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Circulation: Heart Failure

ORIGINAL ARTICLE

# Detailed Assessment of the "I Need Help" Criteria in Patients With Heart Failure: Insights From the HELP-HF Registry

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**BACKGROUND:** The "I Need Help" markers have been proposed to identify patients with advanced heart failure (HF). We evaluated the prognostic impact of these markers on clinical outcomes in a real-world, contemporary, multicenter HF population.

**METHODS:** We included consecutive patients with HF and at least 1 high-risk "I Need Help" marker from 4 centers. The impact of the cumulative number of "I Need Help" criteria and that of each individual "I Need Help" criterion was evaluated. The primary end point was the composite of all-cause mortality or first HF hospitalization.

**RESULTS:** Among 1149 patients enrolled, the majority had 2 (30.9%) or 3 (22.6%) "I Need Help" criteria. A higher cumulative number of "I Need Help" criteria was independently associated with a higher risk of the primary end point (adjusted hazard ratio for each criterion increase, 1.19 [95% CI, 1.11–1.27]; $P$<0.001), and patients with >5 criteria had the worst prognosis. Need of inotropes, persistently high New York Heart Association classes III and IV or natriuretic peptides, end-organ dysfunction, >1 HF hospitalization in the last year, persisting fluid overload or escalating diuretics, and low blood pressure were the individual criteria independently associated with a higher risk of the primary end point.

**CONCLUSIONS:** In our HF population, a higher number of "I Need Help" criteria was associated with a worse prognosis. The individual criteria with an independent impact on mortality or HF hospitalization were need of inotropes, New York Heart Association class or natriuretic peptides, end-organ dysfunction, multiple HF hospitalizations, persisting edema or escalating diuretics, and low blood pressure.

**Key Words:** heart failure ■ hospitalization ■ mortality ■ patient readmission ■ prognosis

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Progressive worsening to an advanced stage is a hallmark of heart failure (HF).[1] This late stage of advanced HF is characterized by impaired quality of life and poor prognosis despite conventional HF treatments,[2] with an estimated median time from advanced HF diagnosis to death of ≈1 year.[3] Early and appropriate identification of advanced HF is of paramount importance in the clinical management of patients with HF. Specifically, a timely referral for the evaluation of heart replacement therapies (such as heart transplantation or left ventricular assist device implantation) is fundamental.[4] Furthermore, advanced HF recognition allows a proper follow-up, which is particularly relevant in a syndrome with often unpredictable disease trajectories.[1]

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## WHAT IS NEW?

- In a real-world, contemporary population of patients with heart failure (HF) and at least 1 high-risk marker for advanced HF, a higher number of "I Need Help" criteria was associated with a worse prognosis, with the need of inotropes, high New York Heart Association class or natriuretic peptides, end-organ dysfunction, multiple HF hospitalizations, persisting edema or escalating diuretics, and low blood pressure being the individual criteria with an independent impact on mortality or HF hospitalization.

## WHAT ARE THE CLINICAL IMPLICATIONS?

- Beyond its role in the early identification of patients with advanced HF (screening), the "I Need Help" classification also has a prognostic role. Patients with HF and multiple "I Need Help" markers, particularly in case of need of inotropes, worsening symptoms or persistently high natriuretic peptides, end-organ renal or liver dysfunction, recurrent HF hospitalizations, worsening edema or need of escalating diuretics, and low blood pressure, have a poor prognosis, and referral to advanced HF centers needs to be considered, if indicated.

## Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **HELP-HF** | Assessment of the I Need Help Markers in Heart Failure |
| **HF** | heart failure |
| **HR** | hazard ratio |
| **LVEF** | left ventricular ejection fraction |
| **NT-proBNP** | N-terminal pro-B-type natriuretic peptide |
| **NYHA** | New York Heart Association |

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Therefore, along with several advanced HF definitions and criteria that have been proposed,[1,2,5,6] the "I Need Help" markers have been developed as a useful mnemonic tool to screen and timely identify advanced HF in clinical practice.[2,4,7]

The aim of our study was to evaluate the distribution of the "I Need Help" criteria and their relationship with clinical outcomes in a contemporary, real-world, multicenter HF cohort.

# METHODS

## Study Design

The design of the HELP-HF (Assessment of the I Need Help Markers in Heart Failure) registry was already described.[8] In brief, this was an observational, retrospective, multicenter registry including both inpatients hospitalized for acute HF and outpatients with chronic HF evaluated between January 1, 2020, and November 30, 2021, at 4 participating centers. All consecutive patients who fulfilled at least 1 of the following "I Need Help" criteria were included: (1) previous or ongoing need of inotropes; (2) New York Heart Association (NYHA) classes III and IV or persistently high natriuretic peptide levels; (3) end-organ renal or liver dysfunction in the setting of HF; (4) left ventricular ejection fraction (LVEF) below 20%; (5) recurrent appropriate defibrillator shocks; (6) >1 HF hospitalization in the last year; (7) persisting fluid overload (edema) or increasing diuretic requirement (escalating diuretics); (8) consistently low blood pressure (systolic blood pressure, <90–100 mm Hg); and (9) inability to uptitrate or need to reduce/discontinue prognostic medications (angiotensin-converting enzyme inhibitor or angiotensin receptor neprilysin inhibitor, β-blocker, or mineralocorticoid receptor antagonist). These criteria were assessed, adjudicated, and reported at the time of inclusion by local investigators at each participating center.

All patients were treated according to the HF guidelines.[9] Anonymous individual patient data on medical history, clinical presentation, medical therapy, echocardiographic and laboratory parameters, therapies, and clinical outcomes were collected. Institutional review board approval was waived for this registry because of its retrospective design with collection of anonymized data and without any study-specific intervention. Follow-up was performed by means of review of outpatient visits and hospitalizations or by means of telephone contacts.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Study End Points

The primary end point of this analysis was the composite of all-cause mortality or first HF hospitalization. All-cause mortality alone was the secondary outcome of interest.

## Statistical Analysis

Continuous variables are reported as median and interquartile range and were compared with the Wilcoxon rank-sum test for trend. Categorical variables are presented as numbers and percentages and were compared with the $\chi^2$ test for trend. Baseline characteristics, echocardiography data, laboratory data, and clinical outcomes were compared between patients with a different number of "I Need Help" criteria. Due to the low number of patients with 7, 8, and 9 criteria, these 3 categories were merged into 1 single category (7-8-9 criteria). The Kaplan-Meier method was used to assess the occurrence of primary and secondary end points at 1-year follow-up. For each end point, follow-up was analyzed at the date of the event or at the last available follow-up.

Univariable and multivariable Cox proportional hazard regression analyses were performed to evaluate the prognostic impact of the cumulative number of "I Need Help" criteria and of each individual criterion on the primary and secondary end points. Results are reported as unadjusted or adjusted hazard ratio (HR) with 95% CI. To evaluate the impact of the cumulative number of criteria, the presence of 1 criterion was set as the reference category, and the other categories were compared with this reference category. At multivariable Cox regression analyses, the impact of the cumulative number of

"I Need Help" criteria was adjusted for relevant covariates of interest that were previously identified and validated in the main HELP-HF publication.[8] In detail, the following covariates were included in the multivariable model for the primary end point: age, sex, advanced HF diagnosis according to the Heart Failure Association of the European Society of Cardiology definition, inpatient versus outpatient status, NYHA classes III and IV, estimated glomerular filtration rate with the Chronic Kidney Disease Epidemiology Collaboration equation, peripheral artery disease, prior stroke or transient ischemic attack, history of atrial fibrillation, prior myocardial infarction, chronic obstructive pulmonary disease, and systolic blood pressure at inclusion. In the multivariable model testing the impact on all-cause mortality alone, heart rate at inclusion was also included along with the aforementioned covariates.[8] In 2 subanalyses, the impact of the cumulative number of criteria was evaluated only among inpatients and only among patients with LVEF ≤40%, respectively.

In the multivariable Cox regression analyses testing the impact of each "I Need Help" criterion on both end points in the overall population, each individual criterion was adjusted for the other 8 "I Need Help" criteria. After multivariable analysis, a formal test of equality (Wald test) of the obtained adjusted HRs was performed, thus evaluating whether each HR (for a specific criterion) was significantly different as compared with any other HR. An overall *P* value reflecting global differences across all the adjusted HRs was also calculated for both end points.

All reported *P* values were 2 sided, and $P<0.05$ was considered statistically significant. Statistical analyses were performed using STATA, version 16.0 (STATA Corp, College Station, TX).

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# RESULTS

A total of 1149 patients with HF and at least 1 "I Need Help" marker were included in the HELP-HF registry. As shown in Figure 1A, the 3 most common "I Need Help" criteria in the study population were NYHA class/natriuretic peptides (61.8%), edema/escalating diuretics (57.3%), and inability to uptitrate or need to reduce/discontinue prognostic medications (31.2%). The majority of included patients had 2 (30.9%), 3 (22.6%), or 1 (21.2%) "I Need Help" criteria at inclusion (Figure 1B).

## Patients' Characteristics

Baseline patients' characteristics are reported in Table 1. Patients with a higher number of "I Need Help" criteria were younger, less likely to have new-onset (de novo) HF and to be enrolled as inpatients, and had more frequent HF hospitalizations during last year and NYHA classes III and IV. In terms of comorbidities, patients with more "I Need Help" criteria had less commonly hypertension and were more likely to have a history of atrial fibrillation, prior myocardial infarction, and chronic kidney disease. Regarding clinical presentation, patients with a higher number of "I Need Help" criteria had more frequent cardiogenic shock, acute pulmonary edema, peripheral edema and need of intravenous loop diuretics, inotropes/vasopressors, intensive care unit admission, mechanical circulatory support, mechanical ventilation, and continuous renal replacement therapy or ultrafiltration. The Heart Failure Association of the European Society of Cardiology definition of advanced HF was more commonly fulfilled in these patients.

As shown in Table 2, patients with more "I Need Help" criteria had lower LVEF and were more likely to have moderate/severe mitral regurgitation, right ventricular dilatation or dysfunction, and moderate/severe tricuspid regurgitation. NT-proBNP (N-terminal pro-B-type natriuretic peptide) was higher, and estimated glomerular filtration rate was lower in these patients.

## Clinical Outcomes

At a median follow-up of 260 days (interquartile range, 105–390 days), the primary composite end point occurred in 496 patients (43.2%), and 265 patients (23.1%) died. As shown in Figure 2, the incidence of the

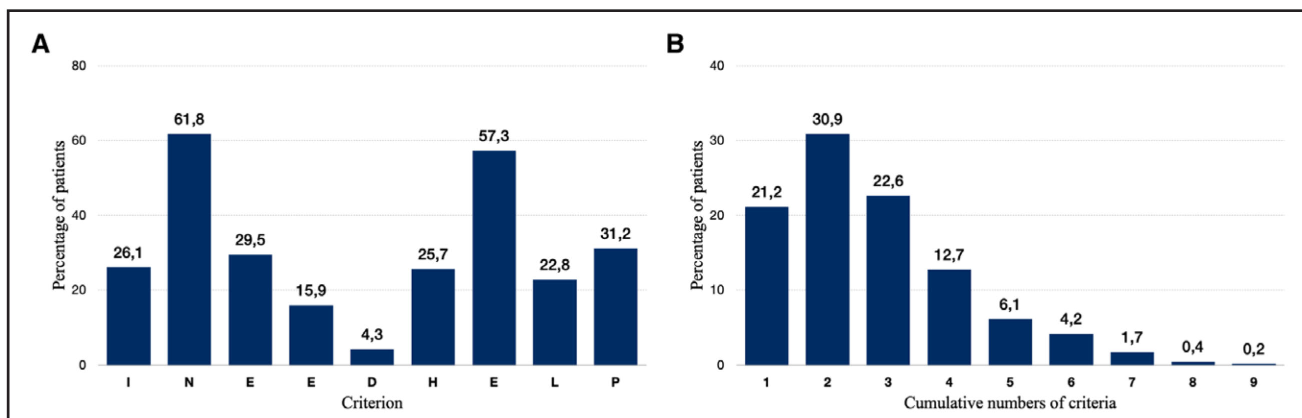


**Figure 1. Distribution of the "I Need Help" criteria.**
The figure depicts the proportion of patients fulfilling each of the 9 "I Need Help" criteria in the study population (**A**) and the proportion of patients fulfilling different cumulative numbers of the "I Need Help" criteria (from 1 to 9) in the study population (**B**).

**Table 1. Baseline Characteristics**

| | 1 criterion (n=243) | 2 criteria (n=355) | 3 criteria (n=260) | 4 criteria (n=146) | 5 criteria (n=70) | 6 criteria (n=48) | 7–9 criteria (n=27) | *P* value |
|---|---|---|---|---|---|---|---|---|
| Age, y | 78 (71–84) | 78 (69–84) | 77 (68–82) | 77 (70–83) | 77 (68–82) | 72 (65–81) | 74 (68–79) | 0.003 |
| Male sex | 158 (65.0) | 241 (67.9) | 178 (68.5) | 93 (63.7) | 45 (64.3) | 39 (81.3) | 19 (70.4) | 0.33 |
| BMI, kg/m$^2$ | 26.7 (23.7–30.4) | 26.4 (23.2–30.5) | 25.3 (22.7–29.1) | 25.0 (22.2–29.0) | 24.9 (22.2–28.5) | 25.3 (23.0–28.9) | 23.1 (22.3–25.2) | <0.001 |
| New-onset HF | 68 (28.0) | 74 (20.9) | 30 (11.5) | 13 (8.9) | 2 (2.9) | 0 (0.0) | 0 (0.0) | <0.001 |
| HF hospitalizations during the last year | 33 (13.6) | 90 (25.4) | 116 (44.6) | 73 (50.0) | 47 (67.1) | 35 (72.9) | 21 (77.8) | <0.001 |
| NYHA class III or IV | 108 (44.4) | 220 (62.0) | 180 (69.2) | 113 (77.4) | 53 (75.7) | 40 (83.3) | 24 (88.9) | <0.001 |
| Type of inclusion | | | | | | | | <0.001 |
| Outpatient visit | 94 (38.7) | 128 (36.1) | 94 (36.2) | 36 (24.7) | 15 (21.4) | 3 (6.3) | 2 (7.4) | |
| Inpatient hospitalization | 149 (61.3) | 227 (63.9) | 166 (63.9) | 110 (75.3) | 55 (78.6) | 45 (93.8) | 25 (92.6) | |
| Comorbidities | | | | | | | | |
| Hypertension | 181 (74.5) | 264 (74.4) | 184 (70.8) | 97 (66.4) | 44 (62.9) | 36 (75.0) | 11 (40.7) | 0.001 |
| Diabetes | 87 (35.8) | 133 (37.5) | 116 (44.6) | 48 (32.9) | 27 (38.6) | 26 (54.2) | 10 (37.0) | 0.21 |
| History of AF | 130 (53.5) | 180 (50.7) | 163 (62.7) | 77 (52.7) | 41 (58.6) | 32 (66.7) | 18 (66.7) | 0.025 |
| Prior myocardial infarction | 65 (26.8) | 119 (33.5) | 81 (31.2) | 58 (39.7) | 29 (41.4) | 18 (37.5) | 10 (37.0) | 0.010 |
| Prior PCI | 67 (27.6) | 103 (29.0) | 69 (26.5) | 45 (30.8) | 25 (35.7) | 18 (37.5) | 9 (33.3) | 0.11 |
| Prior CABG | 28 (11.5) | 46 (13.0) | 37 (14.2) | 32 (21.9) | 13 (18.6) | 13 (27.1) | 2 (7.4) | 0.007 |
| Peripheral artery disease | 52 (21.4) | 56 (15.8) | 39 (15.0) | 27 (18.5) | 15 (21.4) | 12 (25.0) | 4 (14.8) | 0.87 |
| Prior stroke or TIA | 35 (14.4) | 44 (12.4) | 51 (19.6) | 22 (15.1) | 7 (10.0) | 10 (20.8) | 4 (14.8) | 0.45 |
| COPD | 46 (18.9) | 84 (23.7) | 73 (28.1) | 26 (17.8) | 16 (22.9) | 12 (25.0) | 9 (33.3) | 0.26 |
| Chronic kidney disease | 99 (40.7) | 193 (54.4) | 162 (62.3) | 93 (63.7) | 47 (67.1) | 36 (75.0) | 20 (74.1) | <0.001 |
| Cardiac implantable electronic devices | | | | | | | | <0.001 |
| Pacemaker | 40 (16.5) | 50 (14.1) | 45 (17.3) | 20 (13.7) | 9 (12.9) | 3 (6.3) | 0 (0.0) | |
| ICD | 32 (13.2) | 49 (13.8) | 34 (13.1) | 25 (17.1) | 20 (28.6) | 12 (25.0) | 11 (40.7) | |
| CRT-D | 25 (10.3) | 30 (8.5) | 35 (13.5) | 35 (24.0) | 17 (24.3) | 15 (31.3) | 11 (40.7) | |
| CRT-P | 4 (1.7) | 4 (1.1) | 5 (1.9) | 0 (0.0) | 0 (0.0) | 1 (2.1) | 1 (3.7) | |
| Clinical presentation | | | | | | | | |
| Cardiogenic shock | 16 (6.6) | 27 (7.6) | 21 (8.1) | 29 (19.9) | 26 (37.1) | 19 (39.6) | 15 (55.6) | <0.001 |
| Acute pulmonary edema | 28 (11.5) | 44 (12.4) | 28 (10.8) | 23 (15.8) | 13 (18.9) | 10 (20.8) | 7 (25.9) | 0.006 |
| Rales >1/3 lung fields | 93 (38.3) | 150 (42.3) | 105 (40.4) | 69 (47.3) | 32 (45.7) | 25 (52.1) | 16 (59.3) | 0.009 |
| Peripheral edema | 115 (47.3) | 205 (57.8) | 156 (60.0) | 99 (67.8) | 48 (68.6) | 31 (64.6) | 19 (70.4) | <0.001 |
| Systolic blood pressure, mm Hg | 125 (110–140) | 130 (110–145) | 120 (107–135) | 110 (100–130) | 108 (95–120) | 105 (97–115) | 95 (90–100) | <0.001 |
| Heart rate, bpm | 73 (63–85) | 75 (63–90) | 74 (64–90) | 75 (65–86) | 78 (70–88) | 76 (70–89) | 88 (64–105) | 0.016 |
| Intravenous loop diuretics | 158 (65.0) | 233 (65.6) | 169 (65.0) | 105 (71.9) | 55 (78.6) | 35 (72.9) | 23 (85.2) | 0.004 |
| Use of inotropes/vasopressors | 26 (10.7) | 42 (11.8) | 48 (18.5) | 61 (41.8) | 41 (58.6) | 36 (75.0) | 23 (85.2) | <0.001 |
| Need of temporary MCS | | | | | | | | <0.001 |
| IABP | 6 (2.5) | 10 (2.8) | 8 (3.1) | 6 (4.1) | 3 (4.3) | 5 (10.4) | 2 (7.4) | |
| Impella | 1 (0.4) | 2 (0.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (7.4) | |
| VA-ECMO | 1 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (2.1) | 1 (3.7) | |
| Need of mechanical ventilation | | | | | | | | <0.001 |
| Noninvasive | 24 (9.9) | 48 (13.5) | 29 (11.2) | 25 (17.1) | 16 (22.9) | 12 (25.0) | 5 (18.5) | |

(*Continued*)

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**Table 1. Continued**

| | 1 criterion (n=243) | 2 criteria (n=355) | 3 criteria (n=260) | 4 criteria (n=146) | 5 criteria (n=70) | 6 criteria (n=48) | 7–9 criteria (n=27) | *P* value |
|---|---|---|---|---|---|---|---|---|
| Invasive | 6 (2.5) | 9 (2.5) | 5 (1.9) | 5 (3.4) | 2 (2.9) | 2 (4.2) | 6 (22.2) | |
| Need of CRRT/ultrafiltration | 3 (1.2) | 8 (2.3) | 6 (2.3) | 7 (4.8) | 5 (7.1) | 10 (20.8) | 6 (22.2) | <0.001 |
| Need of ICU admission | 33 (13.6) | 56 (15.8) | 52 (20.0) | 50 (34.3) | 23 (32.9) | 23 (47.9) | 16 (59.3) | <0.001 |
| HFA-ESC advanced HF definition | 5 (2.1) | 26 (7.3) | 40 (15.4) | 42 (28.8) | 28 (40.0) | 32 (66.7) | 20 (74.1) | <0.001 |
| INTERMACS profile 1–3 | 3 (1.2) | 11 (3.1) | 12 (4.6) | 26 (17.8) | 17 (24.3) | 22 (45.8) | 13 (48.2) | <0.001 |
| ACC/AHA stage D | 16 (6.6) | 21 (5.9) | 33 (12.7) | 37 (25.3) | 24 (34.3) | 34 (70.8) | 20 (74.1) | <0.001 |
| Oral HF medications at inclusion | | | | | | | | |
| β-Blockers | 188 (77.4) | 278 (78.3) | 201 (77.3) | 105 (72.4) | 57 (81.4) | 32 (68.1) | 21 (77.8) | 0.37 |
| ACE inhibitor, ARB, or ARNI | 142 (58.4) | 201 (56.6) | 120 (46.2) | 63 (43.5) | 29 (41.4) | 17 (36.2) | 13 (48.2) | <0.001 |
| ARNI | 42 (17.3) | 58 (16.3) | 37 (14.2) | 30 (20.7) | 13 (18.6) | 7 (14.9) | 9 (33.3) | 0.22 |
| MRA | 122 (50.2) | 180 (50.7) | 153 (58.9) | 88 (60.7) | 41 (58.6) | 27 (57.5) | 19 (70.4) | 0.004 |
| Loop diuretics | 201 (80.7) | 299 (84.2) | 234 (90.0) | 129 (89.0) | 66 (94.3) | 46 (97.9) | 27 (100.0) | <0.001 |

Data are presented as n (%) and median (Q25–Q75). ACC indicates American College of Cardiology; ACE, angiotensin-converting enzyme; AF, atrial fibrillation; AHA, American Heart Association; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; CRRT, continuous renal replacement therapy; CRT-D, cardiac resynchronization therapy with defibrillator; CRT-P, cardiac resynchronization therapy with pacemaker; HF, heart failure; HFA-ESC, Heart Failure Association of the European Society of Cardiology; IABP, intra-aortic balloon pump; ICD, implantable cardioverter defibrillator; ICU, intensive care unit; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; MCS, mechanical circulatory support; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

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primary composite end point at 1 year was progressively higher in patients fulfilling a higher number of "I Need Help" criteria (log-rank *P*<0.001), with risk estimates ranging from 33.2% in the patients with 1 criterion to 87.6% and 91.2% in the patients with 6 and 7-to-9 criteria, respectively. Similarly, all-cause mortality at 1 year was progressively higher in patients fulfilling a higher number of criteria (log-rank *P*<0.001; Figure 3), with estimated rates ranging from 15.0% in the patients with 1 criterion to 61.0% and 77.4% in the patients with 6 and 7-to-9 criteria, respectively.

The impact of the cumulative number of "I Need Help" criteria at inclusion on the primary and secondary end points is shown in Table 3. At univariable analysis, the presence of 3, 4, 5, 6, and 7-to-9 criteria was associated with a significant and progressively higher impact on the primary composite end point as compared with 1 criterion (HRs, 1.88, 2.04, 2.27, 5.45, and 5.77, respectively; all *P*<0.001). The prognostic impact of 2, 3, 4, 5, 6 and 7-to-9 criteria was also confirmed after multivariable adjustment. The adjusted HR for each criterion increase on the primary composite end point was 1.19 ([95% CI, 1.11–1.27] *P*<0.001). Similar findings were observed for the secondary end point of all-cause mortality alone (Table 3). The prognostic impact of a higher number of "I Need Help" criteria was confirmed at 2 subanalysis evaluating only inpatients (Table S1) and only patients with LVEF ≤40% (Table S2), respectively.

The prognostic impact of each "I Need Help" criterion is reported in Table 4. At multivariable analysis, the criteria independently associated with a higher risk of the primary composite end point were need of inotropes (adjusted HR, 1.64 [95% CI, 1.33–2.02]; *P*<0.001), persisting NYHA classes III and IV or persistently high natriuretic peptides (adjusted HR, 1.37 [95% CI, 1.12–1.66]; *P*=0.002), end-organ dysfunction (adjusted HR, 1.44 [95% CI, 1.19–1.73]; *P*<0.001), >1 HF hospitalization in the last year (adjusted HR, 1.29 [95% CI, 1.06–1.57]; *P*=0.012), persisting edema or escalating diuretics (adjusted HR, 1.55 [95% CI, 1.28–1.88]; *P*<0.001), and low blood pressure (adjusted HR, 1.47 [95% CI, 1.16–1.86]; *P*=0.001). Overall, a significant difference was observed across all the adjusted HRs for the primary end point (*P*=0.019), and individual comparisons between adjusted HRs are reported in Table S3. Regarding the secondary end point, the criteria independently associated with all-cause mortality after multivariable adjustment were need of inotropes, NYHA classes III and IV and high natriuretic peptides, end-organ dysfunction, persisting edema or escalating diuretics, and low blood pressure (Table 4). An overall significant difference across all adjusted HRs was observed also for all-cause mortality (*P*<0.001), and individual comparisons between adjusted HRs are reported in Table S4.

**Table 2. Echocardiographic Data and Laboratory Findings**

| | 1 criterion (n=243) | 2 criteria (n=355) | 3 criteria (n=260) | 4 criteria (n=146) | 5 criteria (n=70) | 6 criteria (n=48) | 7–9 criteria (n=27) | *P* value |
|---|---|---|---|---|---|---|---|---|
| Echocardiographic data | | | | | | | | |
| LVEF, % | 43 (30–54) | 40 (28–55) | 35 (25–50) | 30 (24–45) | 27 (20–40) | 25 (20–39) | 20 (15–22) | <0.001 |
| LVEF categories | | | | | | | | <0.001 |
| HFrEF (LVEF ≤40%) | 114 (46.9) | 195 (54.9) | 161 (61.9) | 105 (71.9) | 57 (81.4) | 40 (83.3) | 27 (100) | |
| HFmrEF (LVEF 41%–49%) | 39 (16.1) | 40 (11.3) | 25 (9.6) | 11 (7.5) | 4 (5.7) | 3 (6.3) | 0 (0.0) | |
| HFpEF (LVEF ≥50%) | 90 (37.0) | 120 (33.8) | 74 (28.5) | 30 (20.6) | 9 (12.9) | 5 (10.4) | 0 (0.0) | |
| Moderate/severe MR | 135 (57.9) | 191 (54.6) | 151 (59.9) | 99 (69.2) | 50 (75.8) | 34 (75.6) | 23 (88.5) | <0.001 |
| RV dilatation | 57 (26.6) | 115 (34.4) | 90 (37.2) | 39 (29.6) | 27 (42.9) | 22 (47.8) | 13 (52.0) | 0.001 |
| RV dysfunction | 72 (31.0) | 138 (39.7) | 116 (45.7) | 77 (55.0) | 36 (56.3) | 26 (55.3) | 17 (65.4) | <0.001 |
| Moderate/severe TR | 112 (49.1) | 169 (49.3) | 141 (57.3) | 73 (52.5) | 41 (63.1) | 30 (65.2) | 19 (73.1) | <0.001 |
| Laboratory findings | | | | | | | | |
| Creatinine, mg/dL | 1.28 (1.00–1.80) | 1.37 (1.02–1.84) | 1.49 (1.14–2.15) | 1.64 (1.18–2.40) | 1.75 (1.30–2.20) | 2.18 (1.31–2.99) | 1.90 (1.44–2.75) | <0.001 |
| eGFR CKD-EPI, mL/min per 1.73 $m^2$ | 48.7 (32.4–70.8) | 45.1 (30.6–62.6) | 41.0 (26.9–57.7) | 34.4 (21.4–54.1) | 35.0 (26.0–49.0) | 27.4 (18.5–50.9) | 31.6 (22.7–42.5) | <0.001 |
| NT-proBNP, pg/mL | 3135 (1636–7476) | 4466 (2272–7950) | 4467 (2294–12 492) | 8199 (4247–18 267) | 10033 (5170–22 390) | 15106 (7697–30 722) | 18780 (6230–49 480) | <0.001 |
| BNP, pg/mL | 530 (278–1119) | 565 (318–1139) | 578 (252–1249) | 818 (291–1365) | 1005 (561–2424) | 1113 (981–1534) | 1802 (740–3301) | <0.001 |
| Hemoglobin, g/dL | 12.3 (10.9–13.6) | 12.0 (10.6–13.5) | 12.1 (10.6–13.7) | 11.7 (10.1–13.5) | 12.0 (10.6–13.3) | 11.7 (9.8–12.9) | 12.0 (10.8–13.0) | 0.043 |
| Sodium, mmol/L | 141 (138–142) | 140 (138–142) | 140 (137–142) | 138 (136–140.5) | 139 (136–140) | 138 (135–140) | 136 (132–141) | <0.001 |
| Potassium, mmol/L | 4.2 (3.9–4.5) | 4.2 (3.8–4.6) | 4.1 (3.7–4.6) | 4.2 (3.9–4.6) | 4.3 (3.7–4.8) | 4.0 (3.8–4.5) | 4.1 (3.6–4.7) | 0.62 |
| AST, UI/L | 25 (19–37) | 24 (18–34) | 25 (19–34) | 28 (20–40) | 27 (19–40) | 32 (22–56) | 29 (21–98) | 0.001 |
| ALT, UI/L | 20 (14–36) | 19 (14–32) | 20 (14–31) | 20 (15–33) | 21 (14–50) | 24 (15–53) | 23 (15–75) | 0.041 |
| Total bilirubin, mg/dL | 0.80 (0.52–1.10) | 0.83 (0.56–1.31) | 0.83 (0.51–1.33) | 0.93 (0.62–1.40) | 1.00 (0.66–1.55) | 0.87 (0.62–1.30) | 1.00 (0.63–2.10) | 0.003 |

Data are presented as n (%) and median (Q25–Q75). ALT indicates alanine transaminase; AST, aspartate transaminase; BNP, B-type natriuretic peptide; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RV, right ventricle; and TR, tricuspid regurgitation.

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## DISCUSSION

Our analysis of the multicenter, contemporary, real-world HELP-HF registry including 1149 patients with HF and at least 1 "I Need Help" criterion demonstrated that an increasing number of "I Need Help" criteria identified those patients with a worse clinical profile and signs of more advanced HF and was independently associated with a higher risk of all-cause mortality or HF hospitalization and of all-cause mortality alone. The subsets of patients with 6 and 7-to-9 "I Need Help" criteria carried the worst prognosis and had a high risk of adverse outcomes. These findings were consistent at subanalyses evaluating only inpatients and only patients with LVEF ≤40%, respectively. When assessing the prognostic impact of each individual "I Need Help" criterion, need of inotropes, persisting NYHA classes III and IV and persistently high natriuretic peptides, end-organ dysfunction, >1 HF hospitalization in the last year, persisting fluid overload and increasing diuretic requirement, and low blood pressure were the criteria independently associated with a higher risk of all-cause mortality or HF hospitalization. Except for multiple HF hospitalizations in the last year, the same criteria were also independently associated with all-cause mortality.

To the best of our knowledge, this is the first study focusing on the prognostic impact of the "I Need Help" classification in patients with HF. The "I Need Help" markers were originally proposed in 2017 as a useful screening tool to easily and timely identify patients with signs and symptoms of advanced HF.[7] Subsequently, the application of these criteria has been suggested to avoid a delayed referral of patients with HF to specialized centers or teams evaluating suitability for heart replacement therapies (such as heart transplantation or left ventricular assist device implantation).[2,4] As expected, in our study,

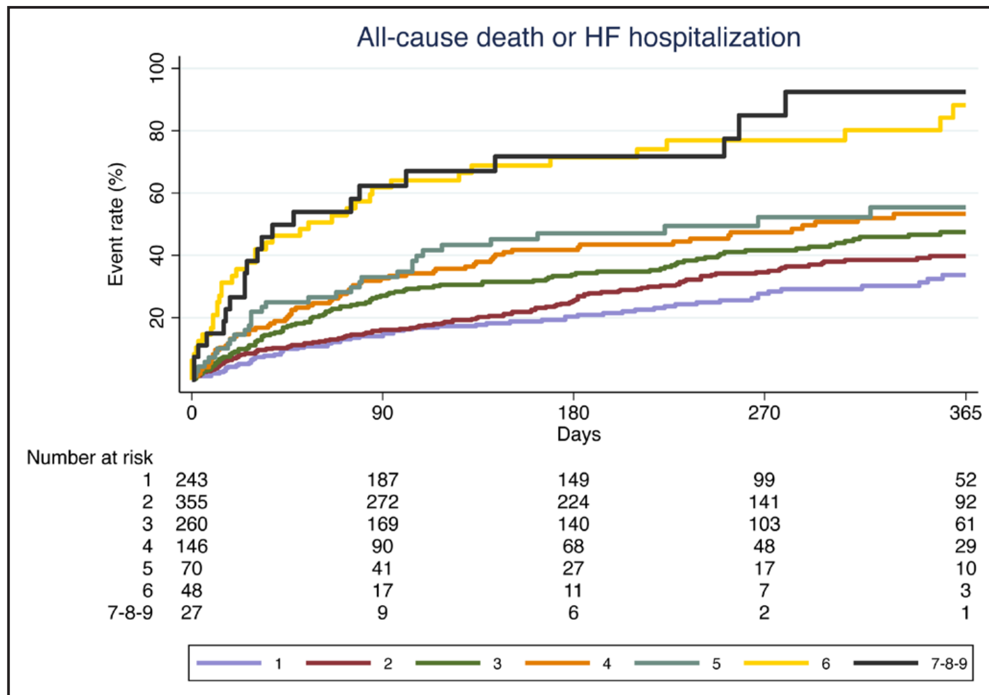


**Figure 2. All-cause mortality or heart failure (HF) hospitalization.**
The figure shows the Kaplan-Meier curves for 1-year composite of all-cause mortality or first HF hospitalization (primary end point) according to the number of "I Need Help" criteria fulfilled.

we observed a worse clinical profile and a progressively higher risk of clinical events in patients with HF fulfilling higher number of "I Need Help" criteria, with those having 6 or 7-to-9 criteria experiencing the worst prognosis. A significantly higher risk of mortality or HF hospitalization was observed for each criterion increase (adjusted HR, 1.19 [95% CI, 1.11–1.27]; $P$<0.001). These findings suggest the potential usefulness of these criteria not only to early identify patients with advanced HF despite the presence of 1 or 2 "I Need Help" markers but also

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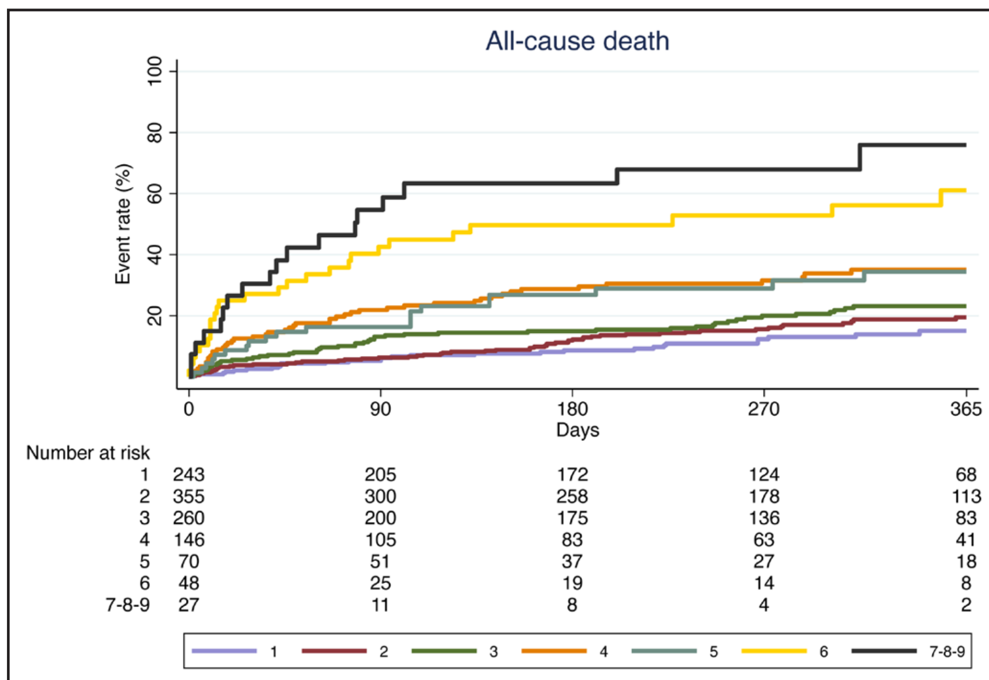


**Figure 3. All-cause mortality.**
The figure shows the Kaplan-Meier curves for 1-year all-cause mortality (secondary end point) according to the number of "I Need Help" criteria fulfilled.

**Table 3. Impact of the Cumulative Number of "I Need Help" Criteria on Clinical Outcomes**

| No. of "I Need Help" criteria | n | All-cause death or HF hospitalization | | | | All-cause death | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Univariable analysis | | Multivariable analysis* | | Univariable analysis | | Multivariable analysis† | |
| | | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| 1 (reference) | 243 | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| 2 | 355 | 1.33 (0.99–1.78) | 0.06 | 1.31 (0.96–1.79) | 0.09 | 1.42 (0.91–2.21) | 0.12 | 1.49 (0.92–2.43) | 0.11 |
| 3 | 260 | 1.88 (1.40–2.53) | <0.001 | 1.68 (1.22–2.33) | 0.002 | 1.92 (1.23–2.99) | 0.004 | 1.72 (1.04–2.85) | 0.034 |
| 4 | 146 | 2.04 (1.47–2.84) | <0.001 | 1.49 (1.03–2.16) | 0.032 | 3.29 (2.09–5.18) | <0.001 | 2.29 (1.35–3.87) | 0.002 |
| 5 | 70 | 2.27 (1.51–3.43) | <0.001 | 1.69 (1.08–2.65) | 0.022 | 2.73 (1.54–4.83) | 0.001 | 1.75 (0.92–3.32) | 0.09 |
| 6 | 48 | 5.45 (3.67–8.10) | <0.001 | 3.59 (2.26–5.70) | <0.001 | 6.34 (3.73–10.76) | <0.001 | 3.87 (2.05–7.32) | <0.001 |
| 7–9 | 27 | 5.77 (3.56–9.35) | <0.001 | 3.52 (2.05–6.06) | <0.001 | 9.68 (5.37–17.46) | <0.001 | 4.48 (2.23–8.98) | <0.001 |
| Each criterion increase | | 1.31 (1.24–1.38) | <0.001 | 1.19 (1.11–1.27) | <0.001 | 1.40 (1.31–1.50) | <0.001 | 1.22 (1.12–1.33) | <0.001 |

Data are presented as HR and 95% CI. eGFR indicates estimated glomerular filtration rate; HF, heart failure; HFA-ESC, Heart Failure Association of the European Society of Cardiology; HR, hazard ratio; and NYHA, New York Heart Association.

*Adjusted for age, sex, HFA-ESC–defined advanced HF, inpatient vs outpatient status, NYHA classes III and IV, eGFR, peripheral artery disease, prior stroke or transient ischemic attack, history of atrial fibrillation, prior myocardial infarction, chronic obstructive pulmonary disease, and systolic blood pressure.

†Adjusted for age, sex, HFA-ESC–defined advanced HF, inpatient vs outpatient status, NYHA classes III and IV, eGFR, peripheral artery disease, prior stroke or transient ischemic attack, history of atrial fibrillation, prior myocardial infarction, chronic obstructive pulmonary disease, systolic blood pressure, and heart rate.

to further stratify those patients fulfilling several "I Need Help" markers and experiencing a high risk of clinical events. In detail, the patients fulfilling 6 and 7-to-9 criteria in our study had a 1-year estimated rate of mortality or HF hospitalization of 87.6% and 91.2%, respectively, with 1-year mortality of 61.0% and 77.4%. Along with the use of more strict and validated definitions for advanced HF, such as that proposed by the Heart Failure Association of the European Society of Cardiology in 2018,[8,10] the simple "I Need Help" mnemonic could be useful to screen and also risk stratify patients with HF.

Regarding the prognostic impact of each individual "I Need Help" criterion, previous or ongoing need of inotropes, NYHA classes III and IV and persistently high natriuretic peptides, end-organ renal or liver dysfunction in the setting of HF, >1 HF hospitalization in the last year, persisting fluid overload and increasing diuretic requirement, and consistently low blood pressure were the 3 criteria independently associated with a higher risk of all-cause mortality or HF hospitalization. The prognostic role of these criteria underlines the profound relationship between cardiac-related hemodynamic parameters, persisting or worsening congestion, and noncardiac end-organ function in patients with advanced HF. Blood pressure is strongly related to stroke volume, peripheral hypoperfusion, and use of inotropes and represents a powerful prognostic marker in patients with HF.[11,12] Furthermore, hypoperfusion and the related need of intravenous inotropes are frequently accompanied by markers of end-organ injury that further worsen prognosis in the setting of HF.[13–15] In addition to these factors, NYHA classes III and IV and recurrent HF hospitalizations are relevant and well-known prognostic markers in HF,[1,14,16,17] and persisting edema or increasing diuretic requirement underlines the pivotal role of congestion in patients with worsening HF and advanced HF.[2,18,19]

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**Table 4. Impact of Each "I Need Help" Criterion on Clinical Outcomes**

| "I Need Help" criterion | All-cause death or HF hospitalization | | | | All-cause death | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariable analysis | | Multivariable analysis | | Univariable analysis | | Multivariable analysis | |
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Inotropes | 1.71 (1.41–2.07) | <0.001 | 1.64 (1.33–2.02) | <0.001 | 2.53 (1.98–3.24) | <0.001 | 2.37 (1.81–3.12) | <0.001 |
| NYHA class/natriuretic peptides | 1.40 (1.16–1.69) | <0.001 | 1.37 (1.12–1.66) | 0.002 | 1.62 (1.24–2.11) | <0.001 | 1.58 (1.20–2.09) | 0.001 |
| End-organ dysfunction | 1.58 (1.32–1.90) | <0.001 | 1.44 (1.19–1.73) | <0.001 | 2.03 (1.59–2.58) | <0.001 | 1.84 (1.44–2.37) | <0.001 |
| Ejection fraction <20% | 1.20 (0.95–1.52) | 0.12 | 0.96 (0.75–1.24) | 0.77 | 1.27 (0.92–1.73) | 0.14 | 0.83 (0.59–1.17) | 0.29 |
| Defibrillator shocks | 1.39 (0.92–2.09) | 0.12 | 1.20 (0.78–1.85) | 0.41 | 1.55 (0.91–2.66) | 0.11 | 1.30 (0.74–2.29) | 0.37 |
| >1 HF hospitalization in the last year | 1.55 (1.28–1.87) | <0.001 | 1.29 (1.06–1.57) | 0.012 | 1.45 (1.12–1.88) | 0.005 | 1.10 (0.84–1.44) | 0.51 |
| Edema or escalating diuretics | 1.39 (1.16–1.68) | <0.001 | 1.55 (1.28–1.88) | <0.001 | 1.37 (1.07–1.77) | 0.014 | 1.59 (1.23–2.07) | 0.001 |
| Low blood pressure | 1.60 (1.31–1.94) | <0.001 | 1.47 (1.16–1.86) | 0.001 | 1.91 (1.48–2.46) | <0.001 | 1.57 (1.15–2.13) | 0.004 |
| Prognostic medications | 1.24 (1.03–1.49) | 0.024 | 1.00 (0.80–1.26) | 0.98 | 1.41 (1.10–1.81) | 0.006 | 1.00 (0.75–1.35) | 0.98 |

Data are presented as HR and 95% CI. In the multivariable models, each criterion is adjusted for all other 8 criteria. HF indicates heart failure; HR, hazard ratio; and NYHA, New York Heart Association.

Beyond history of multiple hospitalizations in the previous year, signs of persisting fluid overload and worsening symptoms, that are frequently adopted criteria to identify patients with advanced HF,[1,2] our findings suggest that also other parameters related to signs of hypotension, hypoperfusion, or end-organ damage are powerful predictors of adverse outcome and need to be considered for a timely referral for heart replacement therapies and palliative care.[2,4,9,20–22]

In the context of the several criteria and definitions of advanced HF that have been proposed in the last years,[1,2,5,6,23] the "I Need Help" mnemonic could represent a useful screening tool to consider the presence of advanced HF and subsequently apply stricter classifications. Our analysis suggests that this screening tool may also have a prognostic significance among patients with HF.

## Limitations

Our study has all the limitations associated with its retrospective design. The clinical outcomes were reported by local investigators and not independently adjudicated, and the follow-up was relatively short (median, 260 days) although with a consistent number of events. Most included patients fulfilled 1-to-3 "I Need Help" criteria; therefore, patients fulfilling a high number of "I Need Help" criteria were relatively underrepresented in this study. Larger prospective studies are needed to confirm our findings and better delineate the role of the "I Need Help" criteria in the identification and prognostic stratification of patients with advanced HF.

## Conclusions

In our multicenter, contemporary, real-world study enrolling patients with HF and at least 1 "I Need Help" marker for advanced HF, an increasing number of "I Need Help" criteria was independently associated with a worse prognosis. Need of inotropes, NYHA classes III and IV and high natriuretic peptides, end-organ dysfunction, multiple HF hospitalizations, persisting fluid overload and escalating diuretics, and low blood pressure were the individual "I Need Help" criteria associated with a higher risk of all-cause mortality or HF hospitalization. Further studies are needed to confirm and better characterize the impact of these criteria as screening markers and prognostic indicators in advanced HF.

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## ARTICLE INFORMATION

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### Supplemental Material

Tables S1–S4

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