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Time-dependent prognostic factors of 6-month mortality in frail elderly patients admitted to post-acute care

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Abstract

Objective: to determine the association between functional and nutritional changes caused by an acute illness requiring hospitalisation and 6-month mortality.
Design: hospital-based prospective longitudinal cohort study.
Setting: acute care centre (Hospital General de Vic, Barcelona Province, Spain). Post-acute care centre (Hospital de la Santa Creu de Vic, Barcelona Province, Spain).
Subjects: hundred sixty five patients aged 75 years and older, hospitalised for an acute event.
Methods: functional status (Barthel and Lawton Indices), cognitive status (Short Portable Mental Status Questionnaire), nutritional status (Mini Nutritional Assessment, albumin, cholesterol), depressive symptoms (Geriatric Depression Scale), co-morbidity (Charlson Index) and self-rated health status were collected upon admission to the post-acute care centre. Functional and nutritional status were assessed 1, 3 and 6 months after admission by a trained staff of geriatricians. Six-month mortality was the main outcome variable. Survival analysis was performed with functional and nutritional status as *time-dependent* variables.
Results:the mean age of the cohort was 83.3 years (SD 5.1) and 68.5% were female. Six-month mortality was 29.1% (95% CI: 22.2–36.7). The variables associated with mortality in bivariate analysis were: gender, Barthel Index (2 weeks before admission), Lawton Index (2 weeks before admission), Charlson Index, Barthel Index (*time-dependent*), Mini Nutritional Assessment (MNA) (*time-dependent*) and cognitive status. The variables associated with mortality in multivariate analysis were: gender, Barthel Index (2 weeks before admission), Charlson Index and MNA (*time-dependent*).
Conclusions: functional and nutritional changes due to an acute illness have a statistical and clinical prognostic value and should be assessed along with other well-known relevant prognostic factors.

Keywords: *frail elderly, prognostic factors, geriatric assessment, longitudinal study, mortality*

Introduction

For many elderly patients, an acute medical illness requiring hospitalisation is an important event that often leads to a decline in health: functional loss, institutionalisation and high rates of mortality during the course of the year following discharge [1–4].

In clinical practice, patients who suffer functional decline after hospitalisation unquestionably make up a subgroup with strong indicators of frailty and a need for specialised care [5]. The prognosis for these patients is determined by their clinical evolution and response to the rehabilitation process during the first few months following the acute

event. Most changes affecting the variables that define the patients' geriatric component occur during this period [6].

The prognostic factors of post-hospitalisation mortality described in the bibliography can be grouped in three different categories: sociodemographic factors such as age, gender, living in a nursing home; medical factors such as co-morbidity and medical diagnosis; and other parameters related to geriatric assessment, such as depressive symptoms, and cognitive, functional and nutritional status [7–9]. Of the prognostic factors studied, considerable importance is given to functional status [10, 11] in relation to other well-known negative prognostic factors (e.g. any diseases, and routine physiological measures and co-morbidity) [6].

Most studies on mortality prognosis in geriatric medicine are based on measuring a series of variables at a particular time in the patient's evolution and determining which ones are associated with mortality. However, the information obtained on the patient at admission is not enough to make an accurate prognosis. While some of these factors are constant, such as age and gender, others, such as functional status and malnutrition, are variables that can change after suitable geriatric intervention, thus changing the prognosis of the situation. As Lamarca *et al.* [12] said, 'longitudinal studies estimating the association between disability and mortality in the elderly population have typically assumed disability constant through the follow-up study period'. These studies have considered disability to be a time-fixed variable, without taking into account changes during the follow-up period.

There is a trend in the literature to use more than one measure of the patient's functional status, whether by retrospectively using the functional status recorded prior to admission to acute care, functional status upon admission, or studies that analyse the change that occurred between the prior situation and the situation upon discharge [13–15]. Consensus is lacking as to the number and frequency of measures that should be used. Few studies analyse different prognostic factors such as longitudinal data, and few address changes in the risk of death over time [12, 16].

The objective of this study was to describe the association between the different sociodemographic and medical variables and those obtained through geriatric assessment (i.e. time-fixed variables), as well as the prognostic impact of functional and nutritional trajectories (i.e. *time-dependent* variables), and 6-month mortality of a cohort of frail elderly patients over age 75 who were hospitalised for an acute event.

Methods

Design

Hospital-based prospective longitudinal cohort study.

Subjects

Between September 2000 and November 2001, 198 elderly patients aged 75 and over who had been discharged from the acute care centre (Hospital General de Vic, Barcelona, Spain) were consecutively admitted to our post-acute care centre (Hospital de la Santa Creu de Vic, Barcelona, Spain) and included in the study. Patients admitted in a terminal situation in accordance with Twycross and Lichter criteria [17], patients diagnosed with terminal cancer and patients for whom follow-up could not be guaranteed because they did not belong to our healthcare community were excluded. Admission to post-acute care was the responsibility of the nursing team and geriatricians.

Data collection and follow-up

A multidimensional geriatric assessment (baseline assessment) was performed on the first day after admission to post-acute care by a trained staff of geriatricians using a standard protocol. The following information was collected: demographic data (age, gender), co-morbidity (Charlson Index), cognitive status assessed using the Short Portable Mental Status Questionnaire score (SPMSQ), depressive symptoms assessed using the 15-item Geriatric Depression Scale (GDS), functional status evaluated using the Barthel and Lawton Indices, nutritional status measured using the Mini Nutritional Assessment (MNA), and self-rated health status. We also determined the body mass index (BMI), and albumin and cholesterol serum concentrations. Functional status 2 weeks prior to admission to acute care was determined retrospectively by asking patients or their caregivers to recall their pre-morbid function.

Follow-up visits were scheduled 1, 3 and 6 months after admission to post-acute care to determine the patients' functional and nutritional status.

For all patients, information for all assessments was collected either from the patient (when cognitive performance was intact) or from a caregiver.

Six-month mortality was the main outcome variable. All deaths during the 6-month follow-up period were confirmed by the family, nursing home or attending physician.

Statistical analysis

We analysed continuous variables using the Student's *t*-test and non-continuous variables using the χ^2 test. Non-parametric tests (Mann–Whitney U test) were used for variables that were not distributed normally. A Kaplan–Meier survival analysis was performed to analyse 6-month mortality. The unadjusted association of predictors with mortality was estimated with a bivariate semiparametric Cox model. The independent association of predictors found to be significantly associated in bivariate analysis or clinically significant was assessed in an extension of the multivariate Cox's proportional hazard model with time-dependent co-variates [18, 19]. Hazard ratios and 95% confidence intervals were calculated. Functional status (Barthel Index) and nutritional status (MNA) were introduced in the Cox model as *time-dependent* co-variables. Including *time-dependent* co-variables in the model made it possible to use the patient's baseline information and the data collected at different follow-up visits. Thus, any changes in the patient's

exposure variables during the follow-up period (functional and nutritional status) were taken into account. Significance was set at 0.05 or less. All statistical analysis was performed using SPSS v.12.0. for Windows and STATA v.8.0.

The study was approved by the Hospital General de Vic's Ethics Committee. All participants or caregivers were required to give informed consent.

Results

Of 198 patients fitting the inclusion criteria, 165 (83.3%) agreed to participate in the study. Over the entire 6-month follow-up period, 15 (9.1%) patients were lost to follow-up (Figure 1). No statistically significant differences were observed in terms of age, gender, functional status prior to hospitalisation or functional status upon admission to post-acute care between the patients who did not agree to participate and those who were included in the study.

Table 1 shows the sociodemographic, functional, and clinical characteristics of the total study population. Six months after admission to post-acute care, accumulated mortality was 29.1% (95% CI: 22.2–36.7). Appendix 1 (supplementary data, available online at www.ageing.oxfordjournals.org) shows the 6-month Kaplan–Meier survival curves according to gender. With regard to the place of death, most patients, (42, 87.5%) died at hospital centres or geriatric institutions. Only 8.3% died at home. Of the patients living after 6 months of follow-up, 38.1% (95% CI: 28.5–48.6) presented with functional decline (loss of 20 or more points on the Barthel Index assessed 2 weeks before admission to acute care and at the 6-month visit).

Appendices 2 and 3 (supplementary data, available online at www.ageing.oxfordjournals.org) show the cohort's

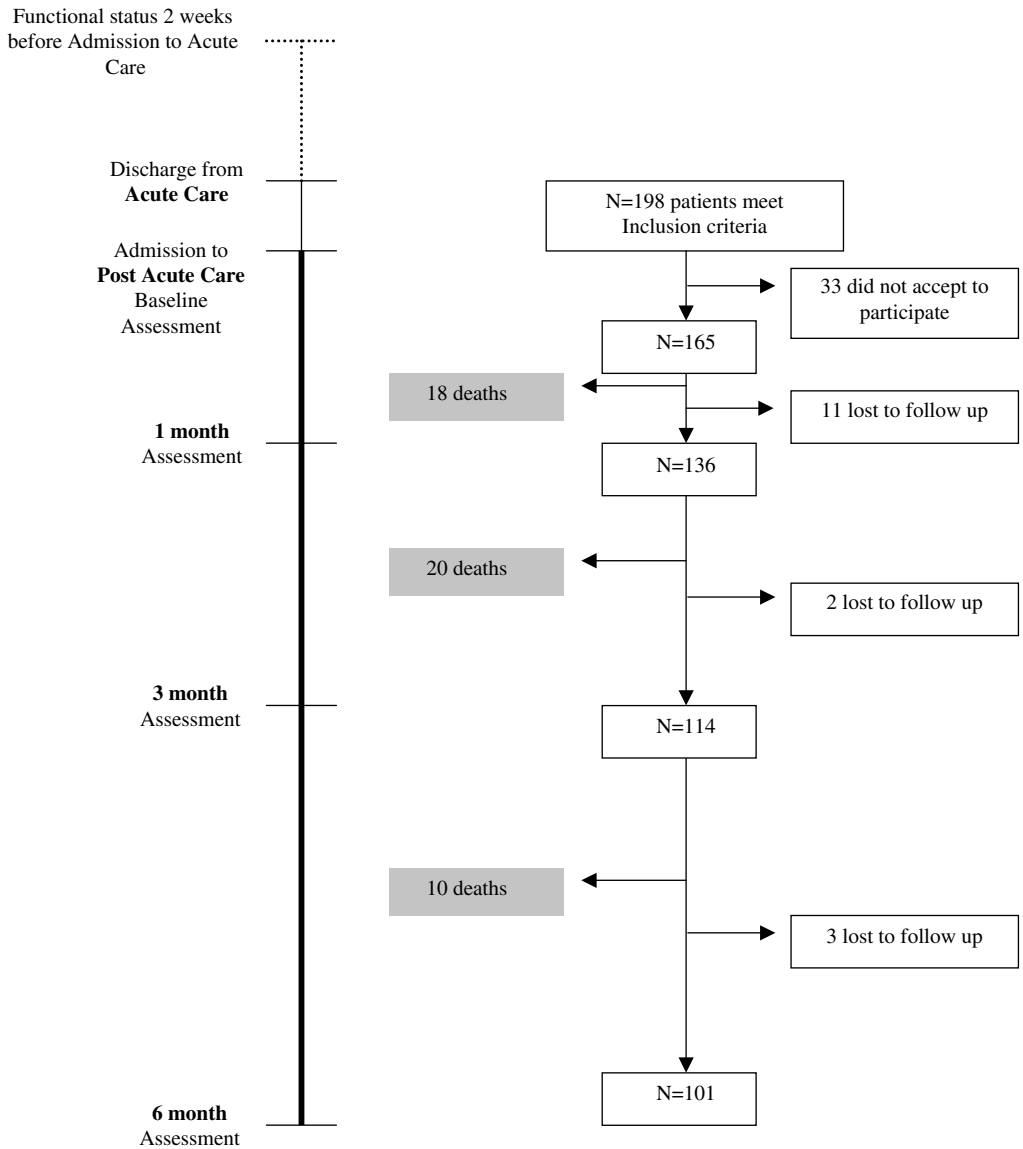

Figure 1. Trial profile.

Table 1. Baseline characteristics of patients

	$N = 165$
Functional status 2 weeks before admission to acute care	
Barthel index	74.5 ± 26.9
Lawton index	1.96 ± 1.80
Acute care	
Length of stay	15.2 ± 8.1
Post-acute care (baseline assessment)	
Age	83.3 ± 5.1
Female gender	113 (68.5)
Charlson index	2.1 ± 1.6
Self-rated health status[a]	
Excellent, very good, good	41 (32.0)
Fair, poor	87 (68.0)
BMI (kg/m^2)	24.6 ± 5.1
Barthel index	31.2 ± 23.2
MNA	16.3 ± 4.0
Serum albumin (g/dl)	3.1 ± 0.4
Serum cholesterol (mg/l)	164 ± 41
SPMSQ score	4.1 ± 3.2
GDS	6.9 ± 3.2

N (%), mean ± standard deviation; BMI: body mass index; MNA: Mini Nutritional Assessment; SPMSQ: Short Portable Mental Status Questionnaire; GDS: Geriatric Depression Scale.

[a] Thirty seven patients did not report self-rated health status.

functional and nutritional trajectories during the follow-up period. Statistically significant differences were observed in functional and nutritional status between the living and dead patients in each of the assessments performed (2 weeks prior to admission to acute care, upon admission to post-acute care and 1 and 3 months after admission to post-acute care) (data not shown). Appendices 4 and 5 (supplementary data, available online at www.ageing.oxfordjournals.org) show the functional and nutritional trajectories by gender.

Table 2 shows the crude and adjusted associations of demographic and clinical variables and 6-month mortality. The variables associated with mortality in bivariate analysis were: male gender (HR 2.54, 95% CI: 1.41–4.60), Barthel Index (2 weeks before admission; HR 0.98, 95% CI: 0.97–0.99), Lawton Index (2 weeks before admission; HR 0.67, 95% CI: 0.54–0.82), Charlson Index (HR 1.28, 95% CI: 1.08–1.51), Barthel Index (*time-dependent;* HR 0.97, 95% CI: 0.96–0.98), MNA (*time-dependent;* HR 0.87, 95% CI: 0.81–0.93) and cognitive status (SPMSQ score; HR 1.17, 95% CI: 1.06–1.29). The variables associated with mortality in multivariate analysis were: male gender (HR 2.74, 95% CI: 1.50–5.00), Barthel index (2 weeks before admission; HR 0.98, 95% CI: 0.97–0.99), Charlson Index (HR 1.22, 95% CI: 1.01–1.48) and MNA (*time-dependent*; HR 0.87, 95% CI: 0.81–0.94).

Table Appendix 6 (supplementary data, available online at www.ageing.oxfordjournals.org) shows the baseline characteristics of patients by gender. Both groups were comparable in terms of functional status prior to the acute event and in terms of functional, nutritional and cognitive status upon admission to post-acute care. Statistically significant differences were observed for co-morbidity and serum cholesterol. Appendix 7 and 8 (supplementary data, available online at www.ageing.oxfordjournals.org) show the crude and adjusted associations of demographic and clinical variables and 6-month mortality by gender. Whereas the only variable associated with mortality in men in multivariable analysis was the Barthel Index (2 weeks before admission; HR 0.98, 95% CI: 0.96–0.99), in the case of women, the variables associated with death were the Charlson Index (HR 1.31, 95% CI: 1.01–1.69), the Barthel Index (*time-dependent*; HR 0.97, 95% CI: 0.95–0.99) and the MNA (*time-dependent*; HR 0.88, 95% CI: 0.79–0.99).

Discussion

Using simple inclusion criteria, a cohort of elderly patients was chosen who were hospitalised for an acute event and had a 6-month mortality rate of 29.1%. The survival curves for men and women were different, and the men's mortality rate was higher [20]. Of the patients living after 6 months, 38.1% presented with functional decline compared with their situation prior to admission. The results of this study carried out at the post-acute care centre show that prognostic factors related to mortality such as gender, Charlson Index, Barthel Index, Lawton Index, SPMSQ score and MNA pertain to different domains of the individual: some reflect sociodemographic features, while others are factors related to medical diagnostics, factors related to functionality (physical and mental) and factors related to nutritional status. These results are consistent with clinical experience, which shows that the cause of death in the elderly is generally multifactorial.

Follow-up of the cohort allowed us to observe that functional and nutritional trajectories underwent many changes within the context of hospitalisation and the subsequent 6 months. This fact reinforces the working hypothesis of using statistical models with repeated measures or *time-dependent* variables to study prognostic factors. Very often, this association has been assessed without considering possible changes in prognostic factors, thereby ignoring the change in the risk of death over time. At certain times, changes taking place in factors associated with mortality can modify the patient's prognosis. Statistical models that do not take these changes into account can be biased with regard to the association between the different prognostic factors and the main dependent variable (mortality, functional decline, etc.) in follow-up studies.

Our results are similar to those obtained by Walter *et al.* [1], the objective of which was to develop and validate a prognostic index for 1-year mortality of older adults after hospital discharge. It was based on a sample with identical age and gender characteristics. Risk factors associated with 1-year mortality in multivariable analysis were gender, function, co-morbidity and a variable such as albumin, which has a nutritional component. Data were collected upon admission except for functional status, for which information was obtained at discharge.

Table 2. Crude and adjusted associations of demographic and clinical variables and 6-month mortality

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Age	1.04 (0.98–1.10)	1.03 (0.96–1.09)
Gender		
Female	1[C]	1[C]
Male	2.54 (1.41–4.60)	2.74 (1.50–5.00)
Barthel index (2 weeks before admission to acute care)	0.98 (0.97–0.99)	0.98 (0.97–0.99)
Lawton index (2 weeks before admission to acute care)	0.67 (0.54–0.82)	NS
Charlson index	1.28 (1.08–1.51)	1.22 (1.01–1.48)
Self-rated health status		
Excellent, very good, good	1[C]	
Fair, poor	1.21 (0.47–3.1)	—
BMI (kg/m^2)	0.98 (0.92–1.03)	NS
Barthel index *(time-dependent)*	0.97 (0.96–0.98)	NS
MNA *(time-dependent)*	0.87 (0.81–0.93)	0.87 (0.81–0.94)
Serum albumin (g/dl)	0.56 (0.25–1.23)	NS
Serum cholesterol (mg/l)	1.00 (0.99–1.00)	NS
SPMSQ score	1.17 (1.06–1.29)	—
GDS		
Depressed (GDS >5)	1.56 (0.58–4.23)	—

HR: Hazard Ratio; CI: Confidence Interval; Unadjusted HR: computed in bivariate Cox regression models. Adjusted: computed in a multivariate model where all the variables of the unadjusted analysis were tested for independent association in a stepwise Cox model; NS: variables failing to reach the threshold for inclusion in the model; —: variables not introduced in the model; BMI: body mass index; MNA: Mini Nutritional Assessment; SPMSQ: Short Portable Mental Status Questionnaire; GDS: Geriatric Depression Scale.

Our study confirmed that nutritional status, assessed using the MNA, is associated with 6-month mortality in bivariate analysis. This association persists after adjusting for gender, age, co-morbidity and functional status. Unlike other studies [21–23], we introduced nutritional status as a *time-dependent* variable, which allowed us to analyse its association with mortality during the entire follow-up period. The fact that this association is significant tells us that the risk remains constant during the 6-month follow-up period. If patients' nutritional status changes during hospitalisation or the post-hospitalisation period, their risk of death also changes.

Co-morbidity is another short-term independent risk factor of mortality. Measuring co-morbidity is one of the challenges of geriatric medicine. Some authors feel there are few differences between the various tools available, while others believe they should be used in accordance with the reason for which they were designed and the environment in which they were designed to be used. The Charlson Index was created to predict intrahospital mortality and meets the criteria for assessing illness and severity [24, 25].

Our data corroborate the fact that functional status prior to admission for an acute illness is an important prognostic factor of mortality. In general, it represents the patient's store of health for fighting the disease [14]. Covinsky *et al.* showed that functional status before the onset of the acute illness is one of the most important prognostic factors of 1-year mortality. However, the sample used in Covinsky's study was characterised by having a low percentage of women (36%).

The pre-admission Barthel Index score (2 weeks before admission to acute care) was considered a more important predictor than the *time-dependent* Barthel Index score. When the results were analysed by gender, it was observed that the Barthel Index as a *time-dependent* variable was a better predictor of death than the pre-admission Barthel Index score in women, which is probably related to the evolutionary pattern of mortality in women. In population-based studies with long follow-up periods, it has been observed that disability is more prevalent in women, and that they present with end-of-life trajectories with progressive disability and have a stronger association with mortality than men [12, 26]. Puts *et al.* also observed that women at baseline are more frail and that dynamic frailty is associated with mortality in the case of women but not in the case of men [16].

Studies that analyse functional status as a prognostic factor of mortality [1, 14, 27] have analysed it at different moments in the evolution of the acute illness. For some authors, functional status prior to admission is the most predictive [14], because it establishes the baseline situation with regard to frailty, whereas for others the most important factor is functional status upon admission to acute care [27], because it provides information on the consequences of the acute illness. However, we feel that this measure can be highly affected by the acute illness itself and by hospital procedures. Still, other authors consider functional status at discharge to be more important [1]. The situation at discharge is the least comparable among different healthcare systems, given that it is conditioned by aspects such as average stay and the

availability of resources after discharge. However, functional status at discharge is an essential parameter for determining the need for further health services. The measure that is the most useful will depend on the objective of the study.

Several methodological limitations of this study should be taken into account. In the analysis by gender, the most important limitations were due to the size of the sample, specifically in the sub-group of men. However, with the percentages of 6-month mortality and frailty, we feel the sample is representative of a sub-group of patients with established frailty that is suitable for the study of prognostic factors of mortality.

It was not possible to determine whether or not, in the multivariable model, cognitive status (associated with 6-month mortality in bivariate analysis) was still independently associated with mortality after adjustment for other co-variables, given that it was not possible to obtain valid information on all patients. Nor do we know whether patient decisions that had the effect of limiting therapeutic treatment may have changed the prognosis.

Prognostic studies using time-fixed variables are useful for case-mix studies where the objective is to classify sub-groups of patients based on the risk of dying. These studies are generally based on the subjects' baseline status. However, prognostic studies designed to help in clinical decision-making should take into account *time-dependent* variables. In this case, the information provided by all the measures available throughout follow-up will be of more use in clinical decision-making than information provided by one specific measure.

Key points

- Functional and nutritional changes due to an acute illness have a statistical and clinical prognostic value and should be assessed along with routine physiological measures and co-morbidity.
- There is a need to consider functional and nutritional status as time-dependent variables to allow for changes that elderly patients may experience over time and the effect of such changes on survival.
- Gender differences: in men, the static definition of function was more predictive of mortality than the dynamic definition of functional status.

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Conflict of interest

None

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