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Original Article

Length of hospital stay, delayed pneumonia diagnosis and post-discharge mortality. The Pneumonia in Italian Acute Care for Elderly units (PIACE)-SIGOT study

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ABSTRACT

Background: High-income countries are currently decreasing length of hospital stay (LOS), with the aim of improving resource utilization. Little is known about the contribution of LOS to short-term post-discharge mortality in older patients with pneumonia.
Aim: to identify factors independently associated with LOS and to determine whether LOS predicts 3-month post-discharge death in older patients hospitalized for pneumonia.
Method: Prospective observation of 318 consecutive patients in the Pneumonia In Italian Acute Care for Elderly units (PIACE) study. Geriatric risk factors and the time between the onset of symptoms and pneumonia diagnosis (time to diagnosis, TTD) were included in the analysis.
Results: Long TTD (odds ratio [OR] 1.104, 95 % confidence interval [CI] 1.008–1.210) and hypoalbuminemia (0.606, 0.392–0.937) were significant correlates of longer LOS ($\geq$ 11 days) in the logistic regression analysis. TTD was shorter in more severe patients, and healthcare associated pneumonia was inversely related to TTD > 1 day (0.471, 0.258–0.859). At Cox regression analysis, longer LOS independently predicted 3-month post-discharge death (hazard ratio [HR] 2.309, 95 % CI 1.229–4.341), together with severity of pneumonia (or of acute illness), comorbidity, disability at discharge and not being discharged to home. LOS was not anymore significant after adjustment for hypoalbuminemia (0.210, 0.118–0.375) and longer TTD (1.103, 1.020–1.193), that independently predicted post-discharge death together with comorbidity and disability at discharge.
Conclusion: Longer LOS characterizes patients with severe hospital presentation and consequently predicts post-discharge death, but delayed pneumonia diagnosis, a modifiable process of care measure, may contribute to both longer LOS and increased post-discharge death.

1. Introduction

The ageing of populations in high-income countries has increased the number of vulnerable older persons requesting medical care, including care for acute and complex illnesses that warrant medical management in equipped hospitals [1]. Despite this epochal epidemiological transition, acute-care hospital beds have been reduced in most high-income countries, in order to optimize the use of hospital resources and to

Abbreviations: LOS, Length Of hospital Stay; CAP, Community-Acquired Pneumonia; PIACE study, Pneumonia in Italian Acute Care for Elderly units study; HCAP, HealthCare Associated Pneumonia; BADL, Basic Activities of Daily Living; SPMSQ, Short Portable Mental Status Questionnaire; CIRS, Cumulative Illness Rating Scale; SOFA, Sequential Organ Failure Assessment; PSI, Pneumonia Severity Index; SO_2, oxygen-hemoglobin saturation; PaO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen; TTD, Time To pneumonia Diagnosis..

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contain economic costs by shifting most of the healthcare services for older persons from acute-care hospitals to the community [2]. As a consequence of decreasing hospital bed capacity, length of hospital stay (LOS), an important metric that defines hospital efficiency, has also decreased in the latest years, and hospital professionals struggle to discharge from hospital a growing number of older and frail patients as soon as some clinical stability is reached [3,4]. Concerns, however, have been raised about the fact that reducing hospital capacity just while the absolute number of sick older persons raises each year may compromise quality and safety of care provided to our most vulnerable patients, as suggested by the phenomenon of emergency department crowding [1–4].

Community-acquired pneumonia (CAP) is one of the most frequent causes of emergency hospitalization among older patients and is often associated with hospital mortality and costs, as well as with adverse post-discharge clinical outcomes [5]. Previous studies have pointed out different variables associated with prolonged LOS in patients with pneumonia, mainly factors clearly associated with poor prognosis (the severity of pneumonia, older age, frailty, specific comorbidities, abnormalities of laboratory variables) [6–8]. However, there is a paucity of data on the impact of LOS on post-discharge short-term death in older patients with pneumonia and it is unknown whether prolonged LOS may indeed represent a useful predictor of post-discharge mortality in pneumonia [8,9]. In fact, even though a prolonged LOS is supposed to characterize sicker patients with reasonable higher risk of death shortly after discharge, being discharged too early, on the contrary, could increase the risk of post-discharge complications and death [3,4,10].

In this study, we analyzed data from the Pneumonia in Italian Acute Care for Elderly (PIACE) units study, with the following aims: to identify independent correlates of prolonged LOS from a wide list of variables, including geriatric factors and a quality of care measure of timeliness of pneumonia diagnosis; to determine whether prolonged LOS predicted increased 3-month post-discharge death after adjusting for recognized predictors of post-discharge death, as well as for the underlying independent correlates of LOS.

2. Methods

2.1. Study design and participants

The PIACE study was a prospective observational cohort study that enrolled patients admitted to 21 Italian acute care geriatric wards for pneumonia. The PIACE study was promoted by the Società Italiana di Geriatria Ospedale e Territorio (SIGOT, Italian Society of Hospital and Community Geriatrics) and coordinated by the Unit of Geriatrics of the Azienda Ospedaliera "Annunziata - Mariano Santo - S. Barbara", Cosenza (Azienda Ospedaliera di Cosenza), Italy. The protocol was first approved by the Ethics Committee of the Azienda Ospedaliera di Cosenza and then by the Ethics Committees of each participating unit. At admission, patients (or their proxies for patients with altered mental status) provided written informed consent to be included in the study. As extensively described elsewhere [11], each participating unit was initially requested to enroll a minimum of 12 consecutive patients. Some units, however, recruited < 12 consecutive patients, who were likewise included in the final sample. The recruitment period started in 2013 and ended in 2016.

Pneumonia was diagnosed as follows [11]: a new pulmonary infiltrate diagnosed by chest radiograph or thoracic computed tomography associated with ≥ 2 of the following criteria: (1) new or increased cough; (2) new or increased sputum production; (3) fever (≥ 38 °C); (4) new-onset or worsening dyspnea; (5) either leukocytosis ($> 10.000/mm^3$) or leukopenia ($< 4.000/mm^3$); (6) physical findings on chest examination compatible with pneumonia according to clinicians' judgment (rales or bronchial breath sounds). Healthcare associated pneumonia (HCAP) was defined as follows [12]: (1) hospitalization for 2 or more days in the last 90 days (before the onset of pneumonia); (2) intravenous therapy (including antibiotics or chemotherapy) or hemodialysis in the last 30 days; (3) residence in a nursing home or a long-term care facility. In the absence of at least one of these criteria, a diagnosis of CAP was made.

2.2. Main study variables

Data regarding symptoms and signs of presentation, clinical characteristics, laboratory variables and comprehensive geriatric assessment were included in the analysis.

Functional status was measured by the Basic Activities of Daily Living (BADL) index [13]. Dependency in 3 or more BADL referred to about 15 days before admission (pre-admission baseline, before the onset of the acute illness), at hospital admission and at discharge were used for analysis. A functional decline between pre-admission and admission, defined as the loss of at least one BADL in the transition from pre-admission baseline to hospital admission in the subgroup of patients with at least one preserved BADL at pre-admission, was also considered. Cognitive impairment was ascertained by a Short Portable Mental Status Questionnaire (SPMSQ) score > 2 [14]. Overall comorbidity was measured by the Cumulative Illness Rating Scale (CIRS) [15] and an analytical variable to identify patients with CIRS comorbidity score > 3 was used for the analysis. Nutritional status was measured by the short form of the Mini Nutritional Assessment [16] and a score between 0 and 11 identified patients at risk of malnutrition.

The overall severity of illness was determined by the Sequential Organ Failure Assessment (SOFA) score [17], while the severity of pneumonia was assessed by the Pneumonia Severity Index (PSI) [18]. Delirium at admission was defined as an acute onset disorder of attention and global cognitive functioning with fluctuations, abnormal arousal, and perceptual disturbances. A Glasgow Coma Scale score of 12 or lower detected patients with depressed level of consciousness at admission.

A diagnosis of acute-on-chronic respiratory failure was attributed to patients who reported home long-term oxygen therapy before admission. In patients without acute-on-chronic respiratory failure, a diagnosis of acute respiratory failure was made in the presence of at least one of the following conditions: oxygen-hemoglobin saturation (SO_2) at hospital admission ≤ 91 % on room air, as measured by arterial blood gas analysis or non-invasively through finger pulse oxymeter; a partial pressure of oxygen (PaO_2) lower than 60 mmHg, as measured on room air at admission; PaO_2/FiO_2 (fraction of inspired oxygen) ratio ≤ 300; non-invasive mechanical ventilation during hospital stay.

Since PIACE case report form requested to indicate the date of initiation of symptoms that led to hospital admission and the date of pneumonia diagnosis, we included a variable called "Time To pneumonia Diagnosis" (TTD) that was the time, measured in days, between the initiation of symptoms and the diagnosis of pneumonia.

Clinical complications of pneumonia, or acute clinical conditions which accompanied pneumonia and were detected during hospital stay, were also collected.

LOS was calculated as the difference between the discharge and the admission dates.

2.3. Analytic strategy, outcomes and statistical analysis

The median value of LOS in the entire population was 11 days. Thus, the study sample was divided in 2 groups: patients with LOS < 11 days ($n = 158$), and patients with LOS ≥ 11 days ($n = 160$). The above mentioned set of clinical and laboratory variables were compared across the two groups by univariate analyses (ANOVA F test or chi-square test). The statistically significant variables were entered as independent variables into a logistic regression analysis, together with age and gender, while the group with longer LOS represented the dependent variable (and the group with shorter LOS was the reference category). Thus, odds ratios (OR) and 95 % confidence intervals (CI) of longer LOS correlates

were calculated.

The same strategy was used to determine the characteristics of patients who had a longer TTD (>1 day; $n = 143$) compared to those with shorter TTD (≤ 1 day; $n = 172$), categorized by population median. Clinical and laboratory variables were compared across the two groups by univariate analyses and significant ones were included in a logistic regression analysis with longer TTD as the dependent variable (shorter TTD as reference category).

Then, the role of LOS as predictor of the study outcome, i.e. 3-month post-discharge mortality (in patients discharged alive) was first investigated by crude and age/gender adjusted Cox regression models. Subsequently, fully adjusted Cox regression models were built in the same population, in order to investigate whether prolonged LOS predicted higher 3-month post-discharge death after adjustment for clinical variables selected according to clinical judgment and previous literature, thereby calculating hazard ratios (HR) and 95 % CI for each clinical variable. Separated fully adjusted Cox models were obtained, including or not the significant underlying correlates of prolonged LOS (previously obtained by the logistic regression analysis), with the aim of determining whether or not prolonged LOS predicted post-discharge death even after adjusting for LOS correlates. Statistical significance was set at $p < 0.05$. All analyses were performed with SPSS version 24 (SPSS Inc., Chicago, IL, USA).

3. Results

Overall, 334 patients were enrolled in the study. Of them, 15 patients were excluded because of insufficient data collection and 1 patient because of length of stay < 1 day, leaving a final sample of 318 participants. Patients who were alive at the time of discharge ($n = 289$) were included in the 3-month post-discharge mortality analysis.

The LOS of the 29 patients who died during hospitalization (12.6 ± 9.5 days) was comparable to LOS of those who were discharged alive (12.6 ± 7.6 days). The Supplementary Table reports the univariate comparisons of other clinical variables that resulted significantly ($p < 0.05$) different in patients who died during hospitalization compared with those discharged alive.

Table 1 shows the clinical characteristics of the two groups divided according to LOS and the univariate comparisons of these variables across the two groups. The prolonged LOS group had doubled higher post-discharge 3-month mortality than the group with shorter LOS (24.1 % vs 12.7 %, p 0.012), while in-hospital mortality was similar. Crude hazard ratio (HR) of prolonged LOS for post-discharge mortality was 1.997 (95 % CI 1.126–3.541, p 0.018) and remained significant after adjustment for age and gender (HR 1.920, 95 % CI 1.079–3.417) by Cox regression analysis. In the latter model, age and gender did not significantly predict post-discharge mortality. Table 2 depicts the results of the logistic regression analysis that included variables associated with prolonged LOS in the univariate comparisons of Table 1, together with age and gender. As reported, only low albumin levels and increased TTD remained significantly associated with prolonged LOS after accounting for the other variables, thereby qualifying as the only independent correlates of prolonged LOS in this population.

In the univariate analyses comparing patients grouped according to TTD, we found significantly ($p < 0.05$) higher rates of dementia, residence in nursing homes or long term care facilities, diagnosis of HCAP, dyspnea at admission, CIRS > 3, dependency in 3 or more BADL 15 days pre-admission, PSI class V (>130) versus classes III-IV (71–130), bilateral versus unilateral lung infiltrate, and acute heart failure during stay, in patients with shorter TTD (0–1 days) compared to patients with longer TTD (> 1 day). Patients with shorter TTD were also older (84.4 ± 7.3 years) than those with longer TTD (82.8 ± 7.5), and more frequently females, but differences were not statistically significant. On the contrary, patients with longer TTD had a significant more frequent use of antibiotics in the 30 days before admission. As showed in Table 3, lower rate of HCAP diagnosis and use of antibiotics before admission were the

Table 1
Univariate comparisons of clinical variables across two groups divided according to length of hospital stay.

	LOS ≤ 10 days (n = 158)	LOS ≥ 11 days (n = 160)	p
Age (years)	83.2 (7.0)	84.3 (7.8)	0.184
Gender, female	61 (38.6)	73 (45.6)	0.205
Dementia	58 (36.7)	52 (32.5)	0.430
Long term pre-admission oxygen therapy	11 (7.0)	19 (11.9)	0.134
Residence in nursing home or long term care facilities	32 (20.3)	21 (13.1)	0.088
Nasogatric tube pre-admission	3 (1.9)	3 (1.9)	0.988
Tracheostomy pre-admission	1 (0.6)	1 (0.6)	0.993
Tracheal intubation in the 30 days pre-admission	1 (0.6)	2 (1.3)	0.569
Hospitalization for at least 2 days in the 90 days before the onset of pneumonia	34 (21.5)	51 (31.9)	0.037
Use of antibiotic(s) in the 30 days pre-admission	46 (29.5)	45 (28.5)	0.844
Pneumonia type			0.207
Community Acquired Pneumonia (CAP)	96 (60.8)	86 (53.8)	
Healthcare associated pneumonia (HCAP)	62 (39.2)	74 (46.3)	
Dyspnea	116 (73.4)	118 (73.8)	0.946
Tachypnea	34 (21.5)	53 (33.1)	0.020
Fever>38 °C	52 (32.9)	46 (28.7)	0.422
Leukocytosis	80 (50.6)	80 (50.0)	0.910
Leukopenia	5 (3.2)	5 (3.1)	0.984
Cough	84 (53.2)	87 (54.4)	0.829
Bronchial secretions	28 (17.7)	38 (23.8)	0.185
Chest pain	20 (12.7)	16 (10.0)	0.454
Acute renal dysfunction	22 (13.9)	23 (14.4)	0.908
Systolic blood pressure, mmHg	117.2 (32.9)	119.5 (29.9)	0.497
Heart rate, beats × minute	88.5 (19.3)	90.2 (20.2)	0.453
Body temperature, °C	37.3 (0.9)	37.1 (0.9)	0.095
Hemoglobin, g/dL	12.2 (1.9)	11.6 (2.0)	0.013
Serum creatinine, mg/dL	1.3 (0.6)	1.5 (1.1)	0.037
eGFR with CKD-EPI, ml/min	55.9 (22.3)	52.2 (25.8)	0.177
Sodium, mEq/L	138.6 (6.2)	137.2 (12.9)	0.213
Potassium, mEq/L	4.0 (0.6)	4.1 (0.7)	0.281
Albumin, g/dL	3.3 (0.8)	3.0 (0.6)	<0.001
Room air oxygen-hemoglobin saturation (SO_2), %	90.7 (6.0)	89.6 (7.2)	0.159
Fasting blood glucose, mg/dL	113.5 (51.2)	121.3 (58.3)	0.235
Arterial partial pressure of oxygen (PaO_2), mmHg	64.9 (17.7)	62.5 (16.5)	0.217
Arterial partial pressure of carbon dioxide ($PaCO_2$), mmHg	37.6 (8.6)	38.1 (9.4)	0.668
Arterial bicarbonate (HCO_3^-), mEq/L	24.7 (4.8)	25.3 (4.7)	0.312
pH	7.42 (0.07)	7.43 (0.06)	0.463
PaO_2 /FiO_2 (fraction of inspired oxygen) < 300	89 (57.4)	105 (67.3)	0.072
Acute respiratory failure	99 (62.7)	119 (74.4)	0.024
Non-invasive ventilation during hospital stay	30 (19.0)	32 (20.0)	0.820
Short Portable Mental Status Questionnaire (SPMSQ) > 2	92 (58.6)	99 (62.7)	0.665
Cumulative Illness Rating Scale (CIRS) >3	84 (53.2)	91 (56.9)	0.506
Mini Nutritional Assessment (MNA) short form ≤ 11	81 (52.3)	96 (61.5)	0.098
Dependency in ≥ 3 Basic Activities of Daily Living (BADL) 15 days pre-admission	76 (48.4)	78 (49.4)	0.865
Dependency in ≥ 3 BADL at admission	92 (58.2)	100 (62.5)	0.436
Dependency in ≥ 3 BADL at discharge	78 (49.4)	91 (56.9)	0.180
Function decline from pre-admission to admission	37 (23.6)	47 (29.7)	0.215
Sequential Organ Failure Assessment (SOFA) >3	76 (48.1)	80 (50.0)	0.735
Pneumonia Severity Index (PSI)			0.003
III-IV 71–130	91 (58.0)	65 (41.1)	
V > 130	66 (42.0)	93 (58.9)	
Time to pneumonia diagnosis, days	2.2 (2.9)	3.2 (4.4)	0.027

(continued on next page)

Table 1 (*continued*)

	LOS ≤ 10 days (*n* = 158)	LOS ≥ 11 days (*n* = 160)	p
Lung infiltrate			0.030
Unilateral	135 (87.1)	122 (77.7)	
Bilateral	20 (12.9)	35 (22.3)	
Extension of infiltrate			0.236
Lobar	121 (83.4)	117 (78.0)	
Multilobar	24 (16.6)	33 (22.0)	
Pleural effusion	46 (31.5)	60 (39.7)	0.139
Other acute illnesses during hospital stay			
Acute coronary syndrome	14 (8.9)	13 (8.1)	0.814
Deep vein thrombosis	8 (5.1)	7 (4.4)	0.772
Ischemic stroke	12 (7.6)	10 (6.3)	0.637
Acute heart failure	40 (25.3)	41 (25.6)	0.950
Sepsis	1 (0.6)	5 (3.1)	0.102
Gastrointestinal bleeding	0 (0.0)	3 (1.9)	0.084
Fluid/electrolyte disorders	4 (2.5)	5 (3.1)	0.750
Acute urinary disorders	0 (0.0)	9 (5.6)	0.002
Anemia	2 (1.3)	6 (3.8)	0.157
Other	82 (51.9)	116 (72.5)	<0.001
Delirium	40 (25.3)	29 (18.1)	0.120
Glasgow Coma Scale score ≤ 12	35 (22.3)	38 (23.8)	0.758
In-hospital death	15 (9.5)	14 (8.8)	0.818
Post-discharge 3-month death*	18 (12.7)	35 (24.1)	0.012
Setting of discharge*			0.032
Home	107 (75.9)	112 (78.3)	
Home with domiciliary care services	8 (5.7)	4 (2.8)	
Post-acute care facilities	0 (0.0)	5 (3.5)	
Rheabilitation facilities	2 (1.4)	6 (4.2)	
Nursing homes	23 (16.3)	13 (9.1)	
Transfer to Intensive Care Units	1 (0.7)	3 (2.1)	

Data are expressed as mean (standard deviation) or number (percentage). LOS, Length Of hospital Stay; eGFR, estimated Glomerular Filtration Rate; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration.

* Patients discharged alive.

Table 2
Logistic regression analysis of variables significantly associated with longer length of hospital stay (11 days or more).

	Odds Ratio	95 % Confidence Interval	p
Age	1.007	0.966–1.050	0.727
Female versus male gender	1.648	0.876–3.103	0.121
Hospitalization for ≥ 2 days in the 90 days before the onset of pneumonia	1.810	0.904–3.626	0.094
Tachypnea	1.421	0.727–2.778	0.304
Hemoglobin	0.901	0.766–1.060	0.208
Creatinine	1.137	0.770–1.677	0.519
Albumin	0.606	0.392–0.937	0.024
Pneumonia Severity Index (PSI) > 130 versus 71–130	1.149	0.568–2.323	0.700
Acute respiratory failure	1.145	0.505–2.594	0.746
Time to pneumonia diagnosis	1.104	1.008–1.210	0.034
Bilateral versus unilateral lung infiltrate	1.689	0.772–3.697	0.190
Complication from other acute illnesses	1.491	0.666–3.341	0.331

Reference category: the group with length of hospital stay of 10 days or less.

only factors significantly associated with longer TTD (versus patients with shorter TTD) in the logistic regression analysis.

Table 4 reports the results of 4 models of Cox regression analysis for identifying independent predictors of post discharge death. These models included LOS and other potential risk factors, such as severity of acute illness (SOFA and PSI, included one by one to avoid statistical collinearity), functional disability at discharge, comorbidity, and discharge to home (including home with domiciliary care services) versus other modalities of hospital discharge. Separated models (labelled with "B") adding albumin and TTD to the above reported variables were constructed. LOS, severity of illness, comorbidity and dependency at discharge independently predicted greater post-discharge death, while discharge to home was an independent predictor of a better outcome after discharge. However, LOS was not independently related to the outcome of interest after accounting for albumin and TTD (models 1B and 2B). In both models, low albumin levels and longer TTD emerged as independent predictors of post-discharge mortality, together with comorbidity and disability at discharge.

Table 3
Logistic regression analysis of variables significantly associated with longer time to pneumonia diagnosis (> 1 day).

	Odds Ratio	95 % Confidence Interval	p
Age	1.012	0.974–1.051	0.551
Female versus male gender	0.840	0.499–1.414	0.512
Dementia	0.584	0.309–1.102	0.097
Residence in nursing home or long-term care facilities	0.995	0.418–2.367	0.990
Recent antibiotic therapy	3.045	1.698–5.461	<0.001
Healthcare associated pneumonia	0.471	0.258–0.859	0.014
Dyspnea	0.634	0.350–1.150	0.133
Cumulative Illness Rating Scale (CIRS) > 3	0.668	0.394–1.131	0.133
Pneumonia Severity Index (PSI) > 130 versus 71–130	0.741	0.436–1.260	0.269
Bilateral versus unilateral lung infiltrate	0.553	0.274–1.118	0.099
Acute heart failure	0.605	0.335–1.095	0.097
Dependency in ≥ 3 Basic Activities of Daily Living (BADL) 15 days before admission	0.881	0.477–1.630	0.688

Reference category: the group with time to pneumonia diagnosis 0–1 days.

4. Discussion

Our findings can be summarized as follows: a delayed diagnosis of pneumonia (longer TTD) and hypoalbuminemia - a proxy for clinical severity - were independently associated with prolonged LOS; in turn, prolonged LOS predicted 3-month post-discharge death together with other measures of clinical severity, mainly comorbidity and disability at discharge; hypoalbuminemia and diagnostic delay, however, were stronger predictors of post-discharge death than prolonged LOS itself; a worse clinical presentation, such as that of HCAP phenotype, was associated with early pneumonia diagnosis (short TTD), due to presumable increased clinical alertness and diagnostic sensitivity dedicated to more critical patients.

In accordance with previous studies, we found that patients with longer LOS presented with more severe pneumonia than those with shorter LOS [6–8]. In fact, hypoalbuminemia, a recognized marker of clinical severity and instability in pneumonia [7,19], emerged as an independent correlate of prolonged LOS. Longer TTD, i.e. a diagnostic delay at admission, was another correlate of longer LOS, suggesting the potential impact of some quality of care measures on the prognosis of older patients with pneumonia (see below).

A longer LOS was a risk factor for post-discharge death, after correction for age, severity of illness, comorbidity, disability at discharge, and not being discharged to home. Indeed, while there is a paucity of data on specific pneumonia populations [8,9], our conclusions suggest that the association between longer LOS and post-discharge outcomes should be interpreted as a natural consequence of the higher clinical severity and vulnerability detected since hospital admission [6,8,20]. Accordingly, disability at discharge and comorbidity measured at admission were better predictors of post-discharge death than LOS (Cox models "B"). In this perspective, supported by the current literature [6,8,20], the better post-discharge outcome observed in patients with shorter LOS indicates their *low* clinical severity [21]. At least for some patients, such better post-discharge outcome following a short LOS may additionally reflect the reduced exposure to the iatrogenic risks

Table 4
Cox regression analyses of LOS as independent predictor of 3-month post-discharge death adjusted for risk factors, including (models B) or not LOS underlying correlates.

	Model 1				Model 1B				Model 2				Model 2B		
	HR	95 % CI	p		HR	95 % CI	p		HR	95 % CI	p		HR	95 % CI	p
LOS ≥ 11 days	2.270	1.236–4.166	0.008	LOS ≥ 11 days	1.967	0.893–4.333	0.093	LOS ≥ 11 days	2.309	1.229–4.341	0.009	LOS ≥ 11 days	1.843	0.820–4.141	0.139
SOFA > 3	2.144	1.130–4.068	0.020	SOFA > 3	0.838	0.374–1.879	0.668	PSI > 130	1.878	1.005–3.511	0.048	PSI > 130	1.221	0.522–2.885	0.645
CIRS > 3	2.434	1.184–5.006	0.016	CIRS > 3	6.043	1.893–19.295	0.002	CIRS > 3	2.410	1.176–4.943	0.016	CIRS > 3	5.570	1.790–17.332	0.003
Dependency in ≥ 3 BADL at discharge	2.930	1.272–6.752	0.012	Dependency in ≥ 3 BADL at discharge	7.046	2.121–23.406	0.001	Dependency in ≥ 3 BADL at discharge	3.046	1.329–6.980	0.008	Dependency in ≥ 3 BADL at discharge	6.869	2.067–22.824	0.002
Discharged to home*	0.395	0.213–0.733	0.003	Discharged to home*	0.678	0.325–1.415	0.301	Discharged to home*	0.355	0.191–0.662	0.001	Discharged to home*	0.710	0.339–1.488	0.364
				Albumin	0.192	0.104–0.353	<0.001					Albumin	0.210	0.118–0.375	<0.001
				Time to pneumonia diagnosis	1.108	1.023–1.199	0.012					Time to pneumonia diagnosis	1.103	1.020–1.193	0.015

LOS, Length Of hospital Stay; HR, Hazard Ratio; CI, Confidence Interval; SOFA, Sequential Organ Failure Assessment; CIRS, Cumulative Illness Rating Scale; BADL, Basic Activities of Daily Living; PSI, Pneumonia Severity Index.
* Discharged to home also included patients discharged to home with domiciliary care service.

of hospitalization (bed-ridden state, hospital-acquired infections, sleep deprivation and others) and a better hospital management, irrespective of clinical severity [9,21,22]. In an Italian study, however, a short LOS was an independent predictor of early hospital readmissions, with increased hospital mortality in re-admitted patients [10]. This is not surprising, because when patients are older, sicker and clinically instable, premature hospital discharge may sometimes lead to post-discharge complications [3,4].

When TTD and albumin levels, the two underlying correlates of LOS, were added to Cox regression models "B", only longer TTD, comorbidity, disability at discharge and hypoalbuminemia resisted as independent predictors of post-discharge death. Therefore, prolonged LOS was no more significant after correction for its underlying correlates. The prognostic value of hypoalbuminemia mirrors its role of marker of clinical instability and systemic inflammation, both strongly affecting prognosis [7,19,23,24]. Since albumin has anticoagulant and anti-platelet properties, hypoalbuminemia may also exert a direct prognostic effect by triggering atherothrombosis [23,24]. In fact, hypo-albuminemia predicted atherothrombotic events in patients with CAP [23] and the infusion of albumin was found to reduce hypercoagulability in patients with coronavirus disease 19 [24].

Although the intrinsic clinical severity is a determinant of both LOS and post-discharge death [6,8,20], there may be a room for improving management of older and frail patients with pneumonia during hospitalization. Our finding that a diagnostic delay (longer TTD) was, at first, a risk factor for longer LOS and, then, a strong predictor of post-discharge death suggests that an early diagnosis of pneumonia may contribute to ameliorate both outcomes, i.e. shortening LOS without increasing the risk of death after discharge. TTD is a process of care and was measured as the time, in days, between the onset of symptoms and the diagnosis of pneumonia. Pneumonia diagnosis should coincide with a chest imaging that demonstrates a lung infiltrate [11]. The median value in our population was 1 day, but in a consistent number of patients TTD well exceeded 1 day. The complexity of clinical presentation of PIACE patients, who frequently had concomitant or complicating acute illnesses, can be confounding and may have contributed to diagnostic uncertainty and delay in many patients. However, we found an interesting association of shorter TTD (0–1 day), i.e. rapid diagnosis, with severe clinical presentation and pre-admission comorbidity/disability, summarized at multivariate analysis by the HCAP phenotype as independent correlate of early pneumonia diagnosis (TTD 0–1 day). This may reflect the fact that a more severe clinical picture and higher vulnerability (HCAP) may raise clinicians' diagnostic alertness. From the other hand, we found a significant association between use of antibiotics in the 30 days before admission and a longer TTD (> 1 day), presumably because a recent antibiotic treatment can be a misleading information in the diagnostic process, due to the notion that a patient back from an antibiotic course is less likely to have a pulmonary infection.

To sum up, severe presentations of pneumonia alert clinicians and anticipate pneumonia diagnosis, but when diagnosis is delayed, patients may be at particular risk to remain longer in the hospital or to die shortly after discharge. TTD was never reported in previous studies, that mostly addressed another quality of care measure called "time to first antibiotic dose", expressed in hours [25]. Studies showed an association between rapid antibiotic administration and reduced LOS [26], an association that could be mediated by an early pneumonia diagnosis. Recent prospective studies, however, did not report lower short-term death in patients who received early their first antibiotic dose [25]. Therefore, it is unlikely that our result of reduced post-discharge mortality associated with quick pneumonia diagnosis is attributable to anticipated initiation of antibiotic therapy. Rather, our findings suggest that a timely diagnosis of pneumonia *per se* is crucial in the process of hospital care, as it presumably prioritizes medical interventions other than antibiotic therapy, such as prevention and treatment of pneumonia complications [25]. An early pneumonia diagnosis is presumably a proxy for more

comprehensive, careful and effective hospital management. Although clinical severity at hospital presentation remains a strong determinant of adverse outcomes [6,8,20], such a careful management may be capable of reducing LOS and, consequently, the potential harms due to prolonged hospitalization. More importantly, timely diagnosis and reduced LOS may provide benefits in terms of lower post-discharge death and should represent key objectives of the hospital care provided to older patients with suspected pneumonia.

4.1. Limitations

The study has limitations. First, although results were obtained in a nationwide multicenter prospective study, further investigation is necessary to confirm that an early pneumonia diagnosis really ameliorates clinical outcomes in pneumonia, and to determine the causative mechanism(s) by which such improvement should occur. Second, we did not report microbiological etiology of pneumonia and information regarding adherence to antibiotic guidelines, both potential determinants of LOS and post-discharge outcomes [6,26,27]. Third, the diagnosis of pneumonia is supposed to be faster within the clinical context of a prospective study specifically focusing on pneumonia, and thus generalizability may be limited.

5. Conclusions

Prolonged LOS was a clear expression of increased pneumonia severity and, consequently, a predictor of post-discharge mortality. Clinicians and, mostly, health authorities should be aware of this risk while planning hospital bed capacities, hospital budgeting and post-discharge services. This study, however, also allows to hypothesize that a better hospital management, i.e. timely pneumonia diagnosis, may decrease LOS and improve post-discharge clinical outcomes of older patients hospitalized for pneumonia.

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Declaration of competing interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2024.12.014.

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