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Original Article

Influence of the length of hospitalisation in post-discharge outcomes in patients with acute heart failure: Results of the LOHRCA study

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ABSTRACT

Objective: To investigate the relationship between length of hospitalisation (LOH) and post-discharge outcomes in acute heart failure (AHF) patients and to ascertain whether there are different patterns according to department of initial hospitalisation.

Methods: Consecutive AHF patients hospitalised in 41 Spanish centres were grouped based on the LOH (< 6/6-10/11-15/ > 15 days). Outcomes were defined as 90-day post-discharge all-cause mortality, AHF readmissions, and the combination of both. Hazard ratios (HRs), adjusted by chronic conditions and severity of decompensation, were calculated for groups with LOH > 6 days vs. LOH < 6 days (reference), and stratified by hospitalisation in cardiology, internal medicine, geriatrics, or short-stay units.

Results: We included 8563 patients (mean age: 80 (SD = 10) years, 55.5% women), with a median LOH of 7 days (IQR 4–11): 2934 (34.3%) had a LOH < 6 days, 3184 (37.2%) 6–10 days, 1287 (15.0%) 11–15 days, and 1158 (13.5%) > 15 days. The 90-day post-discharge mortality was 11.4%, readmission 32.2%, and combined endpoint 37.4%. Mortality was increased by 36.5% (95%CI = 13.0–64.9) when LOH was 11–15 days, and by 72.0% (95%CI = 42.6–107.5) when > 15 days. Conversely, no differences were found in readmission risk, and the combined endpoint only increased 21.6% (95%CI = 8.4–36.4) for LOH > 15 days. Stratified analysis by hospitalisation departments rendered similar post-discharge outcomes, with all exhibiting increased mortality for LOH > 15 days and no significant increments in readmission risk.

Conclusions: Short hospitalisations are not associated with worse outcomes. While post-discharge readmissions are not affected by LOH, mortality risk increases as the LOH lengthens. These findings were similar across hospitalisation departments.

1. Introduction

Heart failure (HF) is a world-wide pandemic associated with significant morbidity, mortality, and cost burden [1,2]. For every health care system, the majority of HF costs are related to hospitalisations during acute decompensations and are proportional to the length of hospitalisation (LOH) required [3]. Therefore, many efforts have been directed at shortening the LOH of patients with acute HF (AHF). Moreover, this strategy is potentially beneficial due to a reduction of the hazards associated with hospitalisation itself, which include exposure to nosocomial infection and complications, iatrogenic harm, or

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the development of delirium in the elderly. Shortening hospitalisation could also impact the rates of post-hospital syndrome, which occurs in recently hospitalised patients who are not only recovering from their acute illness, but also experience a transient period of generalised risk for a wide range of adverse health events [4]. In this sense, data on patients with AHF from the VERITAS trials demonstrated that longer LOH was associated with a higher rate of post-discharge mortality [5]. To meet the objective of limiting the LOH to a minimum, some countries (e.g., Spain) have promoted the creation of short-term units, the purpose of which is to provide quick, coordinated management of patients who have no additional challenges other than decompensation of a chronic condition, such as AHF [6,7].

Nonetheless, while it has been proposed that shortening LOH in AHF is the best way to mitigate expenditures and reduce post-discharge adverse outcome risk [8], it is also feasible that it may worsen short-term outcomes. Certainly, residual congestion or unsolved residual organ damage is more likely to be present at hospital discharge in patients with a very short period of in-hospital supervised management and treatment. In addition, while well-defined discharge planning and structured outpatient follow-up improve AHF patient outcomes [9], very short hospitalisations could interfere with the complete implementation of such measures. To date, the impact of LOH on post-discharge outcomes has been poorly explored in the real world scenario. Although randomised clinical trials are the gold standard to unequivocally demonstrate the benefit of new treatment or disease approaches, inpatient hospital registries remain the primary source of real-world data as they include unselected patients representing the full spectrum of HF [10]. Our purpose was to explore the relationship between the LOH and post-discharge outcomes in a large registry of consecutive patients admitted to hospital for AHF. Our hypothesis is that a short duration of hospitalisation does not negatively impact outcomes in AHF. An exploratory stratified analysis by the main hospitalisation departments of AHF patients was also performed.

2. Methods

2.1. Setting

The LOHRCA (Length Of Hospitalisation and its Relationship with outComes in Acute heart failure) study was an exploratory, secondary analysis within the EAHFE (Epidemiology of Acute Heart Failure in Emergency departments) Registry. This registry was initiated in 2007 and every 2–3 years it carries out a 1–2-month recruitment period of all consecutive patients diagnosed with AHF in Spanish EDs participating in the project. To date, 5 recruitment phases (in 2007, 2009, 2011, 2014, and 2016) have been performed with the participation of 41 EDs from community and university hospitals across Spain (representing about 13% of the hospitals belonging to the Spanish public healthcare system), enrolling a total of 13,791 AHF patients. The LOHRCA study used the 12,843 patients recruited in phases 2 to 5 since data on LOH was not recorded in phase 1. Details of patient inclusion have been reported previously [11,12]. Briefly, the principal investigators of each emergency department participating in the EAHFE Registry attend a general meeting held before every recruitment phase in order to homogenize the logistics, protocol definitions, as well as the inclusion and exclusion criteria. All principal investigators are provided with a common dictionary of terms in order to have standard definitions at all centres (available as Supplementary Table 1). The principal investigators then explain protocol instructions to the emergency physicians of their respective centres during a weekly ED meeting preceding patient recruitment. During the recruitment time frame, patient enrolment is done by any attending emergency physician in the participating EDs. These physicians are responsible for the detection of potential cases of patients with AHF. All suspected cases are confirmed by the principal investigator of each centre to ensure the patients meet the diagnostic criteria of AHF based on the Framingham clinical criteria [13]. If possible, the diagnosis is confirmed by measurement of plasma natriuretic peptide and/or echocardiography during ED or hospital stay, following the current recommendations of the ESC guidelines [14], and this is done in about 92% of cases. The principal investigator of each centre is responsible for the final diagnostic adjudication of the cases. The only exclusion criterion of the EAHFE Registry is a concurrent primary diagnosis of ST-elevation myocardial infarction (STEMI), which occurs in about 3% of AHF cases. The EAHFE Registry is only observational, does not include any planned intervention, and the management of patients is entirely based on the attending ED physician decisions.

2.2. Ethics

The EAHFE Registry protocol was approved by a central Ethics Committee at the Hospital Universitario Central de Asturias (Oviedo, Spain) with the reference numbers 49/2010, 69/2011, 166/13, and 160/15. Due to the non-interventional design of the registry, Spanish legislation allows central Ethical Committee approval, accompanied by notification to the local Ethical Committees. All participating patients gave informed consent to be included in the registry and to be contacted for follow-up. The LOHRCA study was carried out in strict compliance with the Declaration of Helsinki principles.

2.3. Design and variables recorded

All patients hospitalised after an ED diagnosis of AHF and discharged alive, in whom data regarding the LOH and mortality were available, were eligible for this study. The LOHRCA study was designed to analyse outcomes in 4 LOH subgroups. Groups were defined from a previous analysis of outcome prevalence versus time (Fig. 1), and consisted of LOH ≤ 5, 6 to 10, 11 to 15, and $>$ 15 days. The LOH was defined as the calendar day that patients presented to the ED until the calendar day that they were discharged from the hospital.

In addition to the LOH (classificatory variable), another 22 independent variables regarding demographic data (2 variables), comorbidities (12 variables), baseline status (3 variables) and chronic treatments for HF (5 variables) were recorded to delineate the chronic underlying risk profiles that could potentially impact on the primary endpoints. With respect to the severity of the AHF episode itself, we estimated the risk of each patient using the previously developed

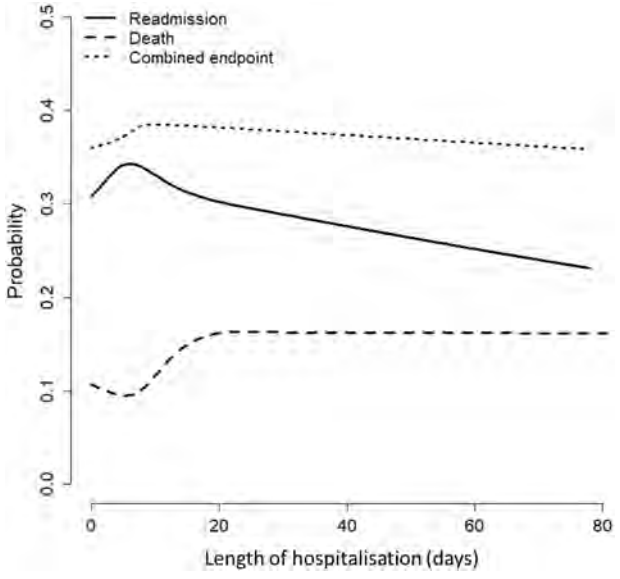

Fig. 1. Probability of adverse outcomes plotted against day by day of length of hospitalisation.

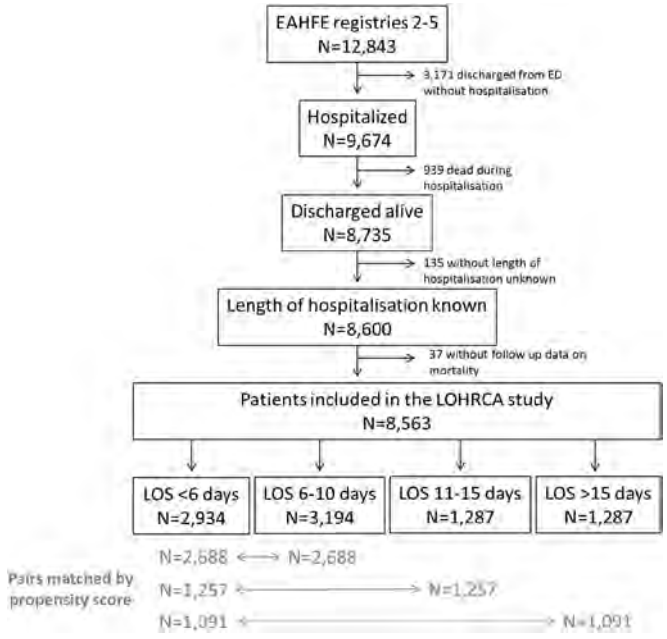

Fig. 2. Flow chart for patient inclusion.
LOS: length of stay.

MEESSI score[11] and EFFECT score [15], which assess the 30-day risk of death in ED AHF and in hospitalised AHF patients, respectively. For both, the higher the score, the higher the risk. The initial department to which the patient was transferred after ED management was considered responsible for hospitalisation because, although the internal transfer rate between different departments is < 10% in Spanish hospitals, we did not record further departments to which a patient was moved when the initial department was not the same as the final department from which the patient was discharged home.

2.4. Outcomes

We recorded three main post-discharge outcomes, defined as starting at the time of discharge from hospitalisation, and included 90-day all-cause death, 90-day readmission due to AHF, and the combined endpoint. The 90-day period was selected because it has been proposed as the vulnerable post-discharge period for patients with AHF [16]. Follow-up was performed by telephone contact and consultation of medical records.

2.5. Statistical analysis

Continuous variables are expressed as mean and standard deviation (SD) or median and interquartile range (IQR) if not normally distributed, and discrete variables as absolute values and percentages. Comparison among groups was carried out using one-way ANOVA for continuous variables and the chi square test for discrete variables. Outcomes among the groups of LOH were compared by means of Cox

Table 1
Overall patient characteristics for the whole series and comparison among the four groups determined by the length of hospitalisation.

	Total *N* = 8563 n (%)	Missing values n (%)	< 6 days *N* = 2934 n (%)	6–10 days *N* = 3184 n (%)	11–15 days *N* = 1287 n (%)	> 15 days *N* = 1158 n (%)	p value
Demographic data							
Age (years) (mean (SD))	80.2 (10.2)	10 (0.1)	80.9 (10)	80.2 (10.2)	80.1 (10.2)	78.7 (10.5)	< 0.001
Female	4742 (55.5)	24 (0.3)	1664 (56.9)	1786 (56.3)	708 (55.1)	584 (50.6)	0.006
Comorbidities							
Hypertension	7215 (84.4)	16 (0.2)	2503 (85.5)	2684 (84.4)	1079 (83.9)	949 (82.2)	0.146
Diabetes mellitus	3665 (42.9)	18 (0.2)	1213 (41.5)	1362 (42.8)	575 (44.7)	515 (44.6)	0.256
Ischaemic heart disease	2467 (28.9)	19 (0.2)	859 (29.3)	894 (28.1)	379 (29.5)	335 (29)	1.396
Heart valve disease	2282 (26.7)	17 (0.2)	789 (26.9)	819 (25.8)	347 (27)	327 (28.3)	0.746
Atrial fibrillation	4235 (49.6)	17 (0.2)	1544 (52.8)	1546 (48.6)	604 (47)	541 (46.9)	< 0.001
Chronic kidney failure (creatinine > 2 mg/mL)	2298 (26.9)	16 (0.2)	719 (24.6)	863 (27.1)	382 (29.7)	334 (28.9)	0.002
Cerebrovascular disease	1155 (13.5)	18 (0.2)	413 (14.1)	384 (12.1)	175 (13.6)	183 (15.9)	0.016
Peripheral artery disease	839 (9.8)	19 (0.2)	281 (9.6)	296 (9.3)	136 (10.6)	126 (10.9)	0.648
Chronic obstructive pulmonary disease	2105 (24.6)	23 (0.3)	681 (23.3)	786 (24.7)	336 (26.1)	302 (26.2)	0.228
Dementia	993 (13)	938 (11)	324 (12.3)	389 (13.7)	161 (13.9)	119 (11.9)	0.488
Active neoplasia	1068 (14)	941 (11)	348 (13.3)	398 (14)	162 (14)	160 (16)	0.424
Prior episodes of acute heart failure	5088 (60.5)	148 (1.7)	1784 (61.8)	1850 (59.2)	763 (60.3)	691 (60.9)	0.44
Baseline status							
Barthel Index (points) (mean (SD))	79.16 (24.56)	969 (11.3)	80.55 (23.54)	78.91 (24.58)	78.01 (26.65)	77.47 (25.72)	0.001
NYHA class III-IV	2029 (25.1)	478 (5.6)	622 (22.3)	747 (24.8)	330 (27.5)	330 (30.5)	< 0.001
Left ventricular ejection fraction (%) (mean (SD))	50.98 (15.16)	3877 (45.3)	51.11 (15.12)	51.27 (14.96)	50.97 (14.96)	49.93 (15.92)	0.278
Chronic treatments at home							
Diuretics (any)	6363 (76)	194 (2.3)	2184 (75.7)	2354 (75.8)	951 (75.7)	874 (77.8)	1.018
Renin-angiotensin system inhibitors	4792 (57.3)	195 (2.3)	1695 (58.7)	1807 (58.2)	695 (55.3)	595 (53)	0.006
Beta-blockers	3416 (40.8)	196 (2.3)	1276 (44.2)	1188 (38.3)	506 (40.3)	446 (39.7)	< 0.001
Mineralocorticoid-receptor antagonists	1428 (17.1)	193 (2.3)	480 (16.6)	511 (16.5)	209 (16.6)	228 (20.3)	0.046
Digoxin	1295 (15.5)	203 (2.4)	460 (16)	487 (15.7)	177 (14.1)	171 (15.2)	0.928
Severity of current heart failure decompensation							
MEESSI score (mean (SD))	−2.69 (1.13)	3526 (41.2)	−2.83 (1.09)	−2.66 (1.14)	−2.58 (1.12)	−2.52 (1.16)	< 0.001
EFFECT score (mean (SD))	115.7 (25.1)	3865 (45.1)	113.7 (24.6)	116.6 (25.2)	117.1 (25.9)	117.6 (24.8)	< 0.001

MEESSI score estimates the 30-day mortality risk and includes 13 parameters: age, Barthel index, NYHA class, decompensation associated with acute coronary syndrome, low output signs and symptoms, systolic blood pressure, respiratory rate, oxygen saturation, potassium, NT-proBNP, troponin, creatinine, and left ventricular hypertrophy in ECG. The higher the score, the higher the risk.
EFFECT score estimates the 30-day mortality risk and includes 10 parameters: age, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, hepatic cirrhosis, cancer, respiratory rate, systolic blood pressure, urea nitrogen and sodium. The higher the score, the higher the risk.

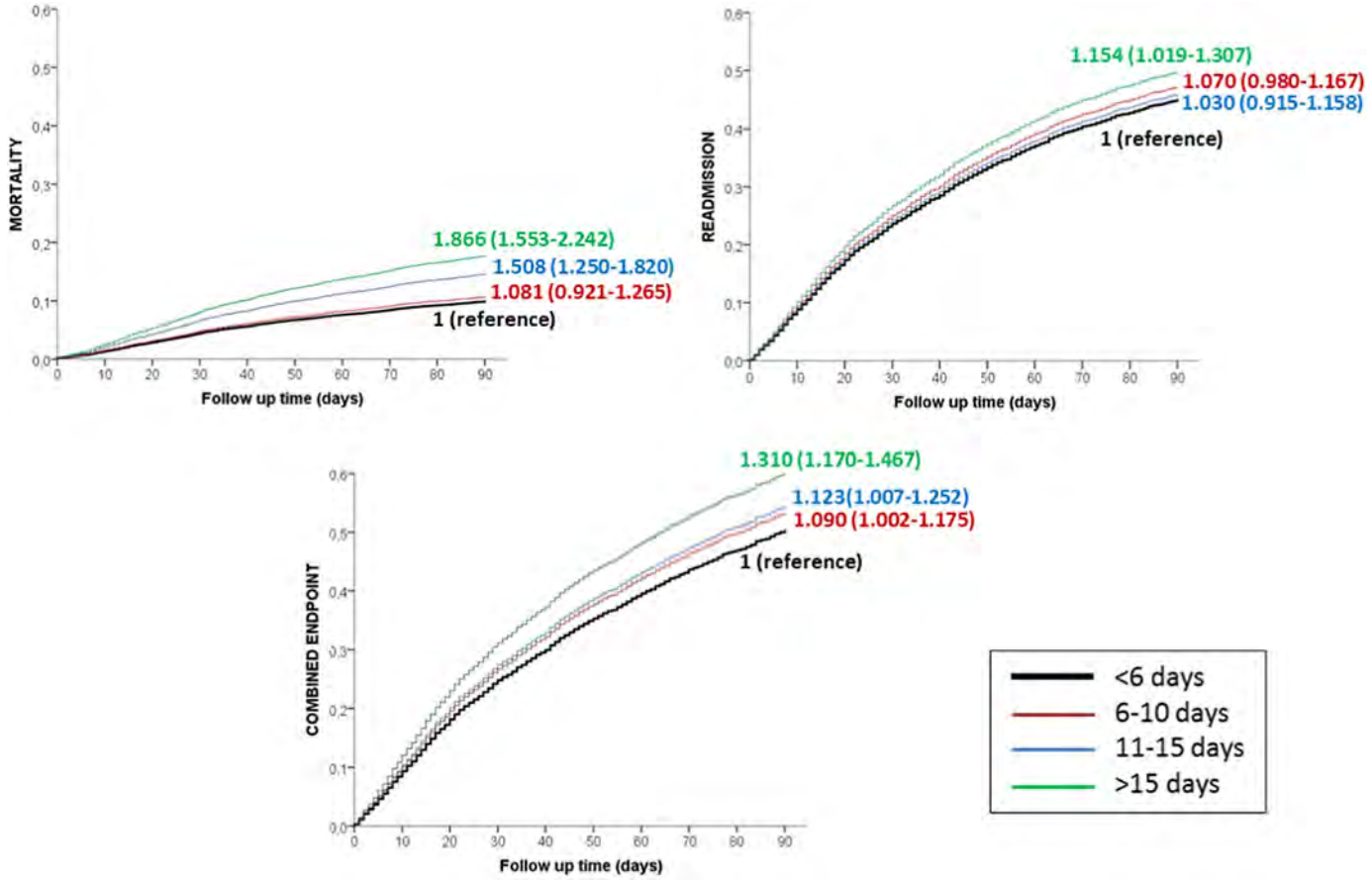

Fig. 3. Unadjusted curves corresponding to proportional hazards of the four length of hospitalisation groups for the three outcomes evaluated in the present study.

regression analysis and expressed as hazard ratios (HRs) with 95% confidence intervals (95% CI) using the shortest LOH stay group (< 6 days) as the reference standard. Curves depicting unadjusted proportional hazards were made. Hazard ratios were adjusted for all independent variables of chronic status with a $p < 0.10$ in the univariate analysis, and by decompensation severity determined by the MEESSI and EFFECT scores. Additional models of adjustment were created by a combination of the above. Missing values were replaced using the multiple imputation technique, generating 5 datasets with no missing values for the variables included in the adjustment. As sensitivity analysis, hospitalisations ≤10 days were analysed in 1-day periods, with LOH of 0–3 days as the reference standard, in order to detect risks in groups in the shortest LOH. We also planned a stratified analysis of the three outcomes for the four main admission wards in patients hospitalised due to AHF: cardiology, internal medicine, geriatrics and short-stay unit. Statistical significance was accepted if the 95% confidence interval (CI) of the excluded the value 1, or the p value was < 0.05. Since this was an exploratory study, a pre-hoc sample size calculation was not made.

3. Results

Of the 12,843 patients included in the EAHFE 2 to 5 registries, 9674 were hospitalised and 8563 were discharged alive and had enough data available to be included in the LOHRCA study (Fig. 2). Overall, the mean age was 80 (SD 10) years, and 55.5% were women. Comorbidities were common, with the most frequent being hypertension (84.4%), atrial fibrillation (49.6%) and diabetes mellitus (42.9%) (Table 1). With respect to baseline status, the mean Barthel index was 79 (SD 25), left ventricular ejection fraction 51% (SD 15), and 25.1% were NYHA class III or IV. A prior episode of AHF was recorded in 60.5% of patients, and 57.3% and 40.8% were receiving chronic treatment with renin-angiotensin system inhibitors and beta-blockers, respectively. Table 1 shows the remaining data regarding baseline and chronic status. With regard to severity of decompensation, the MEESSI and EFFECT scores were − 2.69 (SD 1.13), and 116 (SD 25), respectively (Supplementary Fig. 1).

The median LOH was 7 days (IQR 4–11). The LOH was < 6 days in 2934 patients (34.3%), 6–10 in 3184 (37.2%), 11–15 in 1287 (15.0%), and > 15 in 1158 (13.5%). These groups were different in 10 out of 22 chronic or baseline status variables (Table 1). They also differed in the MEESSI and the EFFECT scores, and the higher the severity of the acute episode (assessed by either score), the longer the LOH (Table 1).

During the 90-day post-discharge period, 975 (11.4%) patients died, 2760 (32.2%) were readmitted, and 3202 (37.4%) achieved the combined endpoint (Fig. 3). With respect to patients with a LOH of < 6 days, unadjusted HRs for mortality showed statistically significant increases of 50.8% and 86.6% if hospitalised 11–15 days and > 15 days, respectively. Unadjusted HRs for 90-day readmission showed a statistically significant increase of 15.4% for patients with LOH > 15 days, and the 90-day combined endpoint showed statistically significant increases of 9.0%, 12.3% and 31.0% for cohorts with LOH of 6–10, 11–15, and > 15 days, respectively (Fig. 3 and Table 2). The models with progressive adjustment showed similar results for 90-day mortality, and statistically significant increases were maintained with the complete adjustment (model 6) for mortality in patients with LOH 11–15 days (36.5% increase vs. LOH < 6 days; 95% CI 13.0% to 64.9%) and > 15 days (72.0% increase vs. LOH < 6 days, 95% CI 42.5% to 107.5%). On the other hand, LOH had a neutral effect on 90-day readmission after complete adjustment (model 6), while patients with LOH > 15 days had significantly higher rates of the combined endpoint (22% increase vs. LOH < 6 days, 95% CI 9% to 37%) (Table 2). The

Table 2
Unadjusted and adjusted hazard ratios (HR) of adverse outcomes per length of hospitalisation group.

	< 6 days	6–10 days	11–15 days	> 15 days
90-day all-cause mortality				
Unadjusted HR	1 (Reference)	1.081 (0.921–1.265) [0.339]	**1.508 (1.250–1.820) [< 0.001]**	**1.866 (1.553–2.242) [< 0.001]**
Adjusted HR (model 1)	1 (Reference)	1.064 (0.906–1.249) [0.447]	**1.441 [1.193–1.740) [< 0.001]**	**1.850 (1.536–2.227) [< 0.001]**
Adjusted HR (model 2)	1 (Reference)	0.996 (0.847–1.171) [0.958]	**1.351 (1.118–1.631) [0.002]**	**1.651 (1.371–1.989) [< 0.001]**
Adjusted HR (model 3)	1 (Reference)	1.049 (0.893–1.232) [0.562]	**1.455 (1.206–1.756) [< 0.001]**	**1.847 (1.537–2.219) [< 0.001]**
Adjusted HR (model 4)	1 (Reference)	0.986 (0.839–1.158) [0.862]	**1.325 (1.097–1.599) [0.003]**	**1.600 (1.329–1.928) [< 0.001]**
Adjusted HR (model 5)	1 (Reference)	1.040 (0.885–1.222) [0.635]	**1.407 (1.164–1.699) [< 0.001]**	**1.797 (1.490–2.167) [< 0.001]**
Adjusted HR (model 6)	1 (Reference)	1.009 (0.859–1.186) [0.911]	**1.365 (1.130–1.649) [0.001]**	**1.720 (1.426–2.075) [< 0.001]**
Adjusted HR (by propensity score matching)	1 (Reference)	0.985 (0.829–1.170) [0.860]	**1.480 (1.174–1.864) [< 0.001]**	**1.830 (1.441–2.324) [< 0.001]**
90-day readmission due to AHF				
Unadjusted HR	1 (Reference)	1.070 (0.980–1.167) [0.131]	1.030 (0.915–1.158) [0.628]	**1.154 (1.019–1.307) [0.024]**
Adjusted HR (model 1)	1 (Reference)	1.057 (0.968–1.154) [0.213]	1.001 (0.889–1.126) [0.992]	1.103 (0.973–1.250) [0.127]
Adjusted HR (model 2)	1 (Reference)	1.052 (0.964–1.148) [0.256]	1.005 (0.893–1.130) [0.939]	1.121 (0.990–1.270) [0.073]
Adjusted HR (model 3)	1 (Reference)	1.063 (0.974–1.160) [0.173]	1.024 (0.910–1.152) [0.696]	**1.148 (1.014–1.300) [0.030]**
Adjusted HR (model 4)	1 (Reference)	1.052 (0.964–1.149) [0.256]	0.993 (0.883–1.118) [0.911]	1.091 (0.962–1.237) [0.175]
Adjusted HR (model 5)	1 (Reference)	1.050 (0.962–1.147) [0.276]	0.993 (0.889–1.126) [0.997]	1.103 (0.974–1.251) [0.123]
Adjusted HR (model 6)	1 (Reference)	1.046 (0.958–1.142) [0.316]	0.987 (0.877–1.111) [0.830]	1.083 (0.955–1.228) [0.215]
Adjusted HR (by propensity score matching)	1 (Reference)	1.019 (0.928–1.119) [0.690]	0.982 (0.856–1.128 [0.799]	1.026 (0.883–1.192) [0.883–1.192]
90-day combined endpoint				
Unadjusted HR	1 (Reference)	**1.090 (1.002–1.175) [0.044]**	**1.123 (1007–1.252) [0.038]**	**1.310 (1.170–1.467) [< 0.001]**
Adjusted HR (model 1)	1 (Reference)	1.075 (0.988–1.169) [0.092]	1.087 (0.974–1.213) [0.136]	**1.248 (1.113–1.400) [< 0.001]**
Adjusted HR (model 2)	1 (Reference)	1.064 (0.978–1.156) [0.148]	1.084 (0.972–1.209) [0.149]	**1.256 (1.120–1.407) [< 0.001]**
Adjusted HR (model 3)	1 (Reference)	1.080 (0.993–1.173) [0.072]	1.115 (0.999–1.173) [0.052]	**1.301 (1.162–1.457) [< 0.001]**
Adjusted HR (model 4)	1 (Reference)	1.062 (0.977–1.155) [0.157]	1.069 (0.958–1.193) [0.235]	**1.222 (1.090–1.369) [0.001]**
Adjusted HR (model 5)	1 (Reference)	1.065 (0.979–1.159) [0.141]	1.077 (0.979–1.202) [0.184]	**1.232 (1.099–1.382) [< 0.001]**
Adjusted HR (model 6)	1 (Reference)	1.058 (0.973–1.151) [0.190]	1.066 (0.955–1.190) [0.256]	**1.216 (1.084–1.364) [0.001]**
Adjusted HR (by propensity score matching)	1 (Reference)	1.031 (0.943–1.127) [0.596]	1.066 (0.936–1.231) [0.335]	**1.174 (1.022–1.347) [0.023]**

AHF: acute heart failure.
Bold numbers denote comparisons with p values < 0.05.
Model 1: adjusted for differences in chronic status (age and sex; atrial fibrillation, chronic kidney disease and cerebrovascular disease as comorbidities; baseline Barthel index and NYHA class; and chronic treatment with renin-angiotensin system inhibitors beta-blockers and mineralcorticosteroid-receptor antagonists).
Model 2: adjusted for the MEESSI score.
Model 3: adjusted for the EFFECT score.
Model 4: adjusted for differences in chronic status and the MEESSI score.
Model 5: adjusted for differences in chronic status and the EFFECT score.
Model 6: adjusted for differences in chronic status, the MEESSI and the EFFECT score.
Propensity score matching comparisons were made between 2688, 1257 and 1091 pairs for the comparison between the reference group (< 6 days) and the 6–10, 11–15 and > 15 days groups, respectively.

detailed daily analysis of LOH during the first 10 days showed no differences in adjusted HRs for mortality, although there were increases in the adjusted HR for readmissions and the composite endpoint in patients with a LOH of 8 and 9 days compared with 0–3 days (Fig. 4).

Stratified analysis was performed according to whether patients had initially been admitted to cardiology (1911 patients, 22.3%), internal medicine (4716, 43.4%), geriatrics (620, 7.2%) or a short stay unit (1408, 16.4%). With few exceptions, similar patterns of HRs were observed in post-discharge outcomes for the four departments (Fig. 5). Increased mortality was observed in patients hospitalised > 15 days, irrespective of the initial admission department, with increments ranging from 66% (internal medicine) to 216% (geriatrics). Conversely, there was no increased readmission risk, and only a significant increment in risk of combined endpoint was observed in patients initially hospitalised in cardiology or short-stay units for > 15 days (29% and 98%, respectively).

4. Discussion

The results of the LOHRCA study were obtained from a consecutive cohort with prospective collection of clinical data of patients hospitalised for AHF in 41 Spanish hospitals and provide three main findings. First, short hospitalisations were not associated with an increased risk of adverse post-discharge outcomes during the subsequent 90 days, while the risk of presenting an adverse event increased in patients hospitalised for > 15 days. Second, while mortality increased with a longer LOH, readmission did not. And third, the department where the patient had initially been hospitalised did not seem to influence the previous two findings.

Our results suggest that short hospitalisations are a safe and even a recommendable option for patients with AHF, since after adjusting for potential differences in baseline and chronic status as well as for the severity of decompensation, neither mortality nor readmission increased when the LOH was 10 or less days. After this time point, we found that mortality progressively increased with a lengthening in the LOH, with a 73% increase in patients in whom the LOH surpassed 15 days compared to those not surpassing 5 days. This finding is in line with recent data from a Polish study of 765 patients discharged from 32 cardiology wards. In this study, mortality increased 120% during an average 414-day follow-up in patients with an index hospitalisation exceeding 21 days compared to patients hospitalised < 7 days [17]. Similarly, Sud et al. reported a 28% increase in 30-day all-cause mortality in 58,230 AHF patients admitted to any hospital ward (not only cardiology) in Ontario, Canada for 9 days or more compared with those with a LOH of 5–6 days [18]. Therefore, our data confirm and expand the direct relationship between LOH and the risk of death reported in such studies. As we prospectively recorded clinical data (in contrast with previous studies that were based on administrative data

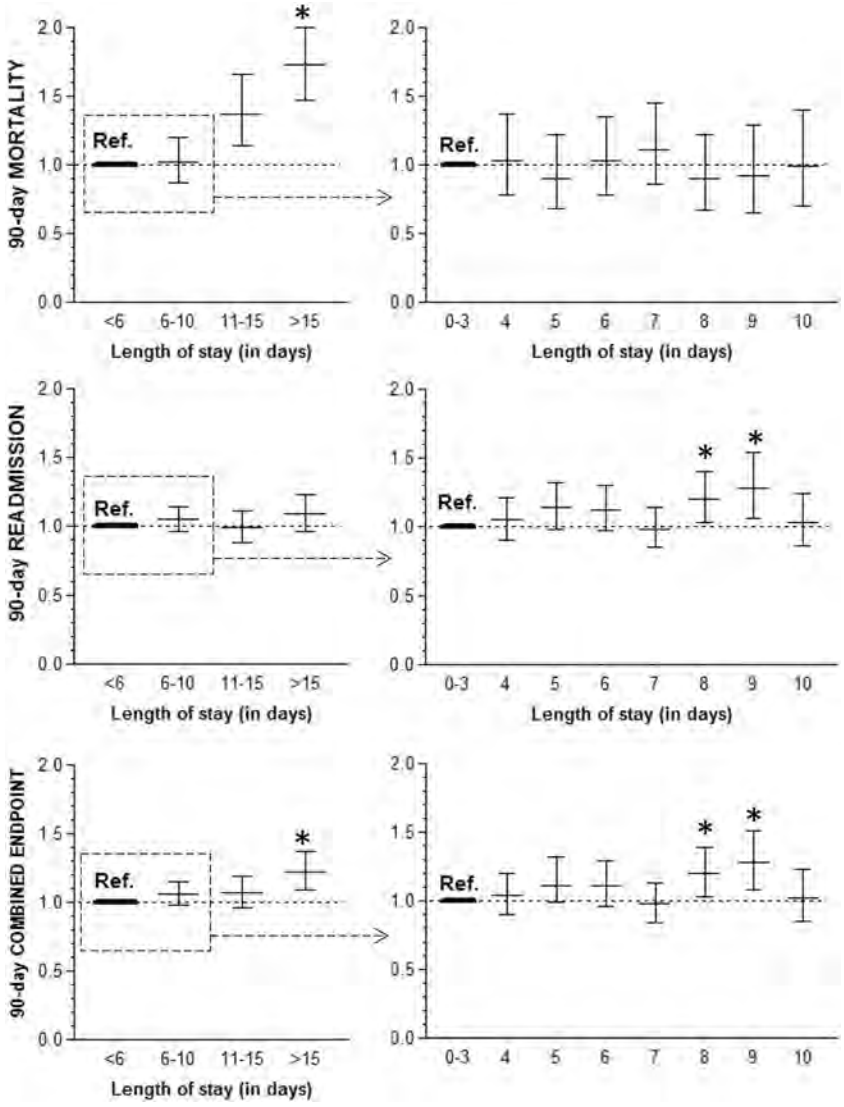

Fig. 4. Comparative hazard ratios for the fully adjusted model (adjusted for differences in baseline and chronic status, the MEESSI score and the EFFECT score) for the three outcomes evaluated in the study: 90-day mortality (up), readmission (middle) and combined endpoint (down). Analysis is presented for the four predefined length of hospitalisation groups (left) and detailed day by day for the first 10 days (right).
Asterisks indicate $p < 0.05$ respect to reference group (Ref.)

collection), we were able to include the severity of decompensation in the adjustment of our estimations. However, although our results were very consistent in all the adjusted models we developed, an increase in mortality with a lengthening of LOH may just signal a more vulnerable population requiring longer hospitalisation and at higher risk of post-discharge death rather than demonstrating a direct influence of LOH in the risk of death.

Conversely, we did not detect an increase in 90-day readmission rates related to LOH. This finding is in contrast with previous studies assessing the relationship between LOH and post-discharge readmission [18–21]. While two American studies have demonstrated that only longer hospitalisations are related to all-cause and HF-related readmissions [19,20], the Canadian Sud et al. study reported the same finding for all-cause readmission but with a U-shape relationship for HF-related readmission, with patients with both the the shortest and longest LOH being at increased risk [18]. By contrast, analysis of the 6827 patients from 27 countries included in the ASCEND-HF trial showed that a longer LOH was associated with a lower risk in readmission [21]. Therefore, our findings are remarkably different from those obtained in these previous studies, as we failed to detect any relationship between LOH and the risk of post-discharge readmission. Hypothetically, the fact that we accounted for the severity of the episode could have contributed to this absence of relationship. Remarkably, only HF-related readmission was taken into account in the LOHRCA study. Nonetheless, from all the information currently available, it seems evident that while the relationship between LOH and post-discharge mortality is clear and direct, the existence and the way of the relationship with post-discharge readmission risk is still unclear and needs further studies.

It is of note that we found a relatively uniform increase in mortality in long hospitalisations across the most frequent departments and specialties involved in in-hospital AHF care. While our results are unique in that this approach to investigate the effect on post-discharge outcomes in individual departments has not previously been performed by other authors, they are contrary to many findings suggesting that the management of AHF by cardiologists may have better outcomes [22–24]. It should be noted that the results of the LOHRCA study cannot be interpreted as a result of differences in the performance of these specialities managing AHF patients during admission, but rather refer to outcomes obtained during the vulnerable phase following patient discharge. As previously commented, one possible explanation is that an increased LOH is just a marker of patients with the highest risk,

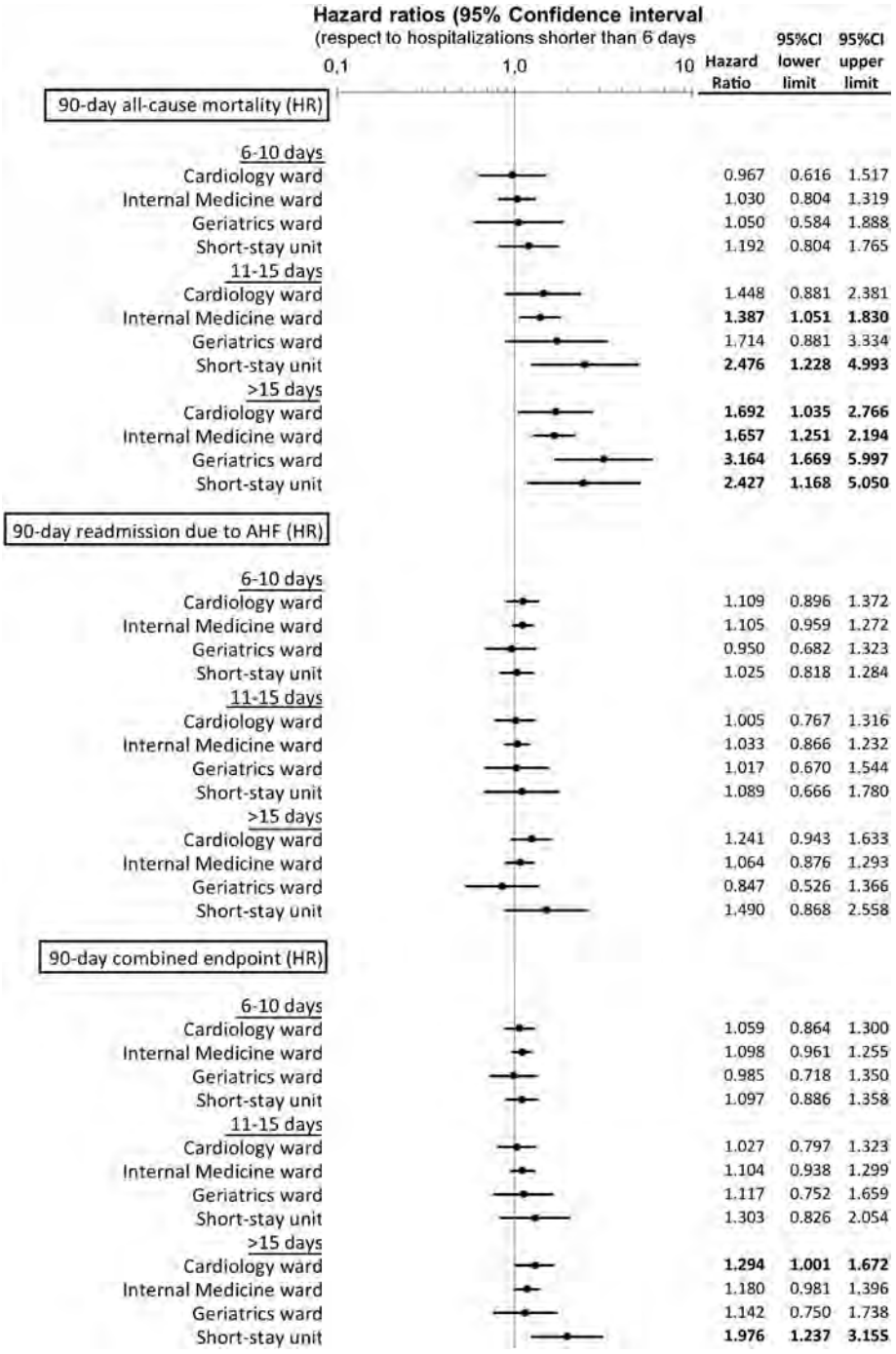

Fig. 5. Stratified analysis of the effect of length of hospitalisation on 90-day outcomes according to the department of hospitalisation (fully adjusted model). Bold numbers in the right columns denote p value < 0.05.

and does not directly cause the increase in mortality observed. We have tried to limit this possibility by making multiple adjustments, thereby minimizing the potential effect of the different chronic or acute patient profiles, although unknown confounders may persist. It is well known that for patients experiencing an episode of AHF, the average survival is 2 years, and the most vulnerable period is the 3-month window immediately after discharge [16,25]. Reducing persistent subclinical congestion, increasing the use of disease-modifying heart failure therapies, and ensuring optimal transitions of care after hospital discharge have been described as essential steps in improving outcomes for AHF patients [24]. Nonetheless, our findings suggest that increases in LOH do not achieve greater or better implementation of these key steps.

Again, a similar pattern of readmission was found for the four departments, with no increase of readmission risk associated with a longer LOH. Only the combined endpoint occurred more often in patients initially managed in the cardiology department or in the short-stay units and who had a LOH > 15 days. One limitation which might explain this finding is that we do not know how frequent discharge plans were implemented by each department. A recent meta-analysis of 41 randomised trials testing transitional care interventions demonstrated that implementation of transitional plans at AHF patient discharge achieves a significant reduction of 8% and 29% in the risk of rehospitalisation and ED visits, respectively [26]. As shown by our results on mortality, it

is clear that a longer LOH with a greater opportunity for intervention was not successful in changing outcomes. Albeit not statistically significant, our finding of a higher increment of readmission (49%) in patients hospitalised longer than 15 days and who were initially admitted to short-stay units (on top of the 143% of increase in mortality) probably contributed to the significant increment (98%) in the combined endpoint in the same group of patients. Many authors have underlined the importance of candidate selection to define which patients should be admitted to short-stay units, as failure to do this usually leads to prolonged hospitalisations [7,8,27,28].

Our study has some limitations. First, this is a secondary analysis limited to hypothesis generation that requires confirmation in future trials. Second, since there was no sample size calculation due to the exploratory nature of the study, a type-II error cannot be excluded in some of the estimations made, especially in the stratified analysis by departments (due to the small number of events in certain outcomes and/or departments). Third, in this real-life cohort without intervention, attending physicians followed their usual local protocols and did not receive any specific instructions about the precise time for hospital discharge and patient transition. Fourth, the patients were from a single country with a universal public health care system, and since international heterogeneity in organisational and transition processes is high [29], external validation of our results should be carried out in further studies in other countries with different healthcare system models. And fifth, we recorded the department which was responsible for admission once emergency department care was completed, but we did not track further patient transfers from the initial department to others. Therefore, post-discharge outcomes cannot entirely be attributed to the management of the department to which patients were initially admitted. An example of this limitation is the short-stay units where, despite most of the participating hospitals having a LOH limited to 96 h, some patients initially admitted to these units had a LOH of > 10 (and even 15) days, probably because they were moved to other departments for reasons we do not know.

Despite these limitations, we can conclude that short hospitalisations in AHF patients are not associated with poorer outcomes, and that for the particular case of all-cause mortality, patients hospitalised longer than 10 days could be at increased risk. No large differences in outcomes were observed among the main departments responsible for the initial hospitalisation.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejim.2019.08.007.

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The authors have nothing to disclose in relationship with this manuscript.

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