ORIGINAL ARTICLE

Planning to reduce 30-day adverse events after discharge of frail elderly patients with acute heart failure: design and rationale for the DEED FRAIL-AHF trial

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Objectives. To demonstrate the efficacy of a system for comprehensive care transfer (Multilevel Guided Discharge Plan [MGDP]) for frail older patients diagnosed with acute heart failure (AHF) and to validate the results of MGDP implementation under real clinical conditions. The MGDP seeks to reduce the number of adverse outcomes within 30 days of emergency department (ED) discharge.

Method. We will enroll frail patients over the age of 70 years discharged home from the ED with a main diagnosis of AHF. The MGDP includes the following components: 1) a checklist of clinical recommendations and resource activations, 2) scheduling of an early follow-up visit, 3) transfer of information to the primary care doctor, and 4) written instructions for the patient. Phase 1 of the study will be a matched-pair cluster-randomized controlled trial. Ten EDs will be randomly assigned to the intervention group and 10 to the control group. Each group will enroll 480 patients, and the outcomes will be compared between groups. Phase 2 will be a quasi-experimental study of the intervention in 300 new patients enrolled by the same 20 EDs. The outcomes will be compared to those for each Phase-1 group. The main endpoint at 30 days will be a composite of 2 outcomes: revisits to an ED and/for hospitalization for AHF or cardiovascular death.

Conclusions. The study will assess the efficacy and feasibility of comprehensive MGDP transfer of care for frail older AHF patients discharged home.

Keywords: Discharge planning. Emergency department. Acute heart failure. Frail elderly.

Planificación del alta desde urgencias para reducir eventos adversos a 30 días en pacientes mayores frágiles con insuficiencia cardiaca aguda: diseño y justificación del ensayo clínico DEED FRAIL-AHF

Objetivos. Demostrar la eficacia de una intervención integral en la transición de cuidados (Plan de Alta Guiado Multinivel, PAGM) para disminuir eventos adversos a 30 días en ancianos frágiles con insuficiencia cardiaca aguda (ICA) dados de alta desde servicios de urgencias (SU) y validar los resultados de dicha intervención en condiciones reales.

Método. Se seleccionarán pacientes ≥ 70 años frágiles con diagnóstico principal de ICA dados del alta a su domicilio desde SU. La intervención consistirá en aplicar un PAGM: 1) lista de verificación sobre recomendaciones clínicas y activación de recursos; 2) programación de visita precoz; 3) transmisión de información a atención primaria; 4) hoja de instrucciones al paciente por escrito. Fase 1: ensayo clínico con asignación al azar por conglomerados emparejado. Se asignará de forma aleatoria 10 SU (N = 480) al grupo de intervención y 10 SU (N = 480) al grupo de control. Se compararán los resultados entre grupo de intervención y control. Fase 2: estudio cuasi-experimental. Se realizará la intervención en los 20 SU (N = 300). Se comparará los resultados entre la fase 1 y 2 del grupo de intervención y entre la fase 1 y 2 del grupo de control. La variable principal de resultado es compuesta (revisita a urgencias u hospitalización por ICA o mortalidad de origen cardiovascular) a los 30 días del alta.

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Conclusiones. El estudio valorará la eficacia y factibilidad de una intervención integral en la transición de cuidados para reducir resultados adversos a 30 días en ancianos frágiles con ICA dados de alta desde los SU.

Palabras clave: Planificación del alta. Servicio de Urgencias. Insuficiencia cardiaca. Anciano. Fragilidad.

Introduction

Heart failure (HF) is a common chronic disease associated with aging that is often accompanied by a pattern of gradual deterioration interrupted by multiple decompensations until the death of the patient[1]. Chronic decompensated HF (CDHF) is one of the most frequent reasons for emergency visits and the main cause of hospital admission in the elderly population[2]. It is considered a geriatric syndrome associated with a high mortality rate, ED visit, hospital admission, functional impairment, institutionalization and worsening quality of life[3].

A period of vulnerability, following an episode of decompensation, of several weeks is known to exist until reaching stability of the disease[4]. During this period, adverse outcomes are more frequent, and even more so in frail elderly patients[5]. For this reason, clinical guidelines recommend a discharge care plan, early outpatient follow-up and screening for fragility in the elderly population in order to prevent poor outcomes[6]. In Spain, approximately 40% of patients attended by acute HF (AHF) are discharged from the emergency department (ED)[3]. There is little information in the literature on low-risk patients discharged directly from the ED. We know that these patients tend to have a higher rate of revisits and short-term admissions compared to those admitted to conventional hospitalization wards[6]. These worse results could be due to different circumstances linked to the idiosyncrasy of emergency care or short-stay medicine applied in the units concerned[7].

Care transition models from hospital to home have not been adapted to older patients served by CDHF in emergencies or related units. Adequate discharge planning reduces the risk of re-admission to hospital in older patients with AHF[8], as well as the importance in this plan of coordination and early scheduled visits with both the primary care physician and HF units[9,10]. A wide variety of models have been published that typically include discharge planning, coordination with the professional in charge of the outpatient process, and early follow-up after discharge. Positive evidence from these programs comes from patients discharged from conventional hospitalization wards and therefore it is unclear whether they have the same effect when applied in EDs[11-15]. On the other hand, comprehensive geriatric assessment (CGA) should be incorporated into the discharge planning process given the high frequency of fragility among older patients with AHF[16]. CGA is a multidimensional and interdisciplinary diagnostic process that allows the elderly patient with a high risk of adverse outcomes to be identified and an individualized treatment and follow-up plan to be developed[17]. ED discharge planning programs that have incorporated CGA have proven effective in reducing revisits and admissions, especially in very elderly patients[18,19]. The main limitation of CGA is that it requires a large amount of human resources and time, and therefore is not easily accomplished in the ED. For this reason, several abbreviated geriatric assessments (AGAs), carried out by non-geriatric healthcare professionals, have been designed in order to briefly and easily identify the affected areas and thus be able to establish a comprehensive care plan[20].

Considering the above, it is necessary to develop discharge planning intervention strategies that are multidimensional and adapted to the emergency setting to ensure continued care and prevent adverse outcomes among older patients discharged by CDHF from the ED. Therefore, the main objectives of this study are to demonstrate the efficacy of a comprehensive intervention in the transition from emergency care (Multilevel Guided Discharge Plan, MGDP) to reduce adverse outcomes at 30 days in frail elderly patients with AHF discharged from emergency or related units and to validate the results of such intervention in a prospective cohort of patients with similar characteristics in real conditions. Secondary objectives include: 1) to assess the effect of MGDP in the revisit to the ED for any cause, HF and cardiovascular origin, HF and cardiovascular origin admission, mortality from any cause and cardiovascular origin, living days out of hospital, and functional impairment at 30 days after discharge; 2) to determine the effect of different MGDP interventions on adverse outcomes at 30 days after discharge; 3) to investigate the effect of MGDP on adverse outcomes at 30 days after discharge as a function of chronological age, degree of comorbidity, fragility, episode risk stratification, ventricular function, length of stay in the ED, degree of complexity and intervention in the centre's HF process; and 4) to know the effect of MGDP on the degree of compliance, patient or caregiver satisfaction with the care transition, and patient quality of life at 30 days after discharge.

Method

The study consists of 2 phases. In phase 1, an open clinical trial will be performed with random assignment by clusters, the center being the randomization unit, matched by the degree of complexity of the hospital in order to demonstrate the efficacy of the MGDP in reducing adverse outcomes at 30 days. Once the pairs of hospitals have been established, depending on the degree of complexity, a random assignment will be made within each pair of the study group, designating 10 EDs (n = 480 patients) to the intervention group and 10 EDs (n = 480 patients) to the control group. Eligible patients will be detected by the attending physician at the time

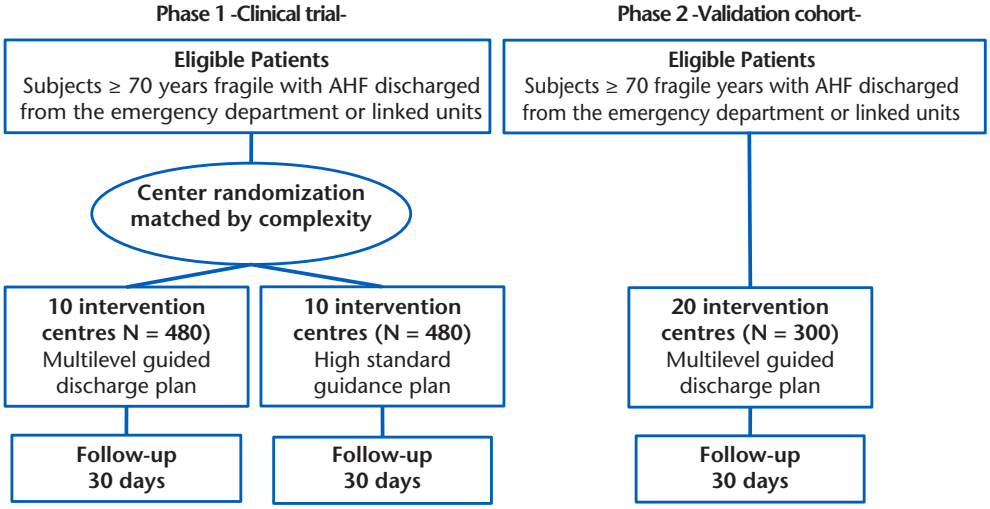

Figure 1. Flowchart of phase 1 and phase 2 of the study. AHF: Acute heart failure.

of discharge planning from the emergency department. A member of the research team will check that the patient meets the established inclusion and exclusion criteria. After consenting to participate in the study, he or she will also perform the patient assessment and collect the information in the data collection notebook. In this first phase, the doctors in the intervention centres will apply the MGDP and the doctors in the control centres will apply the usual medical care. The doctors in the intervention centres will have received a face-to-face training programme and will have a help sheet for the implementation of the MGDP interventions. Researchers will contact the patient or caregiver 30 days after discharge from hospital to collect information on outcome variables, and in the event of an intervention, compliance with the instructions of the MGDP (Figure 1).

In phase 2 a quasi-experimental study will be conducted in a cohort of different patients from the 20 EDs (N = 300 patients) who participated in phase 1 of the study, with the aim of validating the possible short-term effects of the MGDP. All centers will conduct the intervention, after completion of the clinical trial phase, in order to study the effectiveness of the intervention by comparing the results of this new cohort under real conditions with that of the intervention and control groups during the trial phase. The selection criteria, evaluation and 30-day follow-up of patients will not vary from phase 1, with the point being made that phase 1 patients will not be able to participate in phase 2. The main difference with phase 1 is that all participant EDs will apply the MGDP. As in phase 1, all physicians carrying out the intervention will have received a training program on the MGDP and will have a help sheet to implement the interventions of the MGDP (Figure 1).

Eligible persons are frail elderly patients with a primary diagnosis of AHF with a decision to discharge them home directly from the emergency department (including observation units and short stay units) after a period of observation in hospital. Table 1 shows the inclusion and exclusion criteria.

The intervention (MGDP) will be implemented during the discharge planning and will consist in the execution of 4 concrete actions: 1) the checklist that will include a series of clinical recommendations on HF, active comorbidity and fragility, and the activation of resources according to the cognitive, functional, social, nutritional, sensory and pharmacological problems detected; 2) the scheduling of an early visit with a physician responsible for the process; 3) the transmission of information to primary care; and 4) the provision of a written discharge instruction sheet adapted to the elderly patient (Figure 2). The intervention will be limited to the implementation of the actions of the MGDP by the physician at the time of the decision to discharge the patient home from the emergency department (Table 2 and Figure 3).

The primary outcome variable is a composite variable (revisit to emergency department or hospitalisation for HF or mortality of cardiovascular origin) at 30 days after discharge from hospital. Secondary outcomes are: revisit to emergency department for any cause, HF and cardiovascular origin 30 days after discharge, admission for any cause, HF and cardiovascular origin 30 days after discharge, any cause and cardiovascular origin mortality 30 days after discharge, living days out of hospital at 30 days, functional impairment 30 days after discharge (loss of number of independent basic daily activities and variation in Barthel index score referred from baseline situation at 30 days after discharge), degree of patient or caregiver satisfaction about the care transition (percentage of patients who respond very much according to the CTM-15 questions and the 3 items of CTM-3), patient quality of life (total score of the EuroQol-5D adapted question - score from 0 (worst state) to 100 (best imaginable state of health), how good or bad is your state of health today? - and the percentage of patients with and without problems in each dimension of the EuroQol-5D), and medication compliance (compliance if you answer the 4 Morisky-Green test questions appropriately). With regard to the assignment of the causes of revisit, admission and mortality, it will be carried out by two resear-

Table 1. Selection criteria for participation in the study

Inclusion criteria
Age ≥ 70.
Positive fragility screening (ISAR ≥ 2).
Primary diagnosis of acute heart failure. The diagnosis of heart failure must be the primary, it must meet all of the following criteria: a) clinical signs and symptoms of heart failure; b) signs of pulmonary congestion on chest x-ray or pulmonary ultrasound; c) value of NT-proBNP > 1,800 pg/ml.
Planned home discharge from the emergency department (including observation unit or short-stay unit) by the doctor responsible for the patient's care.
Informed consent signature by patient or legal guardian.
Exclusion Criteria
De novo heart failure, except in those cases where the etiology is examined during the index event.
Severe decompensation episode (9th decile of the MEESSI-AHF scale).
Severe non-corrected valve disease (e.g., aortic stenosis or aortic or mitral insufficiency).
Evidence of acute coronary syndrome at present or in the previous 30 days
Surgery or device implantation in the previous 30 days.
Clinically significant arrhythmia: sustained ventricular tachycardia, 2nd or 3rd degree atrial-ventricular block or sinus-auricular block with breaks > 3 seconds.
Arterial hypotension (systolic blood pressure < 100 mmHg), respiratory failure (oxygen saturation < 92%), bradycardia (< 60 bpm), tachycardia (> 110 bpm), electrolytic alteration (natremia < 130 mmol/l and hyperkalaemia >5.5 mmol/l) or anaemia (haemoglobin < 9 gr/dl) not corrected at the time of inclusion.
Expected outpatient inotropic treatment, ventricular assist device, cardiac surgery or transplant in the next 6 months after discharge.
Advanced chronic renal failure (plasma creatinine > 2.5 mg/dl or glomerular filtrate < 30 mL/min/1.73 m^2 or on current or planned dialysis).
Established severe disability (Barthel index < 40 points).
Moderate or severe dementia, active delirium, or psychiatric problems that make intervention difficult.
Terminal illness or life expectancy less than 1 year.
Duration of stay in the emergency department or linked units ≥ 96 hours.
Discharge to residence, subacute hospital, day hospital, home hospitalisation or home support programme.
No possibility of ambulatory follow-up.

ISAR: Identification of Seniors at Risk; MEESSI-AHF: Multiple Estimation of risk based on the Emergency department Spanish Score In patients with acute heart failure.

chers independently and, in case of discrepancy, by a third. The evaluation of the variables related to satisfaction about the transition of care, the patient's quality of life and medication compliance will be carried out by a single masked investigator at the intervention centers.

At the time of discharge planning, a researcher will collect, from the patient's clinical history and the information provided by the patient or caregiver, the following data: identification, triage, demographics, personal history, clinical history, analyses, electrocardiographs and image at the time of arrival at the emergency department and discharge, AGAs, treatment (chronic, during hospital stay and discharge), length of stay in the hospital and final destination of discharge from the ED. In patients in the intervention group of phase 1 and in all patients in phase 2, compliance with the mandatory actions and recommendations made on HF, active comorbidity, and cognitive, functional, nutritional, sensory and polypharmacy will be recorded. All the information will be recorded in an electronic data collection notebook, which will comply with all the requirements established in reference to data protection.

In the calculation of the sample size for phase 1, according to the OAK register, there is a 25% frequency

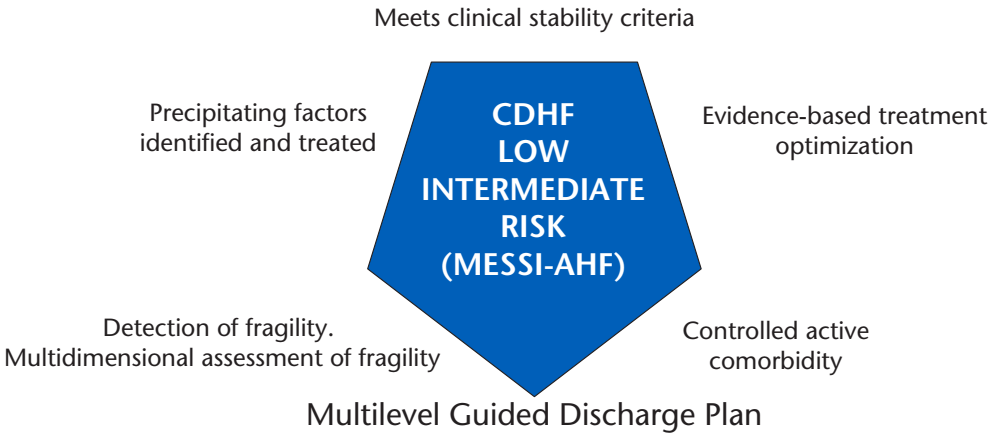

Figure 2. Discharge planning for the patient with decompensated chronic heart failure. MEESSI-AHF: Multiple Estimation of risk based on the Emergency department Spanish Score In patients with Acute Heart Failure, CDHF.

Table 2. Checklist of the recommendations of the Multilevel Guided Discharge Plan

Compulsory actions
Oral and Written Heart Failure Education.
Delivery of the explanatory pharmacological treatment sheet.
Early follow-up with the specialist responsible for the process.
Coordination with primary care.
Clinical recommendations regarding heart failure
Is the patient a candidate for hospital discharge?
Affirmative: Verify that all criteria for clinical and analytical stability are met.
Does the patient have reduced ventricular function?
Affirmative: Initiate or titrate evidence-based pharmacological treatment and evaluate the need for a device.
Clinical recommendations regarding active comorbidity
Does the patient have high blood pressure?
Affirmative: High blood pressure control.
Does the patient have paroxysmal or chronic (permanent/persistent) atrial fibrillation?
Affirmative: Evaluate the risk/benefit ratio of anticoagulant treatment and control of ventricular frequency at discharge.
Has the patient had blood glucose levels of 180 mg/dl during his/her stay in the emergency department?
Affirmative: Dietary recommendations, initiation or modification of antidiabetic treatment and indicate in the discharge report.
Does the patient have anemia or ferropenia?
Affirmative: Assess transfusion of red blood cell concentrates and/or treatment with intravenous iron supplementation.
Does the patient have obstructive pulmonary disease?
Affirmative: To adapt the treatment in case of exacerbation and to value chronic oxygen therapy.
Does the patient have renal insufficiency?
Affirmative: Adapt the dosage of the drugs to the renal function at discharge, review the prescription of nephrotoxic drugs and the levels of potassium in blood at discharge.
Recommendations on cognitive, functional, social, nutritional, sensory and polypharmacy aspects.
Does the patient have a suspected cognitive impairment and no previous diagnosis of dementia?
Affirmative: Affirmative: Referral to the specialist responsible for the process in each center to study probable cognitive impairment.
Has the patient presented or does the patient present acute confusional syndrome?
Affirmative: Educate the caregiver and refer to the specialist responsible in each center for the study of probable cognitive impairment.
Does the patient have a suspected mood disorder and no previous diagnosis of depression?
Affirmative: Refer to the specialist responsible for the process in each center for the study of probable mood disorder.
Is the patient fragile or has significant functional impairment occurred during admission?
Affirmative: Exercise program adjusted to the level of disability, recommend vitamin D deficiency screening, dietary recommendations and educate the caregiver.
Is the patient at risk of malnutrition?
Affirmative: Refer to the specialist responsible for the process in each center to assess protein energy supplements.
Does the patient have social fragility?
Affirmative: Refer to social worker.
Has the patient had 3 or more emergency visits or admissions in the last year?
Affirmative: Contact the person in charge of each centre to contact the primary care doctor or nurse and social worker at the health centre.
Does the patient have polypharmacy or potentially inappropriate prescriptions?
Affirmative: Reconcile chronic medication with the primary caregiver and review potentially inappropriate prescriptions.
Does the patient have an uncorrected visual or auditory deficit?
Affirmative: Refer to appropriate specialist for correction.

of the compound variable 30 days after discharge from the study population, estimating a coefficient of variation (km) of 0.20 between groups within the conglomerate pairs. Considering that the MGDP could reduce the frequency of the main outcome variable by 10%, it will be necessary to include a total of 48 patients in each centre for a power of 80%, a significance level of 5%, and a percentage of losses of 10%. It is estimated that a minimum of 6 months is required for recruitment in level 3 centres and 8 months in level 2 centres.

For phase 2, taking into account the sample size calculated for the group of control centers of phase 1, to achieve a power of 80% with a level of significance of 5% and detect a reduction in the rate of hospital admission similar to that estimated in phase 1, we would need 143 patients for the group of phase 2 from these 10 control hospitals (15 patients per center). The same estimated sample size will be maintained for the phase 2 group from the phase 1 intervention centres (15 patients per centre). A minimum of 3 months is estimated for recruitment in level 3 centres and 4 months in level 2 centres.

Statistical analysis

It will be done by intention to treat and protocol. For the analysis of the outcome variables, random-effect models will be applied for the effect measures within each paired cluster set and multilevel models of logistic, linear and survival regression, introducing as random-effects the hospital and the paired cluster set. These models will be adjusted for those clinically relevant baseline variables between the two study groups. A stratified analysis of the intervention effect will be performed based on the predetermined variables (Figure 4).

Phase 2: Comparison of the outcome variables will be performed: 1) between phase 1 (before the intervention) and phase 2 (after the intervention) in the 10 hospitals of the phase 1 control group to study the effectiveness of the PAGM; 2) between phase 1 (clinical trial) and phase 2 (clinical practice) in the 10 hospitals of the phase 1 intervention group to determine the feasibility of the MGDP under real conditions. Mixed regression effect models will be used, introducing the hospital as a random factor and adjusting for those clinically relevant baseline variables between the two study cohorts (Figure 4).

Results will be presented as crude paired odds ratio (OR) and adjusted next to the 95% confidence interval (CI) for binary outcomes and crude paired mean differences and adjusted next to the 95% CI for continuous outcomes. For the treatment of missing data, analysis of complete cases and analysis by multiple imputation will be performed. A significance value of 5% will be accepted. Analyses will be performed using Stata 12.1 Statistical Packages (Stata Corp; College Station, Texas, USA).

The study will be approved by all participating hospitals' Research Ethics Committees and will be carried out in accordance with the Declaration of Helsinki. All patients or their representatives will provide informed written con-

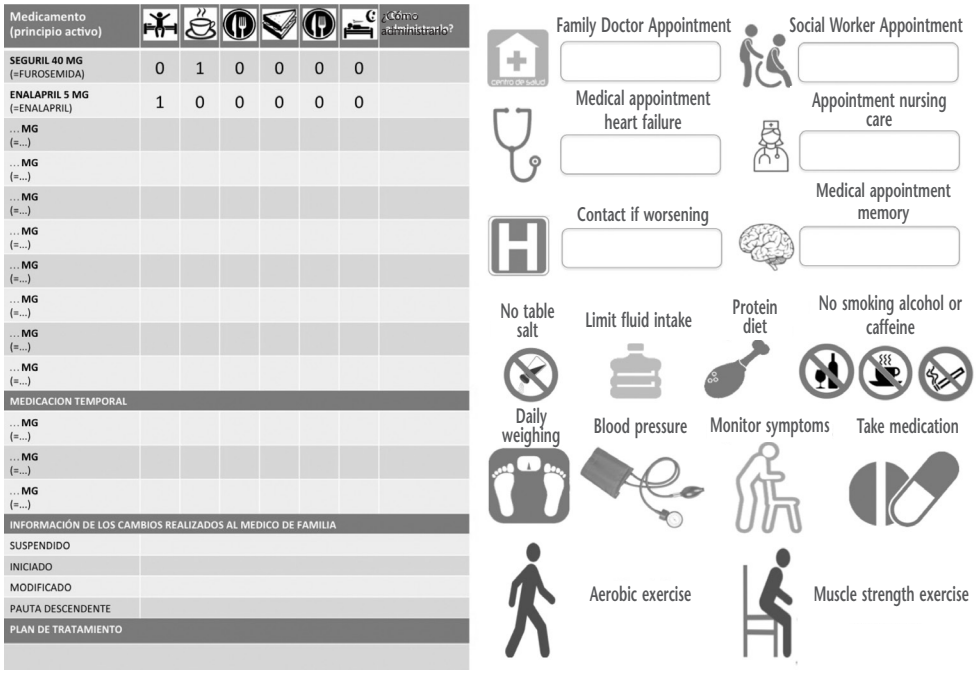

Figure 3. Patient or caregiver information sheet on pharmacological and non-pharmacological treatment and discharge instructions.

sent. The study is registered with ClinicalTrials.gov (NCT03696875).

Discussion

The ageing of the population over the last few decades raises new challenges. HF is a chronic disease that causes a disability intimately linked to old age and that causes an important public health problem in Spain[21]. AHF is one of the main causes of emergency care. Currently, one out of every four elderly patients is discharged directly from the ED[2]. In this group of patients, it has been documented that the frequency of adverse outcomes at 30 days is high (40% of visits to the ED and 20% of admission for other reasons)[2]. Reducing hospitalizations is a priority strategy for hospitals to improve quality of life and reduce process costs[22,23]. Attempts to improve these outcomes with drugs have failed[6].

Care transition strategies in the ED have not been developed well in our setting, and even less so in the very elderly[24]. Therefore, emergency physicians, in conjunction with the other professionals involved in the HF process, have the responsibility to develop new discharge planning strategies that cover all areas of the elderly patient but are easily applicable in emergency care.

The assessment of the acute process in the emergency department is usually one-dimensional, focusing mainly on symptoms and signs of congestion[24]. A series of geriatric variables have been described, the frequency of which increases with age[3], which influence the prognosis of AHF[25,26]. These variables are not usually identified by emergency physicians[27] or considered in the risk stratification and design of the care plan[29,30]. In addition, patients may be discharged at the earliest stages of stabilization, which would increase the risk of residual congestion, under-optimization of evidence-based treatment, and lack of stabilization of active comorbidity. In fact, the presence of adverse outcomes in discharged patients is directly proportional to the percentage of direct discharges from a specific ED[24]. Patients should be discharged when they are hemodynamically stable, euvolaemic, have stable renal function and oral medication has been established for at least 24 hours[10,24]. In older patients, physiological changes secondary to aging and the greater number of diseases and associated drugs as age increases may make it difficult to determine clinical stabilization criteria in order to make a discharge decision.

On the other hand, the poor results described above, together with the lack of well-established strategies in this group of patients, could lead emergency physicians to take the attitude of hospitalizing the majority of the elderly treated by CDHF in the EDs. The problem is that, regardless of costs, hospitalization is not banal. Hospital stay is associated with adverse events related to medications, invasive procedures, nosocomial infections and thromboembolic disease[27]. In older patients, there is also an increased risk of developing geriatric syndromes and disability after discharge[33]. Therefore, it is necessary both to avoid unnecessary admissions and to minimize adverse outcomes after discharge from the emergency department. Experts believe that approximately one in two patients could be safely discharged after an observation period[24].

The present study will assess the efficacy and feasibility of a MGDP to reduce adverse outcomes at 30 days in frail

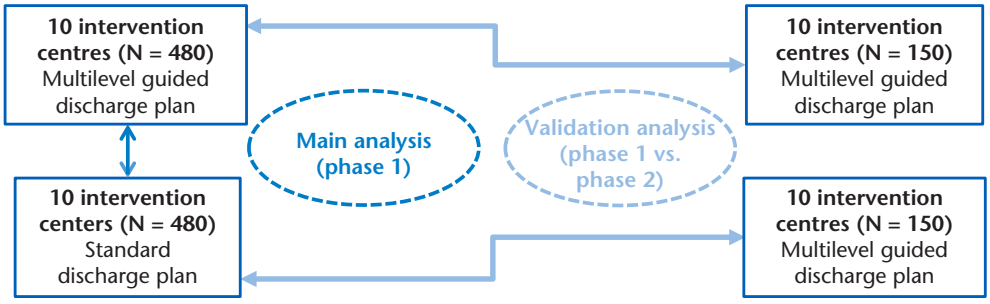

Figure 4. Statistical analysis plan.

elderly patients with AHF discharged from the ED. A number of strategies have been proposed to minimize the limitations of the present study. Well established selection and discharge criteria have been determined in the clinical trial, and the conduct of a subsequent intervention study in a cohort with different patients under real conditions to confirm the outcome of the main variable. An adjustment will be made for the characteristics of the patients and the centre of the groups analysed in order to minimise possible patient and centre selection bias. The assignment of the cause of revisit, re-admission or death will be made by 2 independent researchers and, if there is a discrepancy, by a third. Secondary outcome variables measured by self-referenced scales will be evaluated by a single masked investigator. Compliance with the MGDP will be verified through a telephone follow-up visit and consultation of available databases, and an external audit will be conducted. Tracking losses will be minimized by making up to 3 phone calls, and in the event of not being able to contact, variables may be obtained from hospital and community databases.

Several experts from multiple disciplines (epidemiology, cardiology, geriatrics, emergency medicine, pharmacy and basic sciences) have collaborated in the design of this new strategy for comprehensive discharge planning from the ED in elderly patients with CDHF in order to reduce adverse events in the short term. If our hypothesis based on a previous pilot study is met, the percentage of the 30-day composite variable in the study population could be reduced by 10%[34]. Therefore, the results transferred to clinical practice will generate the necessary scientific bases to support policies of care in emergency services in the elderly patient with HF, supporting decision making and improving innovation capacities in the transition of care from hospital emergency services. This will result in improved adherence to treatment, patient satisfaction and quality of life, all of which could have a significant impact on the costs of the hospitalization process.

Conclusions

The present clinical trial will assess the efficacy and feasibility of a comprehensive intervention in the care transition to reduce adverse outcomes at 30 days in frail elderly with AHF discharged from the ED.

What do we know about it?

– Transition of care to ensure continuity of care upon discharge from hospital has been shown to reduce adverse outcomes in patients with acute heart failure.

– One in four elderly patients with acute heart failure is discharged from the emergency department or its associated units.

– There is a period of vulnerability following an episode of decompensation where there is a high probability of adverse events, this being more likely in older patients with fragility.

– The optimal strategy for transition from care to discharge from the emergency department in frail elderly patients with decompensated chronic heart failure is unknown.

What is new about it?

– This is the first known clinical trial to demonstrate the efficacy of a comprehensive approach to discharge planning from the emergency department in frail elderly patients with decompensated chronic heart failure in reducing the risk of short-term adverse events.

– This strategy of rapid and easily applicable intervention in the emergency setting addresses aspects related to the process of heart failure, but also to comorbidity and fragility.

– The results of this study will provide valuable information on the transition from care to discharge from the emergency department in this high-risk group.

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References

1 Murray SA, Sheikh A. Palliative care beyond cancer: care for all at the end of life. Br Med J. 2008;336:958-9.
2 Llorens P, Javaloyes P, Martín-Sánchez FJ, Jacob J, Herrero-Puente P, Gil V, et al. Time trends in characteristics, clinical course, and outcomes of 13,791 patients with acute heart failure. Clin Res Cardiol. 2018. En prensa.
3 Martín-Sánchez FJ, Marino Genicio R, Rodríguez-Adrada E, Jacob J, Herrero P, Miró Ò, et al. El manejo de la insuficiencia cardiaca aguda en los servicios de urgencias hospitalarios españoles en función de la edad. Rev Esp Cardiol. 2013;66:715-20.
4 Hamo CE, Butler J, Gheorghiade M, Chioncel O. The bumpy road to drug development for acute heart failure. Eur Heart J (Suppl.). 2016;18:G19-G32.
5 Miró Ò, Gil V, Xipell C, Sánchez C, Aguiló S, Martín-Sánchez FJ, et al. IMPROV-ED study: outcomes after discharge for an episode of acute-decompensated heart failure and comparison between patients discharged from the emergency department and hospital wards. Clin Res Cardiol. 2017;106:369-78.
6 Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37:2129-200.
7 Hesselink G, Zegers M, Vernooij-Dassen M, Barach P, Kalkman C, Flink M, et al. Improving patient discharge and reducing hospital readmissions by using Intervention Mapping. BMC Health Serv Res. 2014;14:389.
8 Gonçalves-Bradley DC, Lannin NA, Clemson LM, Cameron ID, Shepperd S. Discharge planning from hospital. Cochrane Database Syst Rev. 2016;CD000313.
9 Albert NM, Barnason S, Deswal A, Hernandez A, Kociol R, Lee E, et al. Transitions of care in heart failure: a scientific statement from the American Heart Association. Circ Heart Fail. 2015;8:384-409.
10 Mebazaa A, Yilmaz MB, Levy P, Ponikowski P, Peacock WF, Laribi S, et al. Recommendations on pre-hospital & early hospital management of acute heart failure: a consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine and the Society of Academic Emergency Medicine. Eur J Heart Fail. 2015;17:544-58.
11 Laugaland K, Aase K, Barach P. Interventions to improve patient safety in transitional care--a review of the evidence. Work. 2012;4:2915-24.
12 Allen J, Hutchinson AM, Brown R, Livingston PM. Quality care outcomes following transitional care interventions for older people from hospital to home: a systematic review. BMC Health Serv Res. 2014;14:346.
13 O'Connell Francischetto E, Damery S, Davies S, Combes G. Discharge interventions for older patients leaving hospital: protocol for a systematic meta-review. Syst Rev. 2016;5:46.
14 Comín-Colet J, Enjuanes C, Lupón J, Caínzos-Achirica M, Badosa N, Verdú JM. Transiciones de cuidados entre insuficiencia cardiaca aguda y crónica: pasos críticos en el diseño de un modelo de atención multidisciplinaria para la prevención de la hospitalización recurrente. Rev Esp Cardiol. 2016;69:951-61.
15 Mabire C, Dwyer A, Garnier A, Pellet J. Meta-analysis of the effectiveness of nursing discharge planning interventions for older inpatients discharged home. J Adv Nurs. 20172018;74:788-99.
16 Martín-Sánchez FJ, Rodríguez-Adrada E, Mueller C, Vidán MT, Christ M, Frank Peacock W, et al. The Effect of Frailty on 30-day Mortality Risk in Older Patients With AHF Attended in the ED. Acad Emerg Med. 2017;24:298-307.
17 Pilotto A, Cella A, Pilotto A, Daragjati J, Veronese N, Musacchio C, et al. Three Decades of Comprehensive Geriatric Assessment: Evidence Coming from Different Healthcare Settings and Specific Clinical Conditions. J Am Med Dir Assoc. 2017;18:192.e1-192.e11.
18 Caplan GA, Williams AJ, Daly B, Abraham K. A randomized, controlled trial of comprehensive geriatric assessment and multidisciplinary intervention after discharge of elderly from the emergency department-the DEED II study. J Am Geriatr Soc. 2004;52:1417e23.
19 Conroy SP, Ansari K, Williams M, Laithwaite E, Teasdale B, Dawson J, et al. A controlled evaluation of comprehensive geriatric assessment in the emergency department: The "Emergency Frailty Unit". Age Ageing 2014; 43:109e14.
20 Martín-Sánchez FJ, Christ M, Miró Ò, Peacock WF, McMurray JJ, Bueno H, et al. Practical approach on frail older patients attended for acute heart failure. Int J Cardiol. 2016;222:62-71.
21 Sayago-Silva I, García-López F, Segovia-Cubero J. Epidemiología de la insuficiencia cardiaca en España en los últimos 20 años. Rev Esp Cardiol. 2013;66:649-56.
22 Delgado JF, Oliva J, Llano M, Pascual-Figal D, Grillo JJ, Comín-Colet J, et al. Costes sanitarios y no sanitarios de personas que padecen insuficiencia cardiaca crónica sintomática en España. Rev Esp Cardiol. 2014;67:643-50.
23 González-Colaço Harmand M, Prada Arrondo PC, Domínguez Rodríguez A. Calidad o cantidad de vida en los ancianos con insuficiencia cardiaca aguda: ¿es hora de hablar? Emergencias. 2018;30:363.

24 Miró Ò, Peacock FW, McMurray JJ, Bueno H, Christ M, Maisel AS, et al. European Society of Cardiology - Acute Cardiovascular Care Association position paper on safe discharge of acute heart failure patients from the emergency department. Eur Heart J Acute Cardiovasc Care. 2017;6:311-20.
25 Martín-Sánchez FJ, Rodríguez-Adrada E, Vidán MT, Díez Villanueva P, Llopis García G, González Del Castillo J, et al. Impacto de las variables geriátricas en la mortalidad a 30 días entre los ancianos atendidos por ICA. Emergencias 2018;30:149-55.
26 Martín-Sánchez FJ, Rodríguez-Adrada E, Vidán MT, Llopis García G, González Del Castillo J, Rizzi MA, et al. Impact of Frailty and Disability on 30-Day Mortality in Older Patients With Acute Heart Failure. Am J Cardiol. 2017;120:1151-7.
27 Graf CE, Zekry D, Giannelli S, Michel JP, Chevalley T. Efficiency and applicability of comprehensive geriatric assessment in the emergency department: a systematic review. Aging Clin Exp Res. 2011;23:244-54.
28 Ouwerkerk W, Voors AA, Zwinderman AH. Factors influencing the predictive power of models for predicting mortality and/or heart failure hospitalization in patients with heart failure. JACC Heart Fail. 2014;2:429-36.
29 Llorens P. Necesidad de evaluar el riesgo de los pacientes con insuficiencia cardiaca aguda en los servicios de urgencias más allá del juicio clínico. Emergencias. 2018;30:75-6.
30 García-Gutiérrez S, Quintana López JM, Antón-Ladislao A, Gallardo Rebollal MS, Rilo Miranda I, Morillas Bueno M, et al. Validación externa de la escala EAHFE-3D para la evaluación del pronóstico en insuficiencia cardiaca aguda. Emergencias. 2018;30:84-90.
31 Formiga F, Chivite D. Insuficiencia cardiaca aguda: básico conocer al paciente. Emergencias. 2018;30:145-6.
32 De Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care. 2008;17:216-23.
33 Long SJ, Brown KF, Ames D, Vincent C. What is known about adverse events in older medical hospital inpatients? A systematic review of the literature. Int J Qual Heal Care. 2013;25:542-54.
34 Fernández Alonso C, Fuentes Ferrer M, Jiménez Santana MI, Fernández Hernández L, de la Cruz García M, González Del Castillo J, et al. Intervención multidimensional que mejora el pronóstico a corto plazo entre los ancianos frágiles dados de alta desde una unidad de corta de estancia: estudio cuasiexperimental. Rev Clin Esp 2018;218:163-9.