Departments involved during the first episode of acute heart failure and analysis of emergency department revisits and rehospitalisations: an outlook through the NOVICA cohort

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ABSTRACT (301 words)

Objectives: We investigated the natural history of patients after a first episode of acute heart failure (AHF), focused on: 1) frequency of emergency department (ED) visits and hospitalizations; 2) departments admitting patients during first and subsequent hospitalizations; and 3) factors associated with difficult disease control after being discharged after *de novo* AHF (DNAHF) episode.

Methods: We included consecutive patients with DNAHF diagnosed in 4 ED located in Barcelona (Spain) at three time-points (2009, 2011, 2014). We recorded clinical characteristics at index event, all post-discharge ED visits and hospitalizations (related and unrelated to AHF) until patient death or censure, and departments in charge of patients' hospitalization (during index event and subsequently). We defined patients as having "Uncontrolled disease" during the first year after index event discharge if they were attended at ED (≥ 3 times) or hospitalized (≥ 2 times) for AHF or died.

Results: We included 505 unique DNAHF patients followed up for 1,203 patient/year. In-hospital mortality during the index episode was 7.5%. Among patients 467 discharged alive, 288 died (median survival time 3.9 years, 95%CI, 3.5-4.4), 2,342 ED visits (42.4% requiring hospitalization; 34.0% AHF-related) and 1,054 unplanned hospitalizations (94.1% through ED; 51.4% AHF-related) took place. Main departments involved in AHF-related hospitalizations were internal medicine (28.0%), short-stay unit (26.3%), cardiology (20.8%), geriatrics (14.1%) and intensive care units (2.8%). Only 47.4% of HF-related rehospitalizations were at the same department as the DNAHF index hospitalization, and internal medicine involvement had a significant increment as subsequent admissions occur ($p=0.01$). Uncontrolled disease was observed in 31.0% of patients, and was related to age >80 (adjusted OR 1.80; 1.17-2.77) and ischemic cardiomyopathy as comorbidity (1.61, 1.03-2.53).

Conclusion: The natural history after DNAHF is by the very first time presented and shows different patterns of hospital department involvement and factors related to uncontrolled disease during the year after debuting.

INTRODUCTION

Heart failure (HF) constitutes the common final syndrome for several specific cardiac diseases. Its natural history is characterized by multiple acute decompensations and progressive decline in heart function finally causing patient death. In many cases, HF remains undiagnosed until the development of a first episode of decompensation uncovers it. In fact, episodes of acute heart failure (AHF) are critical steps in the natural history of HF, as they associate a high in-hospital mortality (between 5-10% depending on the series) and shortly after patient discharge (with up to 20% of mortality following the following 90 days)²⁻⁴. In fact, a generic post-hospital syndrome has been recently defined to underline that patients who have recently been hospitalized are not only recovering from their acute illness, but they also experience a transient period of generalized risk for a wide range of adverse health events⁵. In the specific case of AHF, causes of rehospitalisation within 30 days are only related to HF in 35-37% of cases^{6,7}.

However, there is a lack of studies analysing the natural history of patients after being diagnosed with a first episode of AHF. Some reasons have made difficult to have reliable data from the previous registries. First, most registries include AHF patients in a different evolutionary state of disease, mixing patients with a first episode with patients with advanced disease and multiple previous decompensations^{2-4,8}. This associates a high patient heterogeneity that could bias interpretations, especially when analysing outcomes, even after further statistical adjustments, and this mixture of AHF patients has been proposed as a relevant confounding factor in clinical trials⁹. Second, although specific comparisons have been performed between *de novo* and acutely-decompensated HF¹⁰⁻¹³, and even registries exclusively including patients with a *de novo* AHF episode exist¹⁴, they only include hospitalized patients, sometimes just coming from a single hospital department. This imposes the bias of hospitalization, and disregard the subset of AHF patients that are seen at the emergency department (ED, the place where the majority of them are seen first) and are directly discharged home without hospitalization (between one sixth and one third, depending on the countries)¹⁵. And third, there are no registries with a long-lasting patient follow-up period, as all the previously published series including *de novo* AHF patients consisted on cross-sectional descriptive analysis of patients' characteristics and outcomes exclusively corresponding to such a first AHF episode. Information of the subsequent AHF episodes is also important because, although involvement of the same hospital department in every patient hospitalization could be advisable, a patient transfer among specialities sometimes occurs. This is due because of, as in other long-lasting syndromes, the approach to a HF patient is multidisciplinary by definition and some health care providers and medical specialities participate in patient management^{16,17}. Therefore, only a longitudinal approach can provide a real outlook in the natural history of HF and uncover the real interrelations between specialties taking care of AHF patient management.

All these considerations described above prompted us to launch the present study. The main objective was to evaluate, in a homogenous cohort of patients with a prolonged follow-up period, the natural history of HF patients after debuting with a first AHF episode, with special focus on: 1) the frequency of ED visits and hospitalizations, related and unrelated with AHF; 2) the main departments responsible of patient admissions

during the first and subsequent hospitalizations due to AHF; and 3) the factors associated with a difficult control of patients (i.e., early need for ED revisits or rehospitalizations or death) once they have been discharged after *de novo* AHF episode.

METHODS

Setting

The NOVICA-3 (apocope from the Spanish words “*De novo Insuficiencia Cardíaca Aguda*”; in English: *de novo* AHF) study was designed as an exploratory, secondary analysis within the EAHFE Registry. The EAHFE Registry was initiated in 2007 and every 2-3 years carries out a 1-2-month recruitment period of all consecutive patients diagnosed with AHF in Spanish EDs participating in the project. To date, 6 recruitment phases (2007, 2009, 2011, 2014, 2016 and 2018) have been performed with the participation of 45 EDs from community and university hospitals across Spain (representing about 15% of the Spanish public health care system hospitals), enrolling a total of 18,370 AHF patients. Details of patient inclusion have been reported previously^{3,18,19}. Briefly, patient enrolment is done by any attending emergency physician in the participating EDs, who receives specific study protocol instructions during a weekly ED meeting preceding patient recruitment. These physicians are responsible for the detection of potential cases of 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 criteria²⁰. If possible, the diagnosis is also confirmed by measurement of plasma natriuretic peptide and/or echocardiography during ED or hospital stay following the current ESC guideline recommendations (which occurs in about 92% of cases)²¹. The principal investigator of each centre is responsible for the final diagnostic adjudication of the cases. The only exclusion criterion for being included into the EAHFE Registry is a primary diagnosis of ST-elevation myocardial infarction (STEMI) while concurrently developing AHF (which occurs in about 3% of AHF cases), as the majority of these patients bypass the ED and go directly to the catheterization laboratory. The EAHFE Registry does not include any planned intervention, and the management of patients is entirely based on the attending ED physician decisions. However, all of these physicians are aware of the ESC guidelines, which are the main reference for all emergency physician actions.

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, 160/15 and 205/17. 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 NOVICA-3 study was carried out in strict compliance with the Declaration of Helsinki principles. The authors designed the study, gathered, and analysed the data, vouched for the data and analysis, wrote the paper, and decided to publish.

Design and variables recorded

We selected four tertiary university hospitals providing patients to the EAHFE registry that serve adjacent health care areas of Barcelona (Catalonia, Spain): Hospital Universitari de Bellvitge, Hospital Clínic, Hospital de la Santa Creu i Sant Pau, and Hospital del Mar. The assigned population for health coverage for these four

hospitals is 2,2 million people out of the 3.1 million people conforming the first Barcelona's metropolitan crown. With this strategy, we wanted to obtain a homogeneous population coming from a continuous geographical territory served by neighbouring hospitals, as patients from urban zones with more than one hospital sometimes ask for urgent care to different hospitals. In addition, all four hospitals share the same electronic system for medical record repository (HC3, *Història Clínica Compartida de Catalunya*), which is supported by the public health provider (Catalonian Department of Health) and it can be accessed online by medical professionals involved in the patient care.

The NOVICA-3 study was designed to explore the natural history of AHF patients who had presented to ED of one of the four hospitals involved in the study complaining with the first episode of decompensation (*de novo* AHF). The NOVICA-3 study was specially focused on the episodes of ED revisits and hospitalizations following such first episode. With this purpose, the NOVICA-3 study included patients with a *de novo* AHF episode recruited in the EAHFE Registry phases 2 (2009), 3 (2011) and 4 (2014), for whom the expected follow up length at the time of the study initiation (June 2016) was longer than 1 year. Phase 1 patients (2007) were discarded because of some key variables were not recorded at that moment, phase 5 patients (2016) because of they did not have enough time on follow up at the time of study initiation, and phase 6 patients (2018) because of they had not been included in the registry yet. In all cases, patients were followed up from the index event (*de novo* AHF diagnosis at ED) until death or the end of follow up, which was fixed at the time of the patient's medical records review. Such medical reviews were performed between June 2016 to September 2017, and consisted in individual revision of all the medical records of every patient in any of the four participating hospitals and also at any hospital of Catalonia (Spain), as the HC3 gets access to all the medical records produced at any of the 58 Catalanian public hospitals.

Twenty-six independent variables were recorded, including demographic data (2 variables), comorbidities (13 variables), baseline status (3 variables), triggers of the AHF episode (6 variables) and severity of the AHF index episode (2 variables) (see [Supplemental Table 1](#) for definitions). Regarding the two variables assessing the severity of *de novo* AHF episode, they consisted in: 1) the calculation of the MEESI risk score for every patient, as this risk score has recently been reported to accurately estimate the risk of death during the following 30 days in patients diagnosed with AHF in the ED^{18,22,23}, and 2) the consignment of the need of hospitalization during the index episode.

Outcomes

For every patient, we recorded the following outcomes: 1) every ED revisit, and if the revisit was or was not related to an AHF episode; 2) every patient hospitalization (irrespective whether it was elective or urgent), and if the hospitalization was or was not related to an AHF episode, and the department where hospitalization took place; and 3) the vital status of the patient at the end of the study (live or dead). Death and the number of ED visits and hospitalizations due to AHF episodes were used to detect patients with difficult control of signs and symptoms of HF. In this sense, we defined "Uncontrolled disease" as patients that need to consult an ED due to AHF at least 3 times (irrespective if patients was finally hospitalized or was

not), to hospitalize at least 2 times due to AHF (irrespective it was through ED or was not) or died in the year after *de novo* AHF index discharge. Accordingly, patients that died during the index episode (in-hospital mortality) were excluded for this specific analysis. Follow-up was performed through telephone contact during the first year and thereafter by consultation of both, the in-site hospital electronic records and the online HC3 regional electronic system. Adjudication of events was made at an at-site level by two investigators and, in cases with discrepancy, the principal investigator discussed the case until final agreement was achieved.

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 or the Mann-Whitney non-parametric test for continuous variables and the chi square test (for trend, when needed) for discrete variables. Survival tables were obtained and Kaplan-Meier curves were plotted for the first post-discharge ED visit or hospitalization (overall and related to AHF) and for all-cause death. The risk of having uncontrolled disease the year after index event discharge was expressed by odds ratio (OR) calculated by logistic regression, first unadjusted and then adjusted with a multivariate model that included all the variables that showed a significant association in the univariate analysis. Missing values were replaced using the multiple imputation technique, generating 5 datasets with no missing values for the variables included in the final adjusted model. Further adjustment at centre level was also included. Due to the exploratory nature of our investigation, a *pre-hoc* sample size calculation was not made. Statistical significance was accepted if the 95% confidence interval (CI) of the HR excluded the value 1, or the p value was less than 0.05.

RESULTS

The NOVICA-3 study finally included 505 patients in the analysis (**Figure 1**). The mean age was 80 (SD=10) years, and 51.8% were women. The most frequent comorbidities were hypertension (81%), dyslipidaemia (46%), diabetes (38%) and atrial fibrillation (36%). The rest of clinical characteristics are presented in the **Table 1**. Precipitants of the index episode were recognised in 70% of cases, and the most frequent was infection, detected in 26% of cases. With respect to the severity of the acute episode, 59% were classified by the MEESSI scale as low risk, 25% as intermediate risk, 11% as high risk and 5% as very high risk. Overall, 64% of patients were hospitalized during the index episode, and the main departments where hospitalization took place during the first AHF episode were: short stay unit (30%), cardiology (22%), internal medicine (20%) and geriatrics (10%). Only 3% of cases required intensive care admission (**Figure 1**).

The follow up for the whole cohort of 505 patients extended 1,203 patient/year (2.4 years/patient), and the median and mean survival times were 3.78 (3.28-4.27) years and 3.87 (3.56-4.17) years, respectively. Thirty-eight patients died during the index episode (in-hospital mortality 7.5%), and we could follow up 466 out of the 467 remaining patients that were discharged alive (283 after hospitalization and 183 directly discharged from the ED), with a mean follow up time of 2.6 years/patient. During the follow up of these patients, 223 deaths happened, and the median survival time was 3.93 (3.47-4.39) years (**Figures 1 and 2**).

After the index event, we registered 2,342 ED visits (34% related to AHF episodes), with a median time for the first ED post-discharge visit of 80 (55-102) days [434 (314-555) days for the first AHF-related ED visit]. A 42% of these ED revisits needed patient hospitalization, and this was more frequent in AHF-related than in AHF-unrelated ED visits (66% vs. 30%; $p<0.001$). On the other hand, we registered 1,054 hospitalizations (51% related to AHF), and 992 (93.6%) accounted after ED consultation. With respect to 542 post-discharge AHF-related hospitalizations, 528 (97.4%) occurred after an ED visit (the resting 2.6% of patients were directly hospitalized proceeding from walk-in centres, and were not evaluated at the ED before admission to hospital wards). The median time for the first hospitalisation after being discharged from the AHF index episode was 285 (226-347) days [850 (569-1131) days for the first AHF-related hospitalization] (**Figures 1 and 2**).

There were 283 patients hospitalized during the index episode and discharged alive. For them, departments involved in further hospitalizations due to new AHF episodes did not change significantly, with the exception of internal medicine department, which increased the proportion of admitted patients as the number of hospitalization increased ($p=0.01$, **Figure 3**). When we specifically analysed the 263 patients initially managed in one of the four main departments responsible of the first AHF admission (short-stay unit, cardiology, internal medicine and geriatrics), we found that 47.4% of rehospitalizations took place at the same department where patient was hospitalized during the index event, with no statistically significant differences among them (**Figure 4, top**). Similarly, there were no statistically significant changes in the percentage of hospitalizations carried out by the department responsible of the index admission as the number of hospitalizations progressively increased (**Figure 4, down**).

A total of 462 out of the 466 patients discharged alive after the index AHF event could be classified according to definition of controlled/uncontrolled disease proposed by us (in the 4 remaining cases the patient was alive but with a follow-up of less than 1 year): 319 were classified as having a controlled disease (69%) and 143 (31%) as uncontrolled disease. Six factors were associated with uncontrolled disease in the unadjusted analysis, but only two remained significant after adjustment: age >80 (OR 1.80; 1.17-2.77) and ischemic cardiomyopathy as comorbidity (1.61, 1.03-2.53) ([Table 2](#)). Further adjustment by hospital level retrieved nearly identical results ([Table 2](#)).

DISCUSSION

The NOVICA-3 study is the first longitudinal analysis with a long-lasting follow-up of a cohort of unselected patients after debuting with a first episode of AHF, and three main findings have to be highlighted. First, patients discharged alive after *de novo* AHF has a median survival time of 3.9 years, with median times for first AHF-related ED visit and AHF-related hospitalization of 434 and 850 days, respectively. Second, departments involved in patient hospitalizations during *de novo* AHF episode are diverse, and similar proportion of patients are managed by the three most frequently involved ones (short-stay unit, cardiology and internal medicine, which take care of between 20% and 30% of admissions each one). Significant increase in hospitalizations in the internal medicine department was noted along the natural history of HF. Nonetheless, less than 50% of rehospitalizations took place at the same department where patients were first hospitalized during the index event. And third, close to one third of patients had a difficult management of HF during the year following the first *de novo* AHF episode, which was more frequently seen for patients at advanced age and with a previous history of ischaemic cardiomyopathy.

The first hospitalization due to AHF represents an inflection point in the natural history whereby subsequent all-cause mortality risk following discharge has been reported to be 3-fold higher than in patients with HF that have never been hospitalized²⁴. In a community study, Dunlay *et al.* reported that 67% of HF experienced 2 or more hospitalizations (and 43%, 4 or more) during a median follow up period of 4.7 years²⁵. In fact, hospitalizations represent 77% of the lifetime medical costs in patients with HF²⁶. In our series, the mean of hospitalizations per patient was 3.1 during a mean follow up of 2.4 years, which is close the previous reported figures. On the other hand, the median time for post-discharge all-cause mortality was 3.9 years, and 5-year mortality was 61.0%. Our findings are also close to previous long term estimations in other series of *de novo* AHF, that ranged from 47.4%²⁷ to ...,²⁸ although these data come from hospitalized patients. It has to be underlined that survival time since HF diagnosis should be somehow longer than we are reporting, as part of patients debuting with AHF could have been diagnosed with HF previously, and this data was not recorded in the present study.

Departments involved in AHF hospitalizations were diverse in our study. It is remarkably that proportion of hospitalization during the index and subsequent decompensations was maintained quite stable, with the only exception of internal medicine that progressively took care of a higher proportion of patients as the number of hospitalizations progressively increased. Probably, our aged population, with a high number of comorbidities, significant degree of physical dependence being present in 42% of patients and more than a half of patients having preserved left ventricular ejection fraction influenced the increasing role of internal medicine as HF evolves and patient requires repeated hospitalizations. It is also noticeable than less than half of patients are rehospitalized at the same department where patient was managed during the index episode. We did not investigate the causes of that, as we did not assess if that was associated with a proper hand-over among specialists or what circumstances influenced in this exchange. The effect of being controlled by the same team along all the disease natural history on outcomes has not specifically explored previously. It is well

accepted that transition of patients after decompensation plays a central role in obtaining the best results. A very 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, respectively²⁹. In addition, another recent meta-analysis described the benefits of heart failure clinics in reducing hospitalisation for AHF and all-cause mortality, which was greater among patients with recent ED visit or hospitalisation due to decompensation³⁰. We believe that investigation of the effects of long-time management by the same medical team on outcomes of patients with HF remains to be investigated.

Uncontrolled disease was seen in about one third of patients. We define uncontrolled disease by the presence of repeated ED visits (≥ 3) or hospitalization (≥ 2) due to AHF or death during the year following discharge after the de novo AHF episode. A very recent paper, Go YY et al., using proper methodology to isolated the effects of hospitalizations apart of the influence of death (an important confounder in readmission analysis), established the definition of frequent admitters for those patients with AHF having ≥ 2 AHF-related hospitalizations/year³¹, and demonstrated that this subset of patients had longer length of stay, higher economic costs and higher all-cause mortality during a 3-year follow up period. In fact, Solomon et al. have demonstrated that the risk of death increases with each additional HF hospitalization, with a nearly 30% cumulative incremental risk associated with discharge from a second or third HF, and additionally, they also found that risk of mortality is clearly higher during the first 12 months after hospital discharge for such first AHF episode²⁴. They, however, did not explore related factors with this profile more prone to have decompensations and adverse outcomes. We have seen that patients with advanced age and ischaemic cardiomyopathy as comorbidity are at increased risk of having uncontrolled disease after debuting with AHF. Hypothetically, other factors could be associated with lack of proper disease control, although the exploratory nature of present study precludes obtaining a more solid result. Interestingly, the lack of hospitalization during the index AHF event, a fact that accounted in 36% of our patients, did not predispose to uncontrolled disease. In fact, as commented previously, if an actionable plan for transition and a proper follow-up track exist, good results can be achieved in less severe decompensated patients managed in ambulatory care^{29,30}.

The NOVICA-3 has a number of limitations. First, this real life cohort without intervention, and attending physicians followed their usual local protocols and did not receive any specific instructions about the precise time for ED or hospital discharge and patient transition. Second, the diagnosis of AHF was based on clinical criteria, and in some cases the final diagnosis of AHF was not supported in all cases by natriuretic peptide or echocardiographic results. Although these two limitations could impose caution in interpretation of some of our conclusions, they otherwise make our findings more generalizable to the real world practice. Third, although the patients were from a single city with a universal public healthcare system and participating hospitals were located one next to other, national and international heterogeneity in organizational and

transition processes is high³²; therefore, our results should be confirmed in other cities and, specially, in other countries with different healthcare system models. Fourth, this is an observational study and causal relationships cannot be inferred. This specially applies to the investigation of factors related to uncontrolled disease. Our results relating age and ischaemic cardiomyopathy with uncontrolled disease have to be confirmed by studies specifically designed to identify such relationships. And fifth, 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. For example, the trend for decreasing participation of short-stay units as subsequent AHF hospitalizations are needed, or the non-significant increase in risk of uncontrolled disease related to chronic kidney failure (+60%), NYHA class III-IV at baseline (+76%) or increased risk MEESSI category during acute decompensation (+60%), could really exist and become statistically significant if a large number of patients would have been included.

As conclusion, the natural history after *de novo* AHF is by the very first time presented and shows different patterns of hospital department involvement, with increasing participation of internal medicine department in hospitalizations. In addition, factors like advanced age and ischaemic cardiomyopathy seems to be related to lack of proper disease control during the year after debuting.

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Table 1: Characteristics of the 505 patients included in the NOVICA cohort.

	Total N=505 n (%)	Missing values n (%)
Demographic data		
Age (grouped)		0 (0)
-Age <60 years	26 (5.1)	
-Age 60-80 years	185 (38.6)	
-Age > 80 years	284 (56.2)	
Female	261 (51.8)	1 (0.2)
Comorbidities		
Hypertension	407 (80.6)	0 (0)
Diabetes mellitus	193 (38.2)	0 (0)
Dyslipidaemia	234 (46.3)	0 (0)
Ischaemic heart disease	136 (26.9)	0 (0)
Chronic kidney failure (creatinine >2 mg/mL)	115 (22.8)	0 (0)
Cerebrovascular disease	72 (14.3)	0 (0)
Atrial fibrillation	180 (35.6)	0 (0)
Peripheral artery disease	52 (10.3)	0 (0)
Heart valve disease	111 (22.0)	0 (0)
Chronic obstructive pulmonary disease	99 (19.6)	0 (0)
Dementia	46 (10.2)	54 (10.7)
Active neoplasia	79 (17.5)	54 (10.7)
Hepatic cirrhosis	9 (2.0)	54 (10.7)
Baseline status		
Barthel Index (points)		76 (15.0)
-No or minimal dependence (Barthel index >90 points)	250 (58.3)	
-Mild to moderate dependence (Barthel index 90-50 points)	150 (35.0)	
-Severe or total dependence (Barthel index <50 points)	29 (6.8)	
NYHA class		41 (8.1)
-I	176 (37.9)	
-II	240 (51.7)	
-III	45 (9.3)	
-IV	3 (0.6)	
Left ventricular ejection fraction (LVEF, %)		178 (35.2)
-LVEF <40%	61 (18.7)	
-LVEF 40-49%	40 (12.2)	
-LVEF ≥50%	226 (69.1)	
Triggering factor for the current AHF episode		
Infection	112 (25.7)	69 (13.7)
Rapid atrial fibrillation	81 (16.8)	69 (13.7)
Anaemia	26 (6.0)	69 (13.7)
Hypertensive emergency	37 (8.5)	69 (13.7)
Dietetic or therapeutic transgression	16 (3.7)	69 (13.7)
Acute coronary syndrome	15 (3.0)	12 (2.4)
Severity of the AHF episode		
MESSI risk category		148 (29.3)
-Low risk	211 (59.1)	
-Intermediate risk	89 (24.9)	
-High risk	38 (10.6)	
-Very high risk	19 (5.3)	
Need of hospitalization	321 (63.7)	1 (0.2)

Table 2: Analysis of variables related to uncontrolled disease for the 466 patients discharged alive after a *de novo* acute heart failure episode.

	Uncontrolled disease N=143 N (%)	Controlled disease N=319 N (%)	P value	Unadjusted OR (95% CI) for uncontrolled disease	Adjusted OR (95% CI) for uncontrolled disease	Adjusted OR (95% CI) for uncontrolled disease (controlled by centre)
Demographic data						
Age > 80 years	95 (66.4)	157 (49.2)	0.001	2.04 (1.35-3.08)	1.80 (1.17-2.77)	1.81 (1.18-2.80)
Female	79 (49.0)	166 (52.2)	0.52	0.89 (0.59-1.30)	-	-
Comorbidities						
Hypertension	119 (83.2)	250 (78.4)	0.23	1.40 (0.82-2.29)	-	-
Diabetes mellitus	63 (44.1)	114 (35.7)	0.09	1.42 (0.95-2.12)	-	-
Dyslipidaemia	63 (44.1)	154 (48.3)	0.40	0.84 (0.57-1.25)	-	-
Ischaemic heart disease	49 (34.3)	73 (22.9)	0.011	1.76 (1.14-2.71)	1.61 (1.03-2.53)	1.61 (1.03-2.53)
Chronic kidney failure (creatinine >2 mg/mL)	38 (26.6)	66 (20.7)	0.16	1.39 (0.88-2.20)	-	-
Cerebrovascular disease	30 (21.0)	39 (12.2)	0.016	1.91 (1.13-3.22)	1.61 (0.93-2.80)	1.62 (0.94-2.82)
Atrial fibrillation	61 (42.7)	106 (33.2)	0.05	1.49 (1.00-2.24)	-	-
Peripheral artery disease	19 (13.3)	27 (8.5)	0.11	1.66 (0.89-3.09)	-	-
Heart valve disease	37 (25.9)	64 (20.1)	0.16	1.39 (0.87-2.21)	-	-
Chronic obstructive pulmonary disease	21 (14.7)	67 (21.0)	0.11	0.65 (0.38-1.11)	-	-
Dementia	15 (11.4)	19 (6.8)	0.12	1.77 (0.87-3.60)	-	-
Active neoplasia	26 (19.7)	42 (14.9)	0.23	1.40 (0.81-2.39)	-	-
Hepatic cirrhosis	3 (2.3)	4 (1.4)	0.54	1.61 (0.35-7.30)	-	-
Baseline status						
More than minimal dependence (mild to total, Barthel index ≤90 points)	61 (50.0)	91 (33.2)	0.002	2.01 (1.30-3.11)	1.23 (0.74-2.04)	1.24 (0.74-2.07)
NYHA class III-IV	20 (15.2)	21 (7.1)	0.011	2.33 (1.22-4.47)	1.76 (0.88-3.55)	1.73 (0.86-3.50)
Decreased left ventricular ejection fraction (<50%)	22 (23.2)	73 (34.1)	0.06	0.58 (0.33-1.01)	-	-
Triggering factor for the current AHF episode						
Infection	29 (23.0)	68 (24.9)	0.68	0.90 (0.55-1.48)	-	-
Rapid atrial fibrillation	20 (15.9)	55 (20.1)	0.31	0.75 (0.43-1.31)	-	-
Anaemia	11 (8.7)	13 (4.8)	0.13	1.91 (0.83-4.40)	-	-
Hypertensive emergency	8 (6.3)	28 (10.3)	0.21	0.59 (0.26-1.34)	-	-
Dietetic or therapeutic transgression	8 (6.3)	7 (2.6)	0.07	2.58 (0.91-7.27)	-	-
Acute coronary syndrome	6 (4.3)	7 (2.2)	0.24	1.95 (0.64-5.92)	-	-
Severity of the AHF episode						
Increased risk (intermediate/high/very high) according to MEESI scale	49 (49.0)	68 (30.2)	0.001	2.22 (1.37-3.60)	1.60 (0.95-2.68)	1.63 (0.96-1.02)
Need of hospitalization	93 (65.0)	194 (61.0)	0.41	1.19 (0.79-1.79)	-	-

Figure 1: Patient inclusion flow chart for the NOVICA cohort and distribution of patients along with the events registered after the first *de novo* acute heart failure (AHF) episode.

Figure 2: Survival curves for the three post-discharge outcomes (top: death; middle: hospitalization; down: emergency department visit) registered in the NOVICA cohort.

Figure 3: Location of hospitalization during index acute *de novo* heart failure (AHF) episode (left bar) and for subsequent re-hospitalizations.

P values were obtained through chi-square test for trend comparing the proportion patients hospitalized in each department as the number of hospitalizations increase in front of patients not hospitalized in such a department (i.e., hospitalized in the rest of departments).

Figure 4: Relationship between the department responsible for the first hospital admission during the *de novo* acute heart failure (AHF) episode and the department where subsequent rehospitalizations took place, overall (upper panel) and by the ordinal number of rehospitalizations (lower panel).

P values were obtained through chi-square test (up) and chi-square test for trend (down) comparing the proportion of patients rehospitalized in the same department that hospitalized the patient during the first index episode of AHF in front of patients not hospitalized in such a department (i.e., hospitalized in the rest of departments).

Supplemental Table 1: Dictionary of the variables included in the present study.

DEMOGRAPHICS	
Age	Age calculated as the difference in decimal years between the date of inclusion in the study and the date of birth.
Sex	Male/Female
MEDICAL HISTORY	
Hypertension	Indicate if the patient has arterial hypertension because this is shown under previous clinical history or the patient is receiving specific treatment.
Diabetes Mellitus	Indicate if the patient has diabetes mellitus because this is shown under previous clinical history or the patient is receiving specific treatment.
Ischaemic heart disease	Indicate if the patient has any form of ischaemic heart disease (SCAEST, SCACEST, unstable angina, stable angina, ACI, etc) because this is shown under previous clinical history or the patient is receiving specific treatment.
Heart valve disease	Indicate if the patient has any type of clinically significant heart valve disease according to an ultrasound or haemodynamic study reported in the previous clinical history.
Atrial fibrillation	Indicate if the previous history describes permanent or chronic atrial fibrillation or an ECG performed within the previous year shows atrial fibrillation and this continues to be present.
Chronic kidney disease	Indicate if the patient has chronic renal insufficiency or chronic kidney disease or if analyses over the previous year show creatinine values >2 mg/dL.
Cerebrovascular disease	Indicate if the patient has had a previous cerebrovascular accident or cerebrovascular disease because this is described in the clinical history or shown in CT or MR imaging studies within the previous year and reported as cerebrovascular disease.
Peripheral artery disease	Indicate if the patient has peripheral artery disease in either the lower extremities or carotid artery, and if the patient is receiving specific treatment, has undergone specific surgery (bypass of lower extremities, endarterectomy, etc.) or there is previous history of an ankle brachial index <0.90.
Dementia	Indicate if the patient has a previous clinical diagnosis of dementia performed by a doctor.
Active neoplasia	Indicate if the patient has an active neoplasm
Prior episode of heart failure	Indicate if the patient has heart failure, is receiving specific treatment or the clinical history reports previous episodes of AHF.
BASELINE STATUS	
Baseline Barthel index	Barthel index value of the patient at least 15 days prior to the date seen in the ED.
Baseline functional grade for dyspnoea according to the NYHA scale	Indicate the functional grade of basal dyspnoea (in the 15 days prior to the exacerbation episode) of the patient according to the NYHA scale.
Left ventricular ejection fraction	Indicate left ventricular ejection fraction determined by echocardiography during admission of current episode or, if not determined, the last one determined during the six previous months
CHRONIC TREATMENT AT HOME	
Diuretics	Receiving chronic treatment with diuretics, either loop-diuretics, thiazide diuretics or mineralocorticoid receptor antagonists
Angiotensin-converter enzyme (ACE) inhibitors or angiotensin-II receptor blocker	Receiving chronic treatment with ACE inhibitors or angiotensin-II receptor blocker
Beta-blocker	Receiving chronic treatment with beta-blocker
Mineralocorticoid-receptor antagonists	Receiving chronic treatment with aldosterone-receptor antagonists
Digoxin	Receiving chronic treatment with digoxin
VITAL SIGNS AT EMERGENCY DEPARTMENT ARRIVAL	
Systolic blood pressure	Systolic blood pressure (SBP) measured in mmHg of the patient on arrival to the ED. This value can be that obtained during triage or the first taken on initiating care.
Heart rate	Central heart rate measured as beats per minute of the patient on arrival to the ED. V This value can be that obtained during triage or the first taken on initiating care .
Arterial oxygen saturation	Oxygen saturation expressed as percentage obtained by capillary pulsioxymetry on arrival to the ED. This value can be that obtained during triage or the first taken on initiating care.
BLOOD TESTS AT EMERGENCY DEPARTMENT ARRIVAL	
Glucose	In mg/dL
Creatinine	In mg/dL
Haemoglobin	In g/dL
Potassium	In mmol/L
Sodium	In mmol/L
Raised troponin	Indicate if troponin is above the 99th percent provided by the manufacturer
NT-proBNP	In pg/mL

TRIGGERING FACTORS OF THE CURRENT EPISODE OF ACUTE HEART FAILURE	
Infection	Active infection, of any system, considered to have a role in acute decompensation
Rapid atrial fibrillation	Mean heart rate >100 bpm, considered to have a role in acute decompensation
Anaemia	Haemoglobin <80 g/L, considered to have a role in acute decompensation
Hypertensive emergency	Systolic blood pressure >180 mmHg, considered to have a role in acute decompensation
Acute coronary syndrome	Symptoms starting before decompensation, and not developing after dyspnoea appearance
Dietetic/Therapeutic transgression	High water or sodium intake, omission to take drugs prescribed for heart failure treatment
Other	Describe specifically other adjudicated causes of decompensation not included in the previous episodes
Multifactorial	When some factors concur, but none is of sufficient magnitude to explain the decompensation by itself
None identified	When none of the previous factors can be selected