). Illness severity (OR 1.9, 95% CI 1.2–3, $p = .004$) and older age were also predictive of HAD, even after adjustment for each coded primary discharge diagnosis. After adjustment for the occurrence of prehospital functional decline, however, illness severity and older age were not predictive of HAD anymore.

Conclusions: The severity of illnesses was strongly associated with adverse functional outcomes around hospitalization, but frailty, intended as functional vulnerability to the acute disease before hospitalization, was a stronger predictor of HAD than illness severity and age.

Keywords: Comorbidity—Frailty—Functional status—Hospitalization-associated disability—Illness severity

Acute diseases and subsequent hospitalization are crucial events in the trajectory leading to disability in older people and account for about 50% of all new-onset disabilities in the general elderly population (1). Elderly patients can be admitted to hospitals because of typically disabling conditions, such as stroke or hip fracture, but many seemingly nondisabling illnesses, including pneumonia and exacerbations of cardiorespiratory chronic conditions, often lead to acute functional deterioration in vulnerable, frail individuals (2,3).

The functional trajectory around hospitalization is a complex phenomenon including two different time segments (4–8). In the few days before admission to hospital, frail elderly people can experience functional decline in response to the disabling effect of the acute disease; after admission to hospital, some patients improve their function, others remain stable, whereas some other patients undergo functional decline (4,7). Thus, "prehospital" and "in-hospital" functional changes are distinct processes, with the former indicating the functional response to the acute disease and the latter reflecting a

mix of factors, such as quality of and individual response to hospital care and processes, disease severity, age, frailty, length of hospital stay, and others (4–8).

As a result of prehospital and in-hospital functional dynamics, about 30–40% of elderly patients are discharged from hospitals with new disabilities compared with the premorbid function, usually referring to 15 days before hospitalization and retrospectively measured at hospital admission (4,6,7). This phenomenon is termed "hospitalization-associated disability" (HAD) and is recognized as a geriatric syndrome (2,3). When older patients undergo HAD, they are at increased risk of postdischarge negative outcomes, including death, nursing home placement, short-term rehospitalization, and prolonged disability (3,5,9).

Previous research has tried to identify patients' characteristics which may predict the risk of functional decline in the perihospitalization period. Identifying negative prognostic factors is crucial for adequately assessing patients at admission, elaborating effective preventive hospital strategies, and improving correct transitions to the posthospital settings. In general, poor premorbid (15 days before hospitalization) function, older age, functional status at hospital admission, cognitive impairment, and depression have consistently proved to be prognostic factors for HAD (2,3).

The role played by comorbidity in the development of disability is well recognized (10). The severity of the acute illness is supposed to be an independent risk factor for functional decline in hospitalized elderly patients, but prior reports provided variable results (2,3,5,11–14). In addition, to our knowledge, the association between severity of illness and functional trajectories was never studied by distinguishing the prehospital from the hospital phase. This information is pertinent, because most of functional decline occurs in the few days before hospital admission as a direct consequence of the acute disease (6,7), but it is unknown whether an association exists between the severity of diseases and the occurrence of prehospital functional decline. With this regard, and based on a conceptual framework of hospital-related functional trajectories (2,3,5,10), we hypothesized that, in the few days before hospitalization, the number and, particularly, the severity of illnesses may play a key role in precipitating disability in vulnerable, frail patients who exhibit at baseline a range of premorbid vulnerabilities, including older age, dementia, poor functional status, and others.

In order to address this issue, we used data from the Progetto Dimissioni in Geriatria Study (Project Discharges in Geriatrics, Pro.Di.Ge.) and measured comorbidity by the Geriatric Index of Comorbidity (GIC), a measurement tool mostly based on illness severity.

Methods

The Pro.Di.Ge. Study is an Italian observational prospective cohort study of elderly patients hospitalized because of an acute medical illness in geriatric and general medicine units between November 2004 and January 2006. The original study was performed in three acute geriatric units and two general medicine units of three Italian hospitals (7). However, because of the relevant amount of missing data regarding GIC in patients hospitalized in geriatric units, we restricted the analysis of the present study to patients admitted to the medical units (and discharged alive). Details about the study protocol are described elsewhere (7). Briefly, patients were hospitalized through the emergency department, directly from home (elective admission), or were transferred to the study unit from other acute care units of the same or other hospitals. For patients hospitalized

after evaluation in the emergency department, the assignment to geriatric or medicine wards by the emergency physicians (who had to be blinded about the study) was not dictated by specific criteria and was mostly based on the availability of beds. The patients who came from nursing homes were hospitalized after evaluation in the emergency department. Elective admission (directly from home) was intended as a planned hospitalization, due to a recent-onset medical disease, mainly after evaluation in an outpatient setting. Also, the study protocol did not include any change in the model of care usually provided by each unit to elderly patients. After admission to the study units, functional status was measured by a trained physician at three time points: at hospital admission by direct, observational assessment; at about 2 weeks before hospital admission (preadmission), as evaluated retrospectively at admission by asking participants about their functional status as it was 15 days before hospital admission; and on the day before discharge. The functional status was measured by a modified version of Barthel Index (BI), which provides a reliable and accurate description of autonomy in daily living activities and is sensitive even to small changes in functional capacity (7). Items in the BI relate to self-care (feeding, grooming, bathing, dressing, bowel and bladder continence, and toilet use) and mobility (ambulation, transferring, and climbing stairs). The scale ranges from 0, representing a totally dependent, bedridden state, to 100, indicating full independence. Because the minimum change of BI is a 5-point variation (increase or decrease), we considered as change of function a decrease or an increase of at least 5 points of BI (7).

GIC was constructed as follows (15). First, clinicians identified 15 diseases that are recognized as the most prevalent in hospitalized patients: heart disease of ischemic or organic origin, primary arrhythmias, other heart disease (cardiomyopathies, myocarditis, cor pulmonale due to chronic pulmonary embolism, primary pulmonary hypertension or chronic obstructive lung disease), hypertension, stroke, peripheral vascular disease, diabetes mellitus, anemia, gastrointestinal diseases, hepatobiliary diseases, renal diseases, respiratory diseases, parkinsonism and nonvascular neurologic diseases, musculoskeletal disorders, and malignancies. Second, the severity of these conditions was graded according to the Greenfield's Individual Disease Severity (IDS) (16) score on a 0–4 scale: 0 = *absence of the disease*; 1 = *asymptomatic disease*; 2 = *symptomatic disease requiring medication but under satisfactory control*; 3 = *symptomatic disease uncontrolled by therapy*; 4 = *life-threatening disease or the most severe form of the disease*. Third, each patient was assigned to one of the four GIC classes considering two domains: (i) number of diseases and (ii) severity of diseases measured according to the Greenfield's IDS score. GIC Class 1 includes patients with one or more diseases with IDS = 1 or lower. Class 2 includes patients who have one or more diseases with IDS = 2. Class 3 includes patients having one disease with IDS = 3, other diseases with IDS = 2 or lower. Class 4 includes patients with two or more diseases with IDS = 3 or one or more diseases with IDS = 4. It should be emphasized that GIC classes are all inclusive and mutually exclusive, in that a single patient can belong to only one of the four GIC classes. Among several comorbidity indices, GIC was the only measure to independently correlate with disability after adjustment for severity of individual diseases (15).

Patients were also grouped according to the primary coded ICD9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) discharge diagnosis in the following nine disease categories: valvular and organic cardiomyopathies, coronary artery disease, conduction disorders and arrhythmias,

cerebrovascular diseases, neurological diseases, gastrointestinal diseases, pulmonary diseases, cancer, and other diseases.

Because GIC does not specifically include a diagnosis of dementia, this condition was considered as a separate diagnosis for the analysis, if included among the diseases coded at discharge (7).

When the study physician deemed that patients were unable to respond, surrogates were interviewed.

The Ethical Committee of Ospedale Israelitico, Rome, approved the study.

Analytical Strategy and Statistic Analysis

A bivariate analysis was performed using the *t* test, Mann–Whitney test, Chi-square test and Fisher's exact test (2×2), as appropriate, to compare a series of variables between groups, as follows (Table 1):

(i) Interval preadmission baseline–admission: patients with declined function (decliners) versus nondecliners (unchanged or improved function); (ii) interval admission–discharge in the subgroup of patients with prior prehospital functional decline (decline between baseline and admission): patients with unchanged or declined function versus patients with improved function; and (iii) overall interval baseline–discharge: decliners (HAD) versus nondecliners (unchanged or improved function).

Variables that significantly (*p* < .05) distinguished groups were included as independent variables in three logistic regression analyses for calculating the odds ratio (OR) and 95% confidence interval (CI) of factors that may be associated, respectively, with three dependent variables: (i) prehospital functional decline (decline between baseline and admission); (ii) failure to improve function during hospitalization after prehospital functional decline (unchanged or declined function between admission and discharge compared with the group with improved function); and (iii) HAD (decline between baseline and discharge). Length of hospital stay (LOS) was excluded from the logistic regression analysis of prehospital functional decline, because LOS does not predict, but rather is a consequence of, prehospital functional decline. In order to avoid "floor effect," logistic regression analyses for prehospital functional decline and HAD were repeated by excluding patients with preadmission severe disability (baseline BI ≤ 20), because these already-disabled patients are less likely to experience further functional decline as a consequence of the acute medical disease. The association between each primary ICD-9 discharge diagnosis (vs absence of that primary diagnosis) with both prehospital functional decline and HAD was studied by logistic regression analyses which included only the independent variables that were significant in the first logistic regression analyses performed for each of the two dependent variables. The occurrence of prehospital functional decline was also accounted for as independent predictor of HAD after adjustment for other variables.

A *p* value less than .05 was considered statistically significant.

Results

The study sample consisted of 696 patients hospitalized in internal medicine wards and discharged alive. In the interval between preadmission baseline and admission, 240 (34.5%) of these 696 patients declined in physical function (prehospital functional decline), 449 did not change their function, and the other 7 patients even improved their function. Among the 240 patients with prehospital functional decline, 170 improved, 54 remained the same, and 3 declined further between admission and discharge (in 13 patients, functional status at discharge was not measured). In the overall interval between preadmission baseline and hospital discharge, 126 out of the 696 (18%)

patients declined in function, that is, were discharged with worse-than-baseline functional status (HAD).

The percentage decrease in BI between baseline and admission (prehospital functional decline, *n* = 240) was −32.8 ± 18.9 (mean ± *SD*), whereas the percentage decrease in BI between baseline and discharge (HAD, *n* = 126) was −34.8 ± 20.5.

Of the 696 patients, 38 (5.4% of valid cases) were in GIC Class 1; 269 (38.6%) were in GIC Class 2; 252 (36.2%) were in GIC Class 3; and 129 (18.5%) were in GIC Class 4 (in 8 patients GIC was not measured).

GIC 3–4 patients were not significantly older than GIC 1–2 patients (83.1 ± 8.2 vs 82.4 ± 8.3 years), but they had longer LOS (9.1 ± 6.3 in GIC 3–4 vs 6.4 ± 5.1 days in GIC 1–2) and lower preadmission BI (77.2 ± 26 vs 89.6 ± 18.7).

Table 1 shows the results of the bivariate analyses between two groups in each of the three time intervals around hospitalization (see *Methods*).

Variables that proved to be significantly different between groups in this bivariate analysis were entered into logistic regression analysis models designed to identify variables which were independently associated with the following: prehospital functional decline (from baseline to admission), failure to improve function during hospitalization (from admission to discharge) after prehospital functional decline, and HAD (decline from baseline to discharge).

Pertaining the interval admission–discharge, LOS and the number of ICD-9 diseases coded at discharge were included in a logistic regression analysis with unchanged or declined function as dependent variable and improved function as reference category. Greater LOS was the only significant predictor of failed in-hospital improvement after prehospital functional decline (OR 1.06, 95% CI 1.01–1.11, *p* = .009), whereas the number of ICD-9 diseases was not (OR 1.22, 95% CI 0.99–1.5, *p* = .059).

Table 2 shows the results of the logistic regression analysis for the interval baseline–admission (before hospitalization). Older age, emergency admission, admission from other hospital units, and GIC 3–4 were independently associated with declining function between baseline and admission (prehospital functional decline).

When this logistic regression analysis was repeated by including only patients with baseline BI above 20 (thereby excluding patients with baseline BI ≤ 20, ie, with severe premorbid disability), we obtained similar results, with older age, emergency admission, admission from other hospital units, and GIC 3–4 (OR 2.2, 95% CI 1.5–3.3, *p* < .0001), but also low baseline BI (OR 0.989, 95% CI 0.981–0.99, *p* = .01), which emerged as independent predictors of prehospital functional decline (number of valid cases = 670).

The association of each primary diagnosis (yes/no) with declining function between baseline and admission after adjustment for variables that were significant in the first logistic regression analysis (age, admission from emergency room or from other hospital units, and GIC) was evaluated in a series of logistic regression analyses. No primary diagnosis was significantly associated with declining function between baseline and admission, but, again, older age, emergency admission, admission from other units, and GIC 3–4 (*p* < .0001) were significant predictors of prehospital functional decline in all statistics.

Table 3 shows the results of two models of logistic regression analysis for the interval baseline–discharge. In Model 1, older age, emergency admission, admission from other hospital units, GIC 3–4, and LOS were significantly associated with declining function between baseline and discharge (HAD); in Model 2, however, after adjustment for prehospital functional decline (between baseline and

Table 1. Bivariate Comparisons Between Functional Groups in the Two Time Periods (from baseline to admission and from admission to discharge) and in the Overall Perihospitalization Period (from baseline to discharge)

Variables	From Baseline to Admission (n = 696)			From Admission to Discharge (n = 240)			From Baseline to Discharge (n = 696)		
	Declined (n = 240)	Unchanged-Improved (n = 456)	p Value	Unchanged-Declined (n = 57)	Improved (n = 170)	p Value	Declined (n = 126)	Unchanged-Improved (n = 549)	p Value
Males	44.7	50	.19	39.2	45.5	.44	43.9	49	.31
Age, years	85.7 ± 8.1	81.3 ± 7.9	<.0001	85.2 ± 8.2	85.8 ± 8.1	.65	85.4 ± 7.8	82 ± 8.2	<.0001
Admitted from			<.0001			.55			.0001
Emergency room	63.6	39.2		57.1	67.7		54.4	46.2	
Other units	26	20.7		28.6	22.3		32.8	19.3	
Home	9.2	39.9		12.5	8.8		12	34	
Nursing home	1.2	0.2		1.8	1.2		0.8	0.5	
Dementia	6.2	1.5	.001	7	6.5	.99	7.1	2.3	.012
GIC			<.0001			.33			<.0001
1–2	32	51.2		28	36		29.6	49.6	
3–4	68	48.8		72	64		70.4	50.4	
LOS, days	9.2 ± 6.5	7.2 ± 5.5	<.0001	11.5 ± 7.3	8.2 ± 6	.003	10.6 ± 6.9	7.2 ± 5.5	<.0001
Baseline BI	75.2 ± 24	87 ± 22.7	<.0001	72.3 ± 24.9	77.8 ± 22.3	.142	80.4 ± 21.9	84.6 ± 23	.059
Number of ICD-9 diseases	2.36 ± 1.5	2.53 ± 1.63	.16	2.82 ± 1.73	2.22 ± 1.33	.01	2.61 ± 1.64	2.46 ± 1.57	.34
Primary diagnosis			.001			.38			.027
Coronary artery disease	22	14.2		16.3	23.4		17	16.6	
Cerebrovascular	10.6	9.3		18.2	7.8		14.4	8.8	
Neurological	3.2	2.1		3.6	3.2		3.4	2.3	
Pulmonary	18.8	12.6		25.5	16.9		18.6	13.6	
Gastrointestinal	0.9	3.2		0	1.3		1.7	2.7	
Cancer	12.8	11.4		10.9	13		14.4	10.9	
Conduction disorders and arrhythmias	2.7	10.7		1.8	2.6		1.7	9.5	
Valvular and organic cardiomyopathies	6	7		5.5	6.5		8.5	6.4	
Other	23	29.5		18.2	25.3		20.3	29.2	

Notes: Data are mean ± *SD* or percentage.

BI = Barthel Index; GIC = Geriatric Index of Comorbidity; ICD-9 = International Classification of Diseases, Ninth Revision; LOS = length of stay; *n* = number.

admission), only LOS and prehospital functional decline were significant correlates of HAD.

When these logistic regression analyses were repeated by including only patients with baseline BI above 20, similar results were observed, with older age, emergency admission, admission from other hospital units, LOS, and GIC 3–4 (OR 1.99, 95% CI 1.2–3.1, *p* = .003), but also dementia (OR 2.7, 95% CI 1–7.3, *p* = .04), as significant predictors of HAD in Model 1 and with LOS and prehospital functional decline as significant predictors of HAD in Model 2 (number of valid cases = 655 for both the models).

The association of each primary diagnosis (yes/no) with HAD (decline from baseline to discharge) after adjustment for variables that were significant in Model 1 (age, LOS, admission from emergency room or from other hospital units, and GIC) was tested in a series of logistic regression analyses. No primary diagnosis was significantly associated with HAD, but cerebrovascular disease was a nearly-significant predictor (OR 1.77, 95% CI 0.93–3.37, *p* = .078). In all these logistic regression analyses, older age, LOS, emergency admission, admission from other hospital units, and GIC 3–4 were, again, significant predictors of HAD.

The association of each primary diagnosis (yes/no) with HAD (decline from baseline to discharge) after adjustment for variables that were significant in Model 1 (age, LOS, admission from

emergency room or from other hospital units, and GIC) was tested in another series of logistic regression analyses which also included the presence of prehospital functional decline (vs no prehospital decline) among the independent variables. Only cerebrovascular disease was significantly associated with HAD (OR 3.02, 95% CI 1.1–8.3, *p* = .03). In all these logistic regression analyses, similarly to Model 2, only LOS and prehospital functional decline were significant predictors of HAD, whereas age, the origin of patients (being hospitalized from emergency department or from other hospital units), and GIC were not significant predictors of HAD.

Discussion

This study was specifically designed to investigate the potential independent role played by comorbidity, and particularly the severity of diseases at admission, in the functional trajectories around hospitalization for acute medical diseases in older patients. Our main findings may be summarized as follows: comorbidity (the number and the severity of illnesses) and advanced age were closely associated with both prehospital functional decline and overall HAD, after adjustment for possible confounders; however, when the occurrence of prehospital functional decline was considered, illness severity and age were not significantly associated with HAD anymore. This indicates that the intrinsic functional vulnerability to acute diseases, an index of frailty, is more important than the acute illnesses and age in determining the functional dynamics of hospitalization.

To our knowledge, this is the first study that has investigated the independent effect of illness severity on pre- and in-hospital functional trajectories in older patients. We measured comorbidity by GIC, an assessment tool incorporating both the number and severity of diseases. GIC and the Cumulative Illness Rating Scale (CIRS) proved to be the best predictors of death during hospitalization and in the postdischarge period, when compared with other comorbidity indices including the Charlson index [17–19]. GIC has a high prognostic value in hospitalized patients because its hierarchical construction is mostly based on severity of diseases rather than on their numerical sum. For example, one patient with several well-controlled diseases belongs to GIC Class 2, whereas another patient with only one life-threatening disease falls directly into Class 4. In addition, we collapsed GIC classes into two categories (GIC 1–2 vs GIC 3–4), with illness severity being the only domain separating the two categories. As a consequence, our result of a strong association

Table 2. Logistic Regression Analysis of Variables Associated With Functional Decline in the Transition From Preadmission Baseline to Hospital Admission (prehospital functional decline)

Variables	OR (95% CI)	*p* Value
Age	1.05 (1.02–1.07)	<.0001
Baseline Barthel Index	0.99 (0.98–1)	.08
Emergency admission*	6.1 (3.6–10)	<.0001
Admission from other hospital units*	3.7 (2.1–6.5)	<.0001
Dementia	2 (0.7–5)	.1
GIC 3–4 versus 1–2	2.2 (1.5–3.3)	<.0001

Notes: Valid cases = 686; dependent variable (outcome): the group of patients who declined in function between baseline (15 days before admission) and hospital admission (*n* = 236). Reference category: the group of patients with unchanged or improved function from baseline to admission (*n* = 450).

CI = confidence interval; GIC = Geriatric Index of Comorbidity; *n* = number; OR = odds ratio.

*Reference category: admission from home (elective admission).

Table 3. Logistic Regression Analysis of Variables Associated With Functional Decline in the Transition From Preadmission Baseline to Hospital Discharge (HAD, Hospitalization-Associated Disability)

Variables	Model 1		Model 2	
	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Age	1.03 (1–1.06)	.009	1 (0.97–1.03)	.8
LOS	1.07 (1.03–1.1)	<.0001	1.08 (1.03–1.1)	.002
Emergency admission*	2.8 (1.5–5.2)	.001	0.5 (0.2–1.4)	.2
Admission from other hospital units*	3 (1.5–5.9)	.001	1.6 (0.57–4.5)	.3
Dementia	2.2 (0.8–5.7)	.09	1.4 (0.4–4.3)	.5
GIC 3–4 versus 1–2	1.9 (1.2–3)	.004	1.1 (0.6–2)	.6
Prehospital functional decline†	—	—	337 (78–1456)	<.0001

Notes: Valid cases = 666; dependent variable (outcome): the group of patients who declined in function between baseline (15 days before admission) and hospital discharge (*n* = 124). Reference category: the group of patients with unchanged or improved function from baseline to discharge (*n* = 542).

CI = confidence interval; GIC = Geriatric Index of Comorbidity; LOS = length of stay; *n* = number; OR = odds ratio.

*Reference category: admission from home (elective admission).

†Declined function between baseline and hospital admission (reference category: unchanged or improved function in the same interval).

between GIC 3–4 and prehospital functional decline, together with the observed comparable number of ICD-9 diseases in prehospital functional decliners and nondecliners (Table 1), emphasizes the role played by the severity of acute diseases, rather than the number of diseases, in precipitating the transition to disability in the few days before hospital admission (2).

Because there was no significant association between GIC measures and in-hospital dynamics (from admission and discharge), the strong association between GIC 3–4 and prehospital functional decline was responsible for the overall association between GIC 3–4, that is, disease severity, and HAD (decline from preadmission baseline to hospital discharge).

When the latter association between GIC 3–4 and HAD was controlled for the occurrence of prehospital functional decline, however, GIC 3–4 was not significantly predictive of HAD anymore, while prehospital functional decline was the main determinant of HAD. This result suggests that the individual susceptibility to develop new-onset disabilities in response to acute illnesses (ie, prehospital functional decline) is a stronger determinant of HAD than severity and number of diseases. Although the organ-specific and causative link between some diseases and sudden functional deterioration is obvious (ie, the disability due to a stroke-related hemiparesis), the relation between geriatric syndromes and disability is more complex, because the resultant level of disability is not always predictable on the basis of the mere sum of the potential disabling effects of many coexisting diseases (10,15). Thus, the cause–effect model should be replaced by the stimulus–response model, which takes into account the individual vulnerability (frailty) to functional loss in response to the stress generated by both diseases and hospitalization (10,15). Accordingly, older age, a typical predictor of negative functional outcomes during hospitalization in prior studies (4), was no longer significantly associated with HAD after adjustment for prehospital functional decline. Therefore, prehospital functional decline qualifies as a multidimensional clinical epiphenomenon of frailty, which incorporates and goes beyond the information provided by age and the severity of precipitating diseases. Accordingly, a great prehospital functional decline was found to predict 6-month mortality independently of age, basal comorbidity, and severity of illness at hospital admission (20).

When patients with severe premorbid disability, who could not worsen anymore (floor effect), were ruled out from the analysis, a poor baseline function (low baseline BI) and dementia emerged as significant predictors of, respectively, prehospital functional decline and HAD. These findings are congruent with the conceptual framework of hospital-related functional trajectories described earlier (2,3,5,10) and confirm the role of premorbid vulnerabilities in determining functional dynamics around hospitalization for an acute illness. "Frailty" can be defined as a state of decreased reserve of multiple physiological systems putting an older person at higher risk of adverse outcomes in response to stressors (10). Among these adverse outcomes, disability is the most common, and frailty should be differentiated from disability (10). It can be postulated that prehospital functional decline and HAD occur more frequently in frail older persons accumulating abnormalities in multiple domains, including subthreshold neuromuscular impairments or initial disability, cognitive dysfunction, comorbidities, depressive symptoms, a lack of social support, and others. Such abnormalities predispose older persons to rapidly progress to overt disability or to worsen their baseline disability level when they undergo the stress of acute illnesses and hospitalization. In this view, prehospital functional decline and HAD may be seen as a "post hoc" resultant of frailty. Further research is warranted for better identifying premorbid subclinical abnormalities which may herald prehospital functional decline and HAD (2,3).

Prehospital functional decline and HAD were strongly associated with being hospitalized in the study ward in an emergency condition, from the emergency room or from another hospital ward. We believe that the "origin" of patients reflects domains of disease severity that are not captured by GIC, thereby explaining the association between emergency admission and poor functional outcomes. Again, the adjustment for prehospital functional decline removed the association between emergency admission—a proxy for illness severity—and HAD.

We found a strong association between poor functional outcomes and LOS, which was a significant correlate of HAD even after controlling for prehospital functional decline. The association between functional status and LOS is expected and well recognized (5,20–22). In an Italian study which observed both prehospital and in-hospital functional dynamics, LOS progressively increased as functional performances worsened across groups, with the longest LOS observed in the group with severe prehospital functional decline not followed by in-hospital recovery (5). LOS was described to increase with the magnitude of prehospital functional decline (20), as well as to directly relate to HAD (21). In general, older age, poor cognitive status, functional deterioration, comorbidity, and longer LOS identify a phenotype of patients who are difficult to discharge from hospitals and at higher risk of negative posthospitalization outcomes (5,20–23). Thus, longer LOS is presumably a consequence of disability, severity of illness, and frailty, being unlikely that longer LOS per se may play a causative role in worsening in-hospital functional dynamics (5,20–23). Physicians are currently challenged by health policy makers and administrators to reduce LOS, but this hospital policy may enhance the risk of postdischarge complications and 30-day hospital readmissions in frail patients who are discharged too early to posthospital settings where the level of care is not comparable with that provided by hospitals (24). Recently, the term "hospital-dependent patient" has been proposed to indicate a patient whose conditions can improve only with hospital care, independently of the quality of posthospital care (25). These considerations warrant the need of a more "realistic" approach to the issue of hospitalization of older persons and the effective and timely transition of such patients to posthospital settings (25).

In a study by Mehta and colleagues, the adjustment for dependency in two or more activities of daily living on hospital admission—reflecting prehospital functional decline—did not remove the significant prediction for new-onset disabilities at discharge (HAD) of a number of factors, including age, mobility impairment, and dependency in instrumental activities at baseline, metastatic cancer or stroke, dementia, and low albumin values (11). At variance with these results, we found that age, GIC, and emergency admission were not significant predictors of HAD after controlling for prehospital functional decline. Mehta and colleagues, however, studied only patients without overt disabilities at baseline (11), whereas we addressed a heterogeneous group including both patients who were not disabled prior to the acute illness and patients with different severity of premorbid disability; furthermore, we measured disability by the BI, a more sensitive tool than the Katz index (7). These and other differences between the two studies may account for the partially different results. It should be noted, however, that, similarly to Mehta's findings, we observed that cerebrovascular disease (stroke) as first discharge diagnosis significantly predicted HAD even after controlling for prehospital functional decline and other confounders. As described earlier, this is an expected finding, due to the immediate disabling effect of acute cerebrovascular diseases.

This study has limitations. First, our database did not include some important variables, such as biological measures, body mass index, cognitive status measurements, history of falls, socioeconomic status, diagnosis of delirium or depression, and objective measures of physical performance, which might contribute to explain the relation between severity of illness and prehospital functional decline. Second, we did not examine the role of some important hospitalization processes, including continence and nutritional care, use of medications, and in-hospital mobility. These factors are expected to strongly interact with the relationship between comorbidity and HAD (21). Third, in our population, the prevalence of HAD was lower (18%) than in previous studies (at least 30%). In the entire Pro.Di.Ge. population, which also included patients admitted to geriatric wards, the prevalence of HAD was 29% (7), that is, comparable with values observed in other studies (2–4,6,9,11). Thus, the lower HAD of our population is due to the exclusion of frailer older patients admitted to geriatric units (7). This limits the generalizability of our results, which needs to be replicated in larger populations including patients hospitalized in geriatric wards.

In conclusion, the severity of illnesses and advanced age were potent predictors of adverse functional dynamics around hospitalization in older medical patients, but the prehospital functional vulnerability to the acute disease (ie, frailty) was a stronger determinant of HAD than severity of illness and age.

References

1. Gill TM, Allore HG, Holford TR, Guo Z. Hospitalization, restricted activity, and the development of disability among older persons. *JAMA*. 2004;292:2115–2124.
2. Covinsky KE, Pierluissi E, Johnston CB. Hospitalization-associated disability: "She was probably able to ambulate, but I'm not sure". *JAMA*. 2011;306:1782–1793. doi:10.1001/jama.2011.1556
3. Pierluissi E, Francis DC, Covinsky KE. Patient and hospital factors that lead to adverse outcomes in hospitalized elders. In: Malone ML, Capezuti EA, Palmer RM, eds. *Acute Care for Elders. A Model for Interdisciplinary Care*. New York, NY: Humana Press; 2014:21–48.
4. 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;51:451–458.
5. Sleiman I, Rozzini R, Barbisoni P, et al. Functional trajectories during hospitalization: a prognostic sign for elderly patients. *J Gerontol A Biol Sci Med Sci*. 2009;64:659–663. doi:10.1093/gerona/glp015
6. Mudge AM, O'Rourke P, Denaro CP. Timing and risk factors for functional changes associated with medical hospitalization in older patients. *J Gerontol A Biol Sci Med Sci*. 2010;65:866–872. doi:10.1093/gerona/glq069
7. Palleschi L, De Alfieri W, Salani B, et al. Functional recovery of elderly patients hospitalized in geriatric and general medicine units. The PROgetto DImissioni in GEriatria Study. *J Am Geriatr Soc*. 2011;59:193–199. doi:10.1111/j.1532-5415.2010.03239.x
8. Zaslavsky O, Zisberg A, Shadmi E. Impact of functional change before and during hospitalization on functional recovery 1 month following hospitalization. *J Gerontol A Biol Sci Med Sci*. 2015;70:381–386. doi:10.1093/gerona/glu168
9. Boyd CM, Landefeld CS, Counsell SR, et al. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. *J Am Geriatr Soc*. 2008;56:2171–2179. doi:10.1111/j.1532-5415.2008.02023.x
10. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci*. 2004;59:M255–M263. doi:10.1093/gerona/59.3.M255
11. Mehta KM, Pierluissi E, Boscardin WJ, et al. A clinical index to stratify hospitalized older adults according to risk for new-onset disability. *J Am Geriatr Soc*. 2011;59:1206–1216. doi:10.1111/j.1532-5415.2011.03409.x
12. 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;44:251–257.
13. Volpato S, Onder G, Cavalieri M, et al. Characteristics of nondisabled older patients developing new disability associated with medical illnesses and hospitalization. *J Gen Intern Med*. 2007;22:668–674.
14. Orsitto G, Cascavilla L, Franceschi M, et al. Influence of cognitive impairment and comorbidity on disability in hospitalized elderly patients. *J Nutr Health Aging*. 2005;9:194–198.
15. Rozzini R, Frisoni GB, Ferrucci L, et al. Geriatric Index of Comorbidity: validation and comparison with other measures of comorbidity. *Age Ageing*. 2002;31:277–285.
16. Greenfield S, Blanco DM, Elashoff RM, et al. Development and testing of a new index of comorbidity. *Clin Res*. 1987;A35:346.
17. Zekry D, Loures Valle BH, Lardi C, et al. Geriatrics index of comorbidity was the most accurate predictor of death in geriatric hospital among six comorbidity scores. *J Clin Epidemiol*. 2010;63:1036–1044. doi:10.1016/j.jclinepi.2009.11.013
18. Zekry D, Loures Valle BH, Graf C, et al. Prospective comparison of 6 comorbidity indices as predictors of 1-year post-hospital discharge institutionalization, readmission, and mortality in elderly individuals. *J Am Med Dir Assoc*. 2012;13:272–278. doi:10.1016/j.jamda.2010.11.011
19. Martínez-Velilla N, Cambra-Contin K, Ibáñez-Beroiz B. Comorbidity and prognostic indices do not improve the 5-year mortality prediction of components of comprehensive geriatric assessment in hospitalized older patients. *BMC Geriatr*. 2014;14:64. doi:10.1186/1471-2318-14-64
20. Rozzini R, Sabatini T, Cassinadri A, et al. Relationship between functional loss before hospital admission and mortality in elderly persons with medical illness. *J Gerontol A Biol Sci Med Sci*. 2005;60:1180–1183.
21. Zisberg A, Shadmi E, Gur-Yaish N, Tonkikh O, Sinoff G. Hospital-associated functional decline: the role of hospitalization processes beyond individual risk factors. *J Am Geriatr Soc*. 2015;63:55–62. doi:10.1111/jgs.13193
22. Campbell SE, Seymour DG, Primrose WR. A systematic literature review of factors affecting outcome in older medical patients admitted to hospital. *Age Ageing*. 2004;33:110–115.
23. Wallis SJ, Wall J, Biram RW, Romero-Ortuno R. Association of the clinical frailty scale with hospital outcomes. *QJM*. 2015;108:943–949. doi:10.1093/qjmed/hcv066
24. Bueno H, Ross JS, Wang Y, et al. Trends in length of stay and short-term outcomes among Medicare patients hospitalized for heart failure, 1993–2006. *JAMA*. 2010;303:2141–2147. doi:10.1001/jama.2010.748
25. Reuben DB, Tinetti ME. The hospital-dependent patient. *N Engl J Med*. 2014;370:694–697. doi:10.1056/NEJMp1315568