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ORIGINAL RESEARCH

PRADOC: A Multicenter Randomized Controlled Trial to Assess the Efficiency of PRADO-IC, a Nationwide Pragmatic Transition Care Management Plan for Hospitalized Patients With Heart Failure in France

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BACKGROUND: The PRADO-IC (Programme de Retour à Domicile après une Insuffisance Cardiaque) is a transition care program designed to improve the coordination of care between hospital and home that was generalized in France in 2014. The PRADO-IC consists of an administrative assistant who visits patients during hospitalization to schedule follow-up visits. The aim of the present study was to evaluate the PRADO-IC program based on the hypotheses provided by health authorities.

METHODS AND RESULTS: The PRADOC study is a multicenter, controlled, randomized, open-label, mixed-method trial of the transition program PRADO-IC versus usual management in patients hospitalized with heart failure (standard of care group; NCT03396081). A total of 404 patients were recruited between April 2018 and May 2021. The mean patient age was 75 years (±12 years) in both groups. The 2 groups were well balanced regarding severity indices. At discharge, patients homogeneously received the recommended drugs. There was no difference between groups regarding hospitalizations for acute heart failure at 1 year, with 24.60% in the standard of care group and 25.40% in the PRADO-IC group during the year following the index hospitalization (hazard ratio, 1.04 [95% CI, 0.69–1.56]; *P*=0.85) or cardiovascular mortality (hazard ratio, 0.67 [95% CI, 0.34–1.31]; *P*=0.24).

CONCLUSIONS: The PRADO-IC has not significantly improved clinical outcomes, though a trend toward reduced cardiovascular mortality is evident. These results will help in understanding how transitional care programs remain to be integrated in pathways of current patients, including telemonitoring, and to better tailor individualized approaches.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifier: NCT03396081.

Key Words: heart failure ■ mixed-methods study ■ readmission ■ transition program

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CLINICAL PERSPECTIVE

What Is New?

- Transition care programs are dedicated to improving the coordination of care between hospital and home; they appear to be particularly important regarding this vulnerable period following hospitalization for heart failure.
- The PRADO-IC (Programme de Retour à Domicile après une Insuffisance Cardiaque) is a transition care program that was generalized in France in 2014; in the present randomized study, the PRADO-IC has not significantly improved clinical outcomes, though there is a trend toward reduced cardiovascular mortality.

What Are the Clinical Implications?

- These results will help in understanding how transitional care programs remain to be integrated in current pathways of patients, including telemonitoring, and to better tailor individualized approaches.

Nonstandard Abbreviations and Acronyms

CNAM	caisse nationale d'assurance maladie
GP	general practitioner

The prevalence of heart failure (HF) is ≈1% to 2% in adults.[1] HF hospitalizations represent 1% to 2% of all hospital admissions.[2,3] Approximately half of the patients will be admitted at least once within 1 year after diagnosis, and 20% will be readmitted within that same year.[1,4] Thus, optimizing the transition between hospitalization and return to home is crucial. Building an adequate transition care program relies on the conceptual framework of coordination of care and the ability to improve the quality of care.[5] This could imply early follow-up,[6] as well as organizational approaches from a hospital-centered system, a more patient-centered system, including telemonitoring, and requiring various health providers, leading to complex organizational programs. As the holy grail, an "ideal" intervention could be appealing but impossible to translate worldwide into real life. A previous trial evaluated a program comprising nurse-led self-care education, structured hospital discharge summary, and family physician follow-up <1 week after discharge, with structured nurse home visits and heart function clinics for high-risk patients.[7] This could be difficult to apply worldwide, but the study was surprisingly neutral. In contrast, several meta-analyses have shown that transition care programs are effective at preventing HF readmissions, but results were not consistent between studies, the level of evidence was very low, and weak internal validity was present.[8–13] This is clearly an important knowledge gap.[1,14]

In France, all people are covered by public mandatory health insurance, managed by the Caisse Nationale d'Assurance Maladie (CNAM). The CNAM and the French Society of Cardiology designed a transition care program called Programme de Retour à Domicile après une Insuffisance Cardiaque (PRADO-IC). PRADO-IC was generalized in France in 2014 with the aim to reduce the annual death rate by 20% and the annual HF readmission rate by 30%. The target population consists of patients with HF living at home. The PRADO-IC consists of an administrative assistant who visits patients during hospitalization to schedule follow-up visits with the general practitioner (GP) and cardiologist, and to apply for the social benefits of the CNAM, which comprise a nurse follow-up at 2 (for patients classified NYHA I-II) to 6 months (in case of NYHA III-IV) to assess clinical signs and symptoms of HF, provide pragmatic advice on self-care, and fill out a coordination notebook held by the patient. The PRADO is easily available because it is entirely funded by the CNAM without conditions for hospitals or patients and because it is not time-consuming for usual health care workers.

No previous randomized controlled trial of PRADO-IC has been conducted. However, the French PRADO system has been evaluated in a pragmatic approach.[15] In this observational single-center study, the primary end point was 1-year mortality and HF readmission at 1 year. Despite no impact on the primary end point, the authors emphasized that the most severely ill patients were included in the program, suggesting the interest of this approach, which makes sense from a clinical perspective but deserves to be investigated at a higher level through a dedicated study.

Thus, the present study aimed to evaluate the PRADO-IC program using a design based on the hypotheses provided by health authorities.[16]

METHODS

Design

The PRADOC study is a controlled, randomized, open-label, mixed-method trial of the transition program PRADO-IC versus usual management in patients hospitalized with HF. The trial was conducted by a multidisciplinary team. The study protocol and methods were reviewed by the Ethics Committee CPP SE-I (Ref 2017-64) (NCT03396081). All patients gave informed consent to enter the study. The study protocol was published elsewhere in detail.[16]

The PRADO program had been exhaustively implemented at a nationwide level by the CNAM; 10 223, 14 865,

18075, 11320, and 13423 patients were included in the program at the national level during 2017, 2018, 2019, and 2020 (data from the CNAM). During the duration of the study, the CNAM continued to be both supportive of the program in daily practice and to promote the trial. The scientific committee was independent from the CNAM.

A total of 404 patients were recruited between April 2018 and May 2021 from the cardiology wards of 5 centers, including 3 university hospitals, 1 public hospital, and 1 private hospital. Patients were assessed consecutively for eligibility, and eligible patients were included during weekdays.

The selection criteria were mainly those of the PRADO-IC (pragmatic approach): adult patients hospitalized for acute HF (regardless of ejection fraction) who were discharged to home and independent at home, without terminal kidney failure, significant cognitive impairment, or behavioral disorders. Other exclusion criteria were patients in palliative care, patients with a programed treatment of the cause in the short term (valvular surgery, transcatheter aortic valve implantation, removal of arrhythmogenic focus, heart transplantation), patients planning to move into an Elderly Care Home in the next 6 months, not speaking French, pregnant women, prisoners, and patients participating in another interventional research protocol.

Intervention: The PRADO-IC Program

The experimental intervention was a transition care program between acute (hospitalization for acute HF) and ambulatory care. The intervention was the program developed and implemented at the national level, without any additional intervention. Health providers at each hospital were informed of the ongoing trial before its start. The hospital physician in charge assessed the eligibility of patients and prescribed the program, which comprises 3 elements. First, an administrative assistant visits patients during hospitalization and checks whether they need help to make an appointment with their health providers (GP, cardiologist, and nurse). When adapted, the administrative assistant makes the 3 separate appointments early after discharge: during the following week for GP and nurse, and the 2 first months for the cardiologist. Moreover, the administrative assistant organizes an appointment with the social service of the National Social Insurance if needed. Second, a systematic nurse follow-up is set at home. For all patients, an initial pattern of 1 nursing visit per week is scheduled for 2 months (8 visits total). For patients with NYHA III and IV, bimonthly visits are scheduled for an additional period of 4 months. During these half-hour visits, the nurse monitors HF signs and symptoms and delivers education, including self-care development. Nurses have all received the same training using an e-learning program developed by the French Society of Cardiology and the CNAM. Third, a follow-up notebook is delivered to patients during their hospitalization. The notebook contains personalized clinical monitoring advice, the treatment prescribed at discharge, contact details of health providers, dates of appointments, and any pertinent follow-up information that health providers need to share with colleagues.

It was a pragmatic design so that both groups could receive strong recommendations from the hospital team to visit a GP or cardiologist early after discharge. Other health providers, especially the GP, could also prescribe a nurse follow-up or whatever they found appropriate, independent of the hospital physician.

Randomization

Patients were individually randomized using a centralized method based on a minimization algorithm accessible online (Ennov Clinical Software). Stratification criteria were the inclusion center and current attendance by the patient at an independent patient education program. They were allocated to either the standard of care group or the groups benefiting from the PRADO-IC program (PRADO-IC).

Primary Outcome

The primary efficacy outcome was collected over 1 year and comprised hospitalizations for acute HF.

The secondary end points were collected over 1 year and comprised hospitalizations for any cause, death from cardiovascular cause (codes I00 to I99, *International Classification of Diseases, Tenth Revision* [*ICD 10*]), and death from any cause.

Sample Size

The sample size was calculated based on the effectiveness criterion of the main outcome as described in detail elsewhere.[16] Briefly, the objective of the PRADO plan was to achieve a relative reduction of 30% in the risk of re-hospitalization for HF. In the control group, the expected readmission rate was 45% during the first year after the index event.

To demonstrate this risk reduction, with a 5% bilateral alpha risk and a power of 80%, 10% potential dropout and loss of follow-up, 404 subjects needed to be recruited.

Data Analysis

Analyses were performed by the Public Health Department of the University Hospital of Montpellier (France) using the SAS 9.4 statistical software (NC, Cary), and the level of significance for each test was set at 0.05. All data were described using mean and SE or median and quartiles (Q1-Q3) for quantitative variables depending on their distribution, and using frequencies and percentages for qualitative variables.

For censored outcomes, follow-up times were calculated from date of discharge to date of event, and groups were compared using Kaplan–Meier curves and log-rank tests. Hazard ratios were calculated using nonadjusted Cox models.

Sensitivity analyses of the primary outcome were performed to take into account all collected outcomes. Zero inflated negative binomial models were used to analyze recurrent hospitalizations, and win-ratio analyses was used to analyze recurrent events.

Modification of the efficacy of PRADO-IC on the primary outcome by inclusion during lockdown, age, and left ventricular ejection fraction (LVEF) was assessed by testing interactions in a multivariate Cox model. More than half of patients (≈60%) had been included before the lockdown due to the COVID-19 pandemic.

RESULTS

Population

As shown in Figure 1 and Table 1, 404 patients were recruited as expected. The mean age was 75±12 years in both groups. Baseline characteristics are reported in Table 1. The patients were mainly male and had rarely benefited from educational programs (≈5%). The SOC and interventional groups were well balanced regarding severity indices; at admission, 47% and 54% of patients, respectively, presented with NYHA class III and 43% and 38% with NYHA class IV. Furthermore, NT-proBNP (N-terminal pro-B-type natriuretic peptide) was 8991 ng/L and 8678 ng/L in the SOC and intervention groups, respectively, and the main comorbidities were well balanced, including hypertension (64% and 70%) and diabetes (32% and 39%). The first cause for HF was ischemic (52% and 51%).

Intrahospital Evolution

Dyspnea largely improved during hospitalization, with a minority of patients being NYHA III at discharge (8% and 12%). Consistently, the NT-proBNP level decreased ≈50% (4123 ng/L and 4465 ng/L). Nineteen patients were not discharged home, and 1 patient died the night following his discharge (Figure 1).

Treatment at Discharge

At discharge, most patients received loop diuretics (89% in both groups). The patients homogeneously received the recommended drugs, including β-blockers (83% in both groups), sacubitril-valsartan (26% and 27%), or spironolactone (38% and 33%).

Intervention

The intervention is described in Table 2. More than 90% of patients in the PRADO-IC group benefited from the

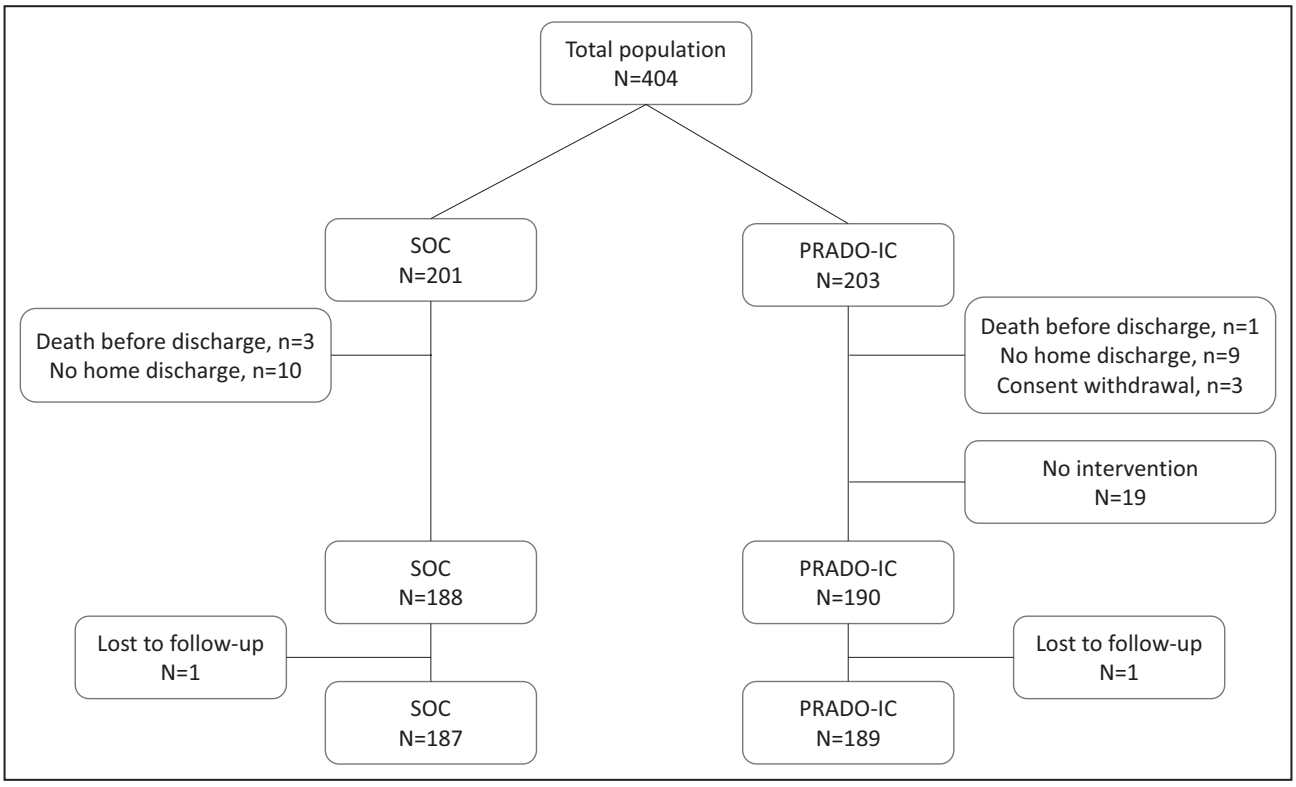

Figure 1. Study flowchart.
PRADO-IC indicates Programme de Retour à Domicile après une Insuffisance Cardiaque; and SOC, standard of care.

Table 1. Baseline Characteristics of the Population

	Standard of care N=201	PRADO-IC N=203	*P* value
General characteristics on admission			
Sex, male	138 (68.66)	143 (70.44)	0.70
Age (y)	74.94±12.25	75.45±11.65	0.83
Previous TE	10 (5.03)	11 (5.47)	0.84
NYHA			
I	0 (0.00)	2 (1.05)	0.22
II	18 (9.57)	13 (6.81)	
III	89 (47.34)	104 (54.45)	
IV	81 (43.09)	72 (37.70)	
NT-proBNP (ng/L)	8991.04±11989.55	8677.51±10122.95	0.71
GFR (mL/min)	58.15±25.45	55.32±24.00	0.30
Hemoglobin (g/dL)	12.87±2.29	12.74±2.25	0.56
Ferritin (µg/L)	248.97±268.61	243.37±300.75	0.64
Transferrin saturation coefficient (%)	19.98±18.54	17.13±12.87	0.41
Comorbidities			
Hypertension	128 (63.68)	143 (70.44)	0.15
Diabetes	65 (32.34)	80 (39.41)	0.14
Dyslipidemia	98 (49.00)	91 (44.83)	0.40
PAD	45 (22.39)	49 (24.38)	0.64
Tabagism	37 (19.07)	38 (19.59)	0.90
SAS	29 (15.85)	36 (20.34)	0.27
Cardiopathy			
Ischemic	104 (51.74)	103 (51.24)	0.92
Valvulopathy	42 (20.90)	43 (21.39)	0.90
Arrhythmias	89 (44.50)	94 (47.00)	0.62
Idiopathic dilated	41 (20.60)	30 (15.00)	0.14
Hospitalization			
Duration (d)	9.76±8.23	9.73±7.37	0.67
Discharge			
NT-proBNP (ng/L)	4123.33±5755.42	4465.41±5860.65	0.64
LVEF (%)	38.45±13.28	41.62±15.78	0.07
NYHA			
I	9 (5.88)	16 (10.39)	0.22
II	129 (84.31)	119 (77.27)	
III	12 (7.84)	18 (11.69)	
IV	3 (1.96)	1 (0.65)	
Treatment at discharge			
β-blockers	165 (82.91)	165 (82.91)	1.00
ACE-i/ARB	83 (41.71)	70 (35.18)	0.18
Sacubitril/valsartan	52 (26.13)	53 (26.63)	0.91
Spironolactone	75 (37.69)	66 (33.17)	0.35
Triple association (ACE-i or ARB or sacubitril/valsartan)	57 (28.64)	48 (24.12)	0.31
Loop diuretic	177 (88.94)	177 (88.94)	1.00

Data are expressed as mean±SD or n (%) as appropriate. ACE-i indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PAD, peripheral artery disease; PRADO-IC, Programme de Retour à Domicile après une Insuffisance Cardiaque; SAS, sleep apnea syndrome; and TE, therapeutic education.

program (91%). Specific reasons for failure to implement the program are detailed in Table 2. It was for internal organizational reasons (eg, too short a delay before discharge) in 32% of the cases, or because they were finally not discharged to home (21%) or were transferred to another department (16%). More than 90% of the patients included in

Table 2. Description of the PRADO-IC Intervention

Description of the intervention	Number of patients (%)
Initiation of the programme (N=203)	
No	19 (9.4)
Reasons for not initiating the programme (N=19)	
Transfer to another hospital department	3 (15.8)
Other programme (similar but dedicated to pneumology)	2 (10.5)
Internal problem implementing the programme before discharge (eg, availability of dedicated operators)	6 (31.6)
No home discharge (recovery, rehabilitation)	4 (21.0)
No phone, no contact	1 (5.3)
Unknown reason	3 (15.8)
Components of the programme	
General practitioner (N=177), number of appointments	164 (92.7)
Delay between discharge and appointment (d)	5 (3–8)
Cardiologist (N=182), number of appointments	165 (90.7)
Delay between discharge and appointment (d)	39 (28–58)
Nurse (N=182), number of appointments	177 (97.3)
Delay between discharge and appointment (d)	3 (1–5)
Social worker (N=160), number of appointments	11 (6.9)

Values are given as n (%) or median (Q1-Q3). PRADO-IC indicates Programme de Retour à Domicile après une Insuffisance Cardiaque.

the program benefited from the appointments as planned with the health providers: 93% with the GP, 93% with the cardiologist, and 97% with the nurse.

Primary End Point

One patient was lost to follow-up in each group. As depicted in Figure 2, there was no difference between the 2 groups regarding hospitalizations for acute HF at 1 year, with 24.60% in the standard of care group and 25.40% in the PRADO-IC group during the year following the index hospitalization (hazard ratio [HR], 1.04 [95% CI, 0.69–1.56]; *P*=0.85). When recurrent events were considered, there was a trend of reduced recurrent events, but it was not significant (data not shown). The efficacy of the PRADO-IC was not modified by the lockdown for COVID-19, age, or LVEF (data not shown).

Secondary End Points

In Cox models, the PRADO-IC did not significantly improve all-cause readmissions (HR, 1.13 [95% CI, 0.83–1.53]; *P*=0.44), cardiovascular mortality (HR, 0.67 [95% CI, 0.34–1.31]; *P*=0.24), or all-cause mortality (HR, 1.10 [95% CI, 0.67–1.80]; *P*=0.71; Figure 2 and Figures S1–S4).

Impact of Socioeconomic Factors

There was no impact of classical patients' socioeconomic factors. Indeed, income was dichotomized (threshold=median in our sample). It was well balanced between groups. Readmissions for acute HF did not differ according to income (22.2% versus 21.7%), nor did all-cause readmissions (38% versus 44%, *P*=0.35), cardiovascular mortality (3% versus 11%, *P*=0.05), or all-cause mortality (11% versus 16%, *P*=0.35). The income did not modify the effect of intervention on any of these outcomes.

The occupational class was well balanced between randomization groups. It was not associated with outcomes and did not modify the effect of intervention.

Impact of Severity of HF at Baseline, as Estimated by the Level of Natriuretic Peptide at Baseline

The level of natriuretic peptide at discharge was associated with readmission for acute HF (36% in high-BNP group versus 19% in low-BNP group, *P* <0.01), all-cause readmissions (57% versus 35%, *P* <0.01), cardiovascular death (12% versus 4%, *P*=0.03), and all-causes death (24% versus 9%, *P* <0.01). Importantly, it did not modify the effect of intervention.

Similarly, the maximal level of natriuretic peptide during hospitalization was associated with readmissions but not with mortality; importantly, it did not modify the effect of intervention.

DISCUSSION

PRADO-IC is a care transitional program implemented by the CNAM everywhere in France, with the aim of reducing the annual HF readmission rate of 30% and the annual death rate of 20%. The present study is the first prospective randomized study evaluating this program based on the initial hypotheses (Figure 3). The population is relatively small, but the number of patients had been determined based on hypotheses provided by the health insurance itself. The main findings were no difference between the 2 groups regarding hospitalizations for HF at 1 year, a trend toward less cardiovascular death in the PRADO-IC group, and no difference regarding all-cause mortality.

Transition care programs aim at improving the transition from hospital to home. They appear to be underestimated and largely understudied, though promising. They can comprise very heterogeneous elements, considered separately or combined, as reported in reviews and meta-analyses,[5,9–12,17–19] including home-visit programs, structured telephone support (nurses, other health providers), telemonitoring (weight, drugs, or others), clinic-based interventions, primarily educational interventions (targeting the patients or health providers, including GPs). Here, a pragmatic easy-to-implement program was developed by the national health insurance and evaluated through this prospective randomized trial.

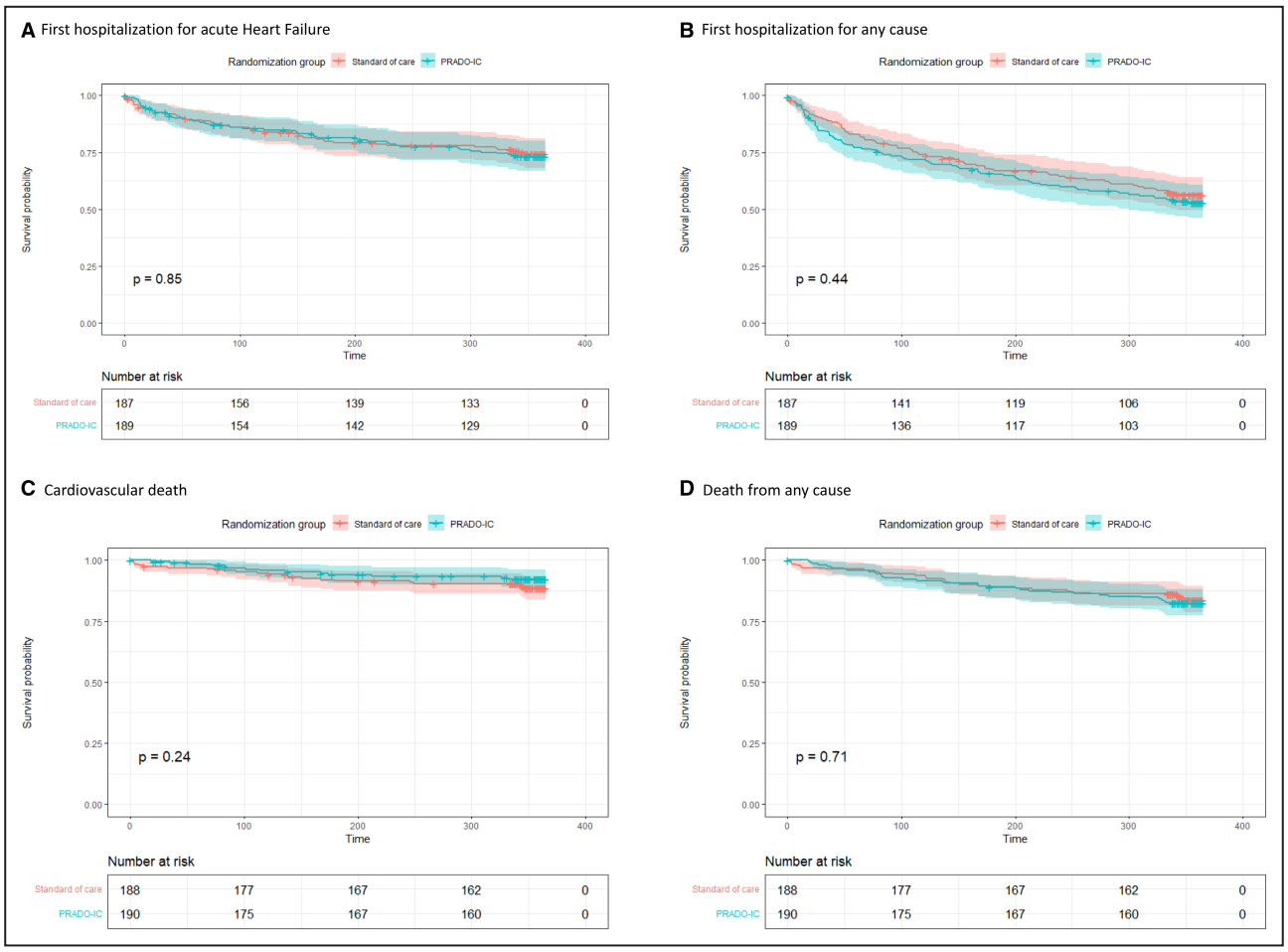

Figure 2. Comparison of outcomes in both study groups.
A, First hospitalization for acute heart failure; **B,** First hospitalization for any cause; **C**, Cardiovascular death; **D**, Death from any cause. Time is in days. *P* values of log-rank tests are given. PRADO-IC indicates Programme de Retour à Domicile après une Insuffisance Cardiaque.

Importantly, these results are not consistent with the data provided by the CNAM at the national level from the claims (no clinical trial); mortality was lower for patients benefiting from the PRADO-IC system (15.7% versus 17.5% in other patients at 6 months). However, these results have been communicated but not published in a peer-reviewed journal. Moreover, these results are from a nonrandomized study. Importantly, patients were selected to participate in a trial and, as expected, probably have less severe disease than in real life, as emphasized by a lower mortality rate at 6 months (11.1% and 11.2% here, respectively). The PRADO-IC program comprises not only medical interventions from the cardiologists and the GP but also by the nurses and social workers. In patients with more severe disease, these interventions could have a greater impact. Consistently, the impact of social deprivation or comorbidities remains to be investigated in order to better tailor the interventions.

The present study is one of the largest trials evaluating a transitional care program for HF. The small population size and generally weak methods are demonstrated in the meta-analyses in the field. In one of the latest meta-analyses, 5 of 18 included trials presented a high risk of overall bias. Only 4123 patients were included in the meta-analysis (ie, mean of ≈230 patients per study), with 2 trials including more patients than the present study. In this meta-analysis, transitional care interventions were suggested to reduce readmissions and emergency visits, but without an impact on mortality.[18] Such meta-analyses remain difficult to build and interpret because of the wide heterogeneity of interventions or the large variety of health providers involved. Among 1007 patients benefiting from a nurse-centered system, including telephone-based monitoring and education in which nurses were able to address individual problems raised by patients, as well as networking of health care providers and training for caregivers, the impact was neutral on a composite primary end point, though mortality decreased significantly.[20] Another monocentric trial found promising results in 488 patients benefiting from a complex multidisciplinary team.

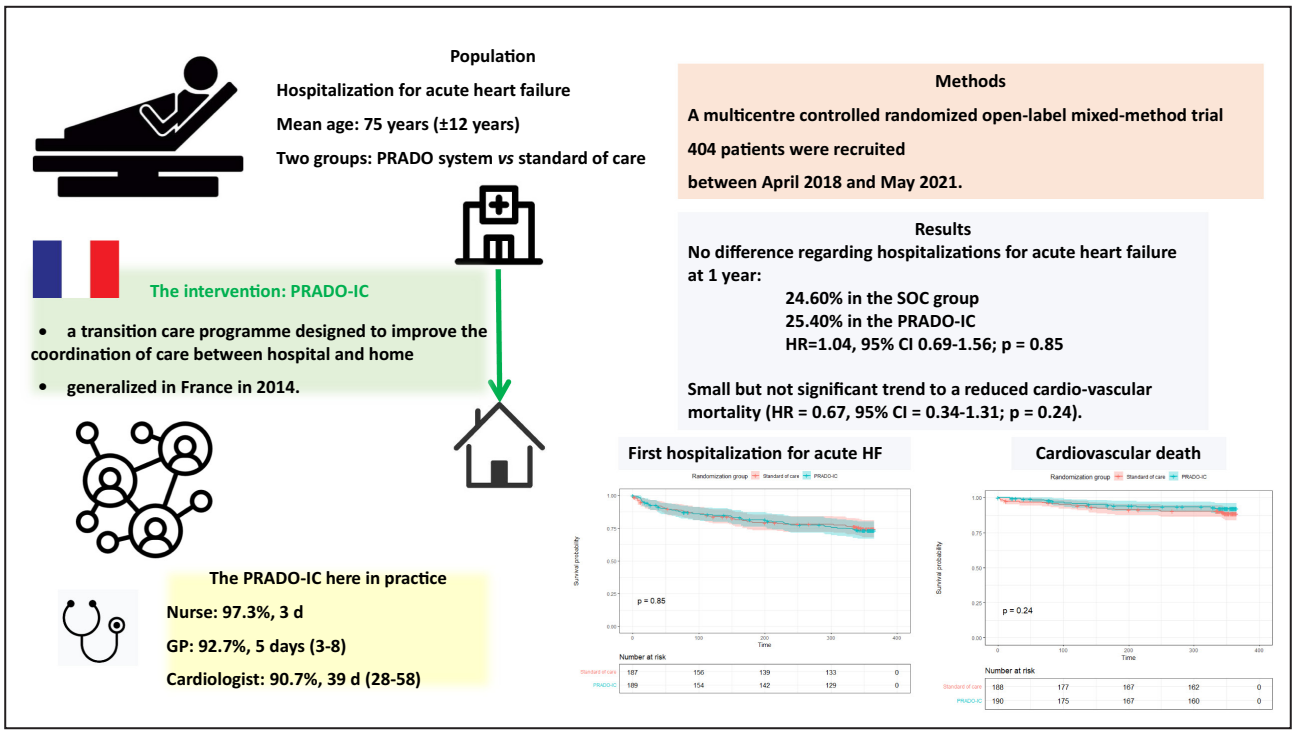

Figure 3. Study summary.
GP indicates general practitioner; HF, heart failure; HR, hazard ratio; PRADO-IC, Programme de Retour à Domicile après une Insuffisance Cardiaque; and SOC, standard of care.

The largest trial to date was conducted among 2494 patients in 2019 in Ontario, Canada.[7] Importantly, hospitals, not patients, were randomized to benefit from the intervention. The intervention could be considered "ideal" but difficult to implement worldwide in real life. It consisted of a nurse-led self-care education, structured hospital discharge summary, and family physician follow-up appointment <1 week after discharge, as well as structured nurse home visits and heart function clinics for high-risk patients. Surprisingly, the study was neutral, and the authors suggested that, even if ineffective in the Canadian context, whether this type of intervention could be effective in other health care systems deserved to be evaluated.

However, building the ideal transitional care program remains a difficult task. Some unexpected side effects could arise. For example, the addition of financial incentives could lead to adverse consequences. In a large database study in the United States, the Hospital Readmissions Reduction Program was associated with a reduction in readmissions among patients with HF but also with an increase of mortality.[13] This highlights that opposite results could be difficult to put in perspective. In other words, obtaining a reduction in mortality could rely on more hospitalizations or heavier costs, because the patients could benefit from more carers to have better outcomes. This could appear logical, but health providers and payers should have this model in mind when tailoring programs, clearly choosing the main goals alongside health providers and society. Clearly, more research is needed to assess the efficacy of the transition care program in detail and probably define the patients who benefit from these approaches. It is not clear whether all patients could be targeted, but perhaps only the older patients, those experiencing social deprivation, or who live far from health facilities, as suggested by some trials on telemonitoring of HF.[21]

This present trial has some strengths. This is one of the rare prospective randomized multicenter trials in the field, assessing a national, rather than local, program. Another strength is that the organizational tool was proposed, developed, and promoted by the health deciders, in a completely independent manner, and this study was built with input from health authorities after the system was implemented at a national level. This transitional care program is pragmatic, reliable, and built to last. In addition, both public and private centers participate, as well as very large tertiary centers or smaller centers; therefore, all types of patients were included here. Above all, in contrast to most of the experimental trials enrolling selected patients, which prevents replication in nonexperimental settings, the present design was built to be as close as possible to the real-life population as targeted by health insurance. The population included here is

closer to the real-life population than those in classical trials on drugs, with a mean age of 75 years and many comorbidities, paving the way for reliable analyses and translation into practice. We believe that the population included appears representative, in spite of some exclusion criteria. Indeed, in this pragmatic study, investigators were allowed to prioritize their clinical judgment to indicate the PRADOC. The comparison with the Observatoire Français de l'Insuffisance Cardiaque Aigue (OFICA) study {Logeart, 2013 #837} (a descriptive French cohort, representative of all patients with HF) shows that our patients are only a little younger (median 78, interquartile range [68–84], versus 79 [70–86] in OFICA), and similarly comorbid (diabetes 36% versus 31%; high blood pressure 68% versus 62%).

However, this work also has limitations. First, because the number of patients to be included had been calculated according to the hypotheses from the initial program decided by the CNAM,[16] a lack of power cannot be excluded. This does not seem to be true regarding readmissions, but it remains likely regarding cardiovascular deaths. However, based on the present HR, 1828 patients would have been mandatory to reach statistical significance if the present result was mainly due to a lack of power. Second, the system was implemented several months or years before the start of the trial, depending on the center. This means that the system should have been stabilized, but this could have induced heterogeneity between centers, because local organizations could have been impacted and necessarily reacted to these deep changes. Third, although the control group was supposed to follow international guidelines, local heterogeneity remains likely. Moreover, the center effect is probably stronger here when compared with trials with drugs because organizational aspects are crucial. To control bias, randomization was stratified on the inclusion center and the current attending of patients to a patient education program, which are the main factors responsible for the heterogeneity of care processes. The stratification should limit the subsequent confounding bias but not the selection bias; therefore, the ability to extrapolate results to other centers could be discussed further. Last, the PRADO-IC system was developed at a national level but with local resources. By definition, local facilities or personnel availabilities could have impacted the program. However, we are not able to assess this impact in detail. Because the study is multicentric, we hope this could have limited this bias.

Despite advances in HF therapy and management, the absolute number of hospital admissions for HF is expected to increase by ≈50% over the next 25 years due to a growing and aging population. The health authorities need results from a high level of evidence from trials to better understand how to articulate the present system with other innovative approaches, including telemonitoring, telemedicine, involvement of new actors, and other organizational innovations. Here, despite the negative result for hospitalizations, a trend of reduced cardiovascular mortality is promising. The present study had not been tailored to assess this hypothesis, but this finding must be kept in mind for further large-scale analyses. The paradigm will likely shift to a broader understanding of the care pathway to integrate the hospitalizations and alternatives to hospitalizations in order to offer the best care, not only to try to reduce hospitalizations. This should include new approaches with more adapted modalities for hospitalization, such as day hospitalization or ambulatory treatments[22] and health providers and payers urged to improve telemonitoring systems,[17] but also should include decisions based on individual risk stratification and dedicated support systems. Indeed, these tools could allow caregivers to better monitor patients with HF by providing access to data provided from simple and noninvasive connected devices (eg, scales or blood pressure cuffs) to sophisticated implanted devices.[17] Importantly, in France, many studies have previously demonstrated the interest of these approaches,[21,23] including medicoeconomic analyses.[24,25] Their integration into transitional care programs appears to be appealing not only to improve the care provided but also to improve the numbers and quality of outcomes evaluated.

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Supplemental Material

Figures S1–S4

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