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ORIGINAL RESEARCH

Effectiveness of an Intervention to Improve Guideline-Directed Medications for Patients With Acute Heart Failure: A Randomized Clinical Trial

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BACKGROUND: Guideline-directed medical therapy during the transitional period is crucial for improving outcomes in heart failure with reduced ejection fraction. We investigated whether a simplified transitional care intervention could increase guideline-directed medical therapy adherence in patients with acute heart failure (HF).

METHODS: This multicenter, open-label randomized trial enrolled 982 patients with acute HF. The transitional care intervention included a discharge checklist, HF education, and telephone monitoring. The primary outcome was achievement of high guideline adherence indicator, defined as the prescription of all 3 guideline-directed medical therapy drugs (renin-angiotensin system blockades, beta blockers, and mineralocorticoid receptor antagonists) at 6 months. Both modified intention-to-treat and per-intervention analyses were conducted to evaluate the effectiveness of intervention components.

RESULTS: Among 982 participants (mean age, 62.4±15.5 years; 64.5% male), there was no statistical difference in the proportion achieving a high guideline adherence indicator between the intervention and control groups (49.6% versus 44.6%; OR, 1.12; 95% CI, 0.86–1.45; *P*=0.37). No significant differences were observed in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score or clinical outcomes. In the per-intervention analysis, patients who received all components showed significantly higher guideline adherence indicator achievement compared with those who received no components (adjusted odds ratio [OR], 1.56 [95% CI, 1.07–2.27], *P*=0.02).

CONCLUSIONS: In this randomized trial of patients with acute HF, although the simplified transitional care intervention did not increase high guideline adherence indicator achievement, implementation of all intervention components was associated with improved guideline adherence. Our findings emphasize that implementation fidelity is the key challenge in optimizing transitional care for HF management.

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Key Words: acute heart failure ■ adherence ■ guidelines ■ implementation ■ transitional care

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CLINICAL PERSPECTIVE

What Is New?

- In this multicenter randomized trial of patients with acute heart failure, a simplified transitional care intervention consisting of a discharge checklist, education, and telephone monitoring improved guideline adherence only when all components were fully implemented.

What Are the Clinical Implications?

- Implementation fidelity is the critical determinant of success for transitional care, as achieving high adherence to guideline-directed medical therapy is strongly associated with significant reductions in 6-month mortality and heart failure-related hospitalizations.

Nonstandard Abbreviations and Acronyms

GAI	guideline adherence indicator
GDMT	guideline-directed medical therapy
KCCQ-CSS	Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score
MRAs	mineralocorticoid receptor antagonists
TCI	transitional care intervention

Heart failure (HF) is one of the leading causes of hospitalization among older adults, with approximately half of patients with acute HF (AHF) readmitted within 6 months.[1–4] The period within 60 to 90 days following hospital discharge is particularly vulnerable, with an increased risk of readmissions and mortality.[5,6] Early initiation and maintenance of guideline-directed medical therapy (GDMT) during this period are crucial to reducing repeated hospitalizations and mortality, especially in HF with reduced ejection fraction.[7–10]

Transitional care interventions (TCIs) are designed to ensure continuity and coordination of care as patients with AHF transition from hospital to home care during the early postdischarge management.[11] Previous studies have shown that comprehensive TCIs including home visits and disease management clinics can reduce mortality, but these resource-intensive interventions may not be feasible in many health care settings.[12,13] More important, the effectiveness of TCIs has been inconsistent across studies, highlighting the need for pragmatic trials evaluating simplified interventions.[14–17]

We designed a simplified TCI focusing on 3 evidence-based components: discharge checklists, HF education, and telemonitoring. These components were selected based on their established effectiveness and feasibility within existing health care systems.[18] The discharge checklist ensures systematic implementation of guideline recommendations, education empowers patients for self-care, and telemonitoring enables early detection of clinical deterioration.

The TRANS-HF (Optimize Heart Failure Care During Transitional Period in Patients With Acute Heart Failure) trial aimed to evaluate whether systematic implementation of these practices through a structured TCI protocol could improve guideline adherence compared with usual care. We hypothesized that this simplified TCI would increase GDMT adherence and that complete implementation of all components would be associated with better outcomes. This study was designed to provide evidence for both the effectiveness of the intervention and the importance of implementation fidelity in transitional care.

METHODS

Data Availability

Deidentified individual participant data underlying the results reported in this article, along with the study protocol, will be available upon reasonable request to the corresponding author. Access will be granted to researchers who provide a methodologically sound proposal for analyses. Data will be shared securely after the approval of the proposal and upon the execution of a formal data use agreement.

Trial Design

We conducted a multicenter, nationwide, prospective, randomized open-label, parallel-group, superiority trial to investigate the effectiveness of a simplified TCI in improving the GAI. This trial was reported in accordance with the Consolidated Standards of Reporting Trials guidelines. Due to the open-label design of the trial, participants, care providers, and data analysts were not blinded to the intervention assignment. Both modified intention-to-treat (mITT) and per-intervention analyses were planned to evaluate the effectiveness of intervention components. The mITT population was defined as all randomized patients excluding those who discontinued the intervention or were lost to follow-up. The per-intervention analysis was pre-specified to evaluate the actual effect of intervention components when fully implemented. This approach was conducted because some components of the intervention (discharge checklist, education) were already implemented as part of usual care in several centers, which could

not be restricted for ethical reasons. Between July 2020 and May 2022, patients with AHF were recruited at 16 tertiary university hospitals (Data S1). The study was approved by the institutional review board of each participating center (number CR320020), and informed consent was obtained from all participants. A detailed study trial protocol was described in the supplement files, and the prespecified statistical analysis plan is detailed in the Statistical Analysis section. Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research. There were no important changes to the trial protocol, prespecified outcomes, or planned analyses after the trial commenced.

Patients

Patients admitted with AHF were enrolled. The inclusion criteria were (1) presence of HF symptoms, or (2) presence of HF signs, or (3) evidence of pulmonary edema on chest radiography, as well as (4) objective evidence of increased left ventricular filling pressure, indicated by elevated natriuretic peptide levels, and (5) left ventricular ejection fraction ≤40%. Patients <19 years and those who did not provide informed consent were excluded. Patients were followed up for 6 months to monitor the occurrence of outcomes.

Randomization

Eligible patients were randomly assigned (1:1) to the TCI or usual care groups before discharge from the index admission. A dedicated clinical research coordinator at the coordinating center generated the random allocation sequence using a pregenerated random table based on the permuted block randomization method with a block size of 4, without any stratification factors. The sequence was maintained within the web-based case report system (iCReaT) of the Korea Disease Control and Prevention Agency. Clinical research coordinators at each participating center enrolled the participants and assigned them to interventions using this web-based system. The allocation sequence was fully concealed from investigators, as the randomization assignment was released only after patient enrollment and entry of baseline information into the system, ensuring adequate allocation concealment. A total of 16 centers participated in the trial, and 982 participants were randomized across these centers.

Intervention

This study was conducted as part of the "Development of Strategies to Enhance the Implementation of Clinical Knowledge on the Prevention, Treatment, Rehabilitation, and Intervention of Cardiovascular Diseases" project by the Korea Disease Control and Prevention Agency. The project aimed to develop a simplified transitional care protocol to improve the implementation of clinical guidelines for HF care. The TCI protocol in the current study included 3 components: (1) a discharge checklist, (2) HF education and distribution of educational materials, and (3) telephone monitoring by a specialized nurse.

To improve adherence to HF treatment guidelines among health care providers, a checklist was developed in collaboration with the Korean Society of Heart Failure and was administered on the day of discharge during the index admission. This checklist ensured the adherence to medications, such as renin-angiotensin-system (RAS) blockers, beta-blockers, mineralocorticoid receptor antagonists (MRAs), and ivabradine; anticoagulation therapy; appropriate blood pressure control; and multidisciplinary consultations with specialists for arrhythmia interventions and device therapy.[19]

For patient interventions, specialized nurses provided HF education before discharge and distributed educational materials approved by the Korean Society of Heart Failure.[20] Additionally, the intervention included at least 2 follow-up telephone consultations by the specialized nurse after discharge. The first call was scheduled within 1 week after discharge and before the first outpatient visit, and the second call was conducted within 2 to 4 weeks after discharge. During these calls, the specialized nurse monitored key clinical parameters including degree of dyspnea, symptom improvement after discharge, body weight, blood pressure, and presence of edema. If any concerning changes were identified, the nurse contacted the physician and guided patients for early heart failure clinic visits as needed. To standardize the interventions for the experimental group, the same educational materials and telephone monitoring protocols were used, and training was provided to ensure consistency (Data S2). In the usual care group, transitional care was provided according to institutional protocols at each site. The implementation of specific components varied across centers, with discharge checklists used in 3 hospitals and HF education programs in 8 hospitals as part of their standard care. Patients in both groups could receive additional HF management programs according to their physicians' discretion. All HF education and follow-up calls were delivered by HF-specialized nurses with formal training and clinical experience in HF management. To ensure consistency and standardization across study sites, all research and education nurses participated in regular 50-minute online workshops every 2 months via Zoom, organized by the coordinating institution and based on the official Korean Society of Heart Failure HF patient education materials and the study protocol. Each session covered standardized aspects of education delivery (timing, target populations, duration) and follow-up call protocols (manuals, prompts, response to

noncontact), and competency was confirmed through case-based discussion and Q&A. Fidelity of intervention delivery was centrally monitored by reviewing case report forms and audit reports. Adherence to the intervention protocol was assessed by recording completion of each component and documenting reasons for noncompletion.

Study Outcomes

The primary outcome was the GAI at 6 months, defined by physician prescription of guideline-directed medications. The GAI was calculated based on documented medication prescriptions in medical records. Patients prescribed all 3 GDMT drugs, including RAS blockers, beta blockers, and MRAs, were classified into the high GAI group, and those missing at least 1 medication were classified into the low GAI group. This is assessed as the percentage of the prescribed medications out of the total number of indicated medications for an individual patient, considering both indications and contraindications.[21–23] The 6-month follow-up assessments were conducted within a predefined window of ±1 month from the index discharge date. This was assessed both by randomized groups (mITT analysis) and by actual implementation status of intervention components. The end of the follow-up time frame for the primary outcome was 6 months (plus or minus 1 month) after discharge for each participant.

Secondary outcomes included differences in the change in the Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score (KCCQ-CSS), all-cause mortality, and HF-related first hospitalization at 6 months. The KCCQ is a 23-item, self-administered tool used to measure symptoms, physical function, quality of life, and social function related to HF.[24] Scores range from 0 to 100, with higher scores indicating a better health status.[24] The KCCQ-CSS is derived from the physical limitation and total symptom domains, providing a concise measure of clinical status in patients with HF. The KCCQ was used with permission from Outcomes Instruments, LLC (License No. 14105). Clinical events included all-cause mortality and HF-related hospitalization. All-cause mortality was defined as death from any cause. HF-related hospitalization was defined as time to the first unplanned admission due to worsening signs or symptoms of HF requiring intensification of therapy, with final adjudication performed by an independent data monitoring committee, and only the first hospitalization was considered in the analysis.

Given the nonpharmacological nature of the TCI, which consisted of a discharge checklist, education, and telephone monitoring, it posed minimal risk to the participants. Consequently, formal systematic ascertainment of intervention-related adverse events was not conducted, and no unintended harms were reported during the study period.

Sample Size

Our hypothesis was that the TCI group would have superior results to the usual care group in achieving a higher GAI at 6 months. Based on pilot data from the our previous study, we assumed an achievement rate of 47.4% for the usual care group and hypothesized a 20% relative improvement in the TCI group, corresponding to an expected high GAI achievement rate of 57%.[23] Using a 2-sided significance level of 0.05 and a power of 80%, the required minimum sample size was calculated to be 424 participants per group with PASS software, version 12 (NCSS, LLC, Kaysville, Utah, USA). The assumed effect size corresponded to an absolute difference of 0.20 (Cohen's h ≈0.25, small-to-moderate effect). Considering a dropout rate of 15% for loss to follow-up in the assessment of the primary outcome, we estimated a required sample size of approximately 499 patients per group. Therefore, the total number of participants required for the study was determined to be 998.

Statistical Analysis

Baseline characteristics were summarized using means±SD or medians (interquartile range) for continuous variables and counts (percentages) for categorical variables. Comparisons between the TCI and usual care groups for continuous variables were conducted using the Student's *t* test or Mann–Whitney *U* test, and categorical variables were compared using the chi-square test. Changes in proportions or continuous variables from baseline to the 6-month follow-up were compared using McNemar's test or paired *t* test, respectively. Continuous variables were assessed for normality using the Shapiro–Wilk test and visual inspection of histograms. When the assumption of normality was violated, nonparametric tests were applied. The assumptions of linearity and homoscedasticity were evaluated by examining residual plots. No interim analyses or stopping guidelines were planned.

For the primary outcome, we performed both mITT and per- intervention analyses. In the mITT analysis, the proportion of patients achieving a high GAI at 6 months in the TCI and usual care groups was compared and the association between the groups was evaluated using odds ratios (ORs) with 95% CIs, estimated from a multivariable logistic regression model adjusted for imbalanced baseline characteristics, such as age, diabetes, systolic blood pressure, heart rate, and cause of HF. In the per-intervention analysis, we evaluated the effect of each intervention component and the number of components received using multivariable logistic regression models, adjusting for baseline characteristics that differed according to intervention status. For the analysis of

each intervention, we further examined the results with post hoc adjustment for multiple comparisons using the Holm–Bonferroni method.[25] There were no missing data for the primary outcome among the participants included in the final mITT analysis, precluding the need for missing data imputation or related sensitivity analyses.

For the secondary outcome, the analysis was performed according to the type of each outcome variable as follows: KCCQ scale scores were presented as mean±SD, and changes in the KCCQ scale scores were compared by ANCOVA model including intervention, age, diabetes, systolic blood pressure, heart rate, cause of HF, and each score at discharge in the model. The difference of change between groups was presented as a least square means with a 95% CIs estimated from the model. Clinical events as all-cause mortality or HF-related hospitalization were summarized as the number of events and cumulative incidence rates estimated from Kaplan–Meier curves. The relationship between the groups and clinical events was evaluated using hazard ratios (HRs) with 95% CIs estimated from a multivariable Cox proportional hazards regression model including intervention, age, diabetes, systolic blood pressure, heart rate, and cause of HF. The proportional hazards assumption was assessed and not violated, as confirmed by testing the scaled Schoenfeld residuals. As a sensitivity analysis for potential contamination in usual care group, we compared outcomes between participants in the TCI group who received all 3 intervention components and those in the usual care group who did not receive any intervention components. The effect of center was controlled by including the center variable as a fixed effect in all multivariable models. Missing values were not replaced or imputed; analyses were conducted based on observed data only. All tests were 2 tailed, with a significance level set at $P<0.05$. The analyses were conducted using SAS software 9.4 (SAS Institute, Cary, NC, USA) and R programming (V.4.4.0; The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline Characteristics

Of 1227 patients assessed for eligibility, 1044 patients were enrolled, with 526 assigned to the usual care group and 518 to the TCI group. All 526 patients in the usual care group received the allocated intervention. In the TCI group, 517 patients received the allocated intervention, and 1 patient did not due to early discharge before the intervention. During the follow-up period, 22 patients in the usual care group were excluded from the final analysis (5 lost to follow-up; 17 discontinued intervention, including 6 deaths), and 40 patients in the TCI group were excluded (8 lost to follow-up; 31 discontinued intervention, including 7 deaths) (Figure 1). After excluding patients who discontinued intervention or were lost to follow-up, 504 patients in the usual care and 478 in the TCI group were included in the final mITT analysis (mean age, 62.4±15.5 years; 64.5% male; mean left ventricular ejection fraction, 26.7±7.0%). The prevalence of hypertension and diabetes was 50.1% and 38.5%, respectively. The average left ventricular ejection fraction was 26.7±7.0%, and the mean N-terminal pro-B-type natriuretic peptide level was 9161.1±14666.6 pg/dL, measured during the index admission. Most baseline variables were well balanced between the 2 groups. However, the TCI group had a younger mean age (60.8±16.0 years versus 63.8±14.8 years, $P=0.003$), higher blood pressure, and a lower prevalence of diabetes than that of the usual care group (Table 1).

The baseline high GAI rate was 63.6% in the TCI and 59.5% in the usual care group, showing no significant difference. The prescription rates for RAS blockers, beta blockers, and MRAs were also similar between the 2 groups (Table S1). Additionally, there was no significant difference in the baseline KCCQ-CSS between the TCI and usual care groups (Table 2).

The first outpatient follow-up visit was conducted at a median of 12 days (interquartile range, 8–151 days) after the index discharge. Overall, 70.9% of participants were seen at the clinic within 14 days. The timing of this follow-up visit was comparable between the TCI and usual care groups (median 12 versus 12 days, $P=0.80$). The 6-month follow-up for the primary outcome was completely ascertained for all patients included in the final analysis (504 in the usual care group and 478 in the TCI group).

Implementation of Transitional Care Intervention

Among 478 patients randomized to the TCI group, the discharge checklist and education were completed in all patients (100%) as per protocol, and telephone monitoring was successfully conducted in 389 patients (81.3%). In the usual care group, 53 patients (10.5%) received the discharge checklist and 217 patients (43.1%) received education as part of routine care, and no patients received telephone monitoring. Overall, 389 patients (81.3%) in the TCI group received all 3 components, and 89 (18.7%) received 2 components. In the usual care group, 287 patients (57.0%) received no components, 164 (32.5%) received 1 component, and 53 (10.5%) received 2 components. (Table S2).

Primary Outcomes

In both groups, the achievement of a high GAI decreased during follow-up, with an absolute reduction of –14.9% points in the usual care group (from 59.5% at discharge to 44.6% at 6 months) and –14.0% points in the TCI group (from 63.6% to 49.6%). The between-group difference

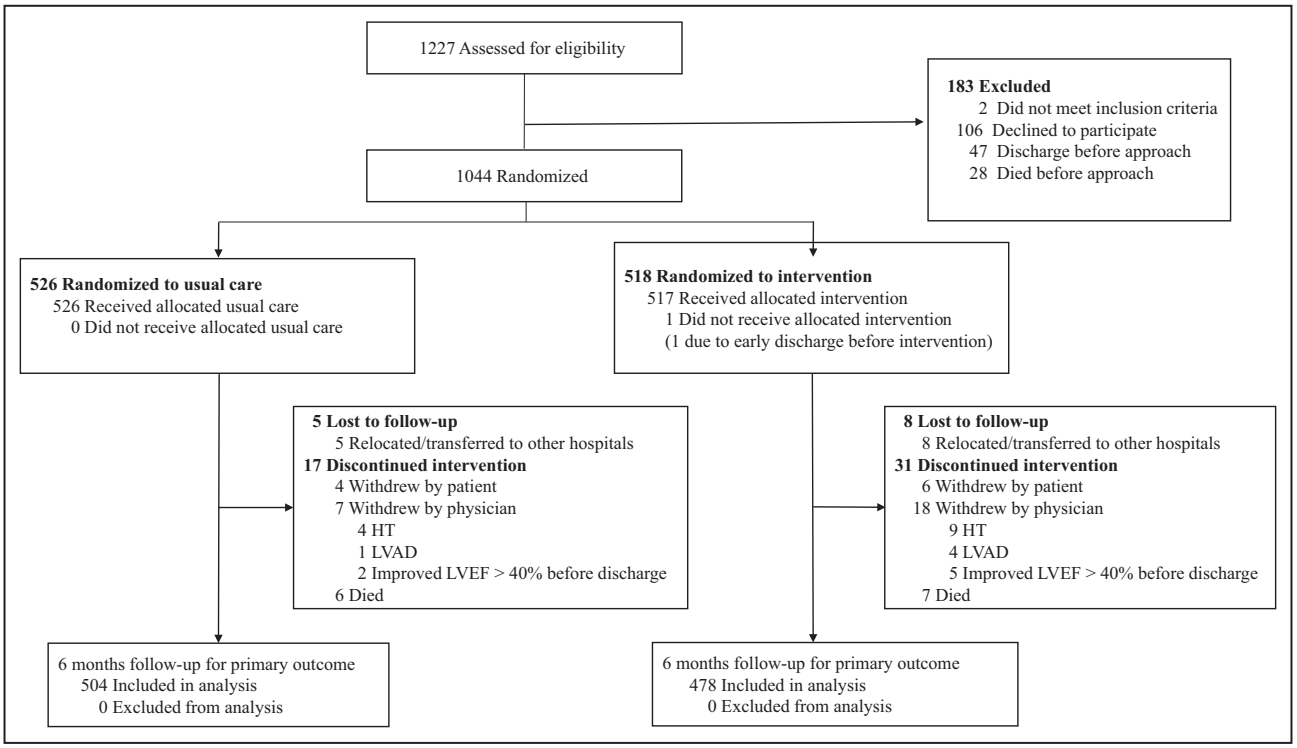

Figure 1. Study algorithm.
HT indicates heart transplantation; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; and TCI, transitional care intervention.

in absolute change was +0.9% points (95% CI, −6.0 to 7.8, *P*=0.80). High GAI achievement at 6 months was observed in 225 patients (44.6%) in the usual care group and in 237 (49.6%) in the TCI group, with no significant difference between the groups (absolute difference, 5.0% [95% CI, −1.8% to 11.8%]; *P*=0.12) (Figure 2A). The changes in target dose achievement for each drug were not significantly different between the groups (Figure 2B and Table S3). In the mITT, the TCI was not associated with the achievement of a high GAI compared with usual care (OR, 1.12 [95% CI, 0.86–1.45], *P*=0.37) (Table 2 and S4).

Analyzing by actual implementation of individual components regardless of group assignment, each component significantly improved GAI achievement (discharge checklist: adjusted OR, 1.55 [95% CI, 1.13–2.11], *P*=0.006; education: adjusted OR, 1.59 [95% CI, 1.09–2.30, *P*=0.02]; telephone monitoring: adjusted OR, 1.38 [95% CI, 1.03–1.83], *P*=0.03) (Table 3 and Figure 3). After post hoc adjustment for multiple comparisons using the Holm–Bonferroni method, all 3 components remained statistically significant (adjusted *P*=0.02, 0.03, and 0.03, respectively). Notably, patients who received all three components showed significantly higher GAI achievement compared with those who received no components (adjusted OR, 1.60 [95% CI, 1.08–2.37], *P*=0.02) (Table 4).

Secondary Outcomes

We evaluated the effect of the TCI on secondary outcomes, including the change in the KCCQ-CSS and clinical end points. There was no significant difference between the TCI and usual care groups in the change of the KCCQ-CSS, with a mean improvement of +27.1 points in the UC group and +25.7 points in the TCI group. The adjusted between-group difference in change was −1.67 points (95% CI −3.97 to 0.62, *P*=0.15). Detailed analysis of individual KCCQ domains showed no significant differences between the TCI and usual care groups (Table S5).

All-cause mortality or HF-related hospitalization occurred in 71 patients (14.8%) in the usual care group and in 67 (14.4%) in the TCI group, with no significant difference between the groups (absolute difference, −0.4%; HR, 1.12 [95% CI, 0.80–1.57], *P*=0.51) (Table 2 and Figure S1). There was no significant difference between the TCI and usual care groups in the change of the risk of clinical events in all subgroup analyses, including the age groups (Table S6).

High GAI and Clinical Events

When analyzing the occurrence of 6-month clinical events based on a high and low GAI, all-cause mortality or HF-related hospitalization occurred in 74 patients

Table 1. Baseline Characteristics in the Study Population

	Total patients (N=982)	Usual care (N=504)	TCI (N=478)	*P* value
Demographics				
Age, y	62.4±15.5	63.8±14.8	60.9±16.1	0.003
Male sex, n (%)	633 (64.5)	320 (63.5)	313 (65.5)	0.52
Body mass index, kg/m^2	24.6±5.1	24.6±4.6	25.2±5.5	0.11
Baseline systolic blood pressure, mm Hg	131.4±27.5	129.5±28.0	133.3±26.9	0.03
Baseline Diastolic blood pressure, mm Hg	82.8±19.0	81.4±18.8	84.3±19.2	0.02
Baseline heart rate, bpm	95.2±24.6	93.5±24.5	97.0±24.6	0.03
New York Heart Association class, n (%)				0.48
II	247 (25.2)	119 (23.6)	128 (26.8)	
III	411 (41.9)	218 (43.3)	193 (40.4)	
IV	324 (33.0)	167 (33.1)	157 (32.8)	
Baseline comorbidity				
Hypertension, n (%)	492 (50.1)	262 (52.0)	230 (48.1)	0.23
Diabetes, n (%)	378 (38.5)	211 (41.9)	167 (34.9)	0.03
Atrial fibrillation, n (%)	195 (19.9)	106 (21.0)	89 (18.6)	0.34
Chronic obstructive pulmonary disease, n (%)	63 (6.4)	34 (6.8)	29 (6.1)	0.66
Cerebrovascular accident, n (%)	79 (8.0)	40 (7.9)	39 (8.2)	0.90
Chronic kidney disease, n (%)	141 (14.4)	71 (14.1)	70 (14.6)	0.80
Baseline laboratory test				
N-terminal pro-brain natriuretic peptide, pg/L	9161.1±14666.6	9530.8±12671.0	8784.7±16459.2	0.48
Median (interquartile range)	4375 (1923–9927)	4550 (2014–11 074)	4276 (1832–9253)	0.11
Hemoglobin, g/dL	13.2±2.4	13.0±2.4	13.3±2.4	0.20
Sodium, mmol/dL	137.7±4.0	137±3.8	137.4±4.3	0.07
Serum urea nitrogen, mg/dL	25.0±14.6	25.3±14.9	24.5±14.1	0.34
Creatinine, mg/dL	1.39±1.38	1.37±1.13	1.42±1.61	0.60
Baseline echocardiographic parameters				
LV ejection fraction, %	26.7±7.0	26.5±6.9	26.8±7.2	0.54
Left atrial volume index, mL/m^2	59.4±26.1	60.4±24.9	58.4±27.3	0.27
LV end-diastolic diameter, mm	61.0±8.3	61.2±8.2	60.9±8.5	0.58
LV end-systolic diameter, mm	52.2±9.4	52.6±9.3	51.9±9.6	0.28
Right ventricular systolic pressure, mm Hg	40.6±16.2	40.0±16.2	41.3±16.2	0.25
Number of HF hospitalizations				
De novo HF, n (%)	552 (56.2)	270 (53.6)	282 (59.0)	0.09
Cause of HF, n (%)				0.01
Ischemic	268 (27.3)	155 (30.8)	113 (23.6)	
Nonischemic	714 (72.7)	349 (69.2)	365 (76.4)	
HF medication taken before randomization, n (%)				
Angiotensin-converting enzyme inhibitors	41 (4.2)	24 (4.8)	17 (3.6)	0.35
Angiotensin receptor blockers	217 (22.1)	123 (24.4)	94 (19.7)	0.07
Angiotensin receptor/neprilysin inhibitor	136 (13.8)	76 (15.1)	60 (12.6)	0.25
Beta blockers	336 (34.2)	186 (36.9)	150 (31.4)	0.07
Mineralocorticoid receptor antagonists	252 (25.7)	136 (27.0)	116 (24.3)	0.33
Loop diuretics	898 (91.4)	462 (91.7)	436 (91.2)	0.80
Sodium-glucose cotransporter-2 inhibitors	271 (27.6)	139 (27.6)	132 (27.6)	0.99

HF indicates heart failure; LV, left ventricular; and TCI, transitional care intervention.

(20.3%) in the low GAI group and in 64 (11.0%) in the high GAI group, indicating a lower incidence in the high GAI group than that of the low GAI group (absolute difference, 9.3%; 95% CI, 4.2% to 14.4%; log-rank *P*<0.001) The cumulative incidence rate of all-cause mortality was 7.7% in the low GAI group and 1.9% in

Table 2. Efficacy End Points

	Usual care (N=504) (Reference)	TCI (N=478)	Estimated difference or ratio (95% CI)	*P* value
Primary end points				
High guideline adherence indicator at 6 mo	225 (44.6%)	237 (49.6%)	1.12 (0.86–1.45)*	0.37*
Secondary end points				
Change in Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score	27.1±24.1	25.7±22.6	−1.67 (−3.97, 0.62)†	0.15†
At discharge	58.2±22.6	58.7±22.7	0.55 (−2.41, 3.51)	0.72‡
At 6 mo	84.6±16.4	84.3±16.3	−0.25 (−2.65, 2.15)	0.84‡
All-cause mortality or HF-related hospitalization	71 (14.8%)§	67 (14.4%)§	1.12 (0.80–1.57)‖	0.51‖
All-cause mortality	23 (4.9%)§	16 (3.4%)§	0.91 (0.48–1.74)‖	0.78‖
HF-related hospitalization	58 (12.1%)§	58 (12.6%)§	1.16 (0.80–1.68)‖	0.43‖

HF indicates heart failure; and TCI, transitional care intervention.

*Odds ratio and *P* value estimated from multivariable logistic regression model adjusting age, diabetes, systolic blood pressure, heart rate, and cause of HF.

†Least square mean and *P* value estimated from analysis of covariance adjusting age, diabetes, systolic blood pressure, heart rate, cause of HF, and each score at discharge.

‡*P* value by Student's *t* test.

§Cumulative incidence rate estimated from Kaplan–Meier curve.

‖Hazard ratio and *P* value estimated from multivariable Cox proportional hazards regression model adjusting age, diabetes, systolic blood pressure, heart rate, and cause of HF.

the high GAI group (log-rank *P*<0.001), and that of HF-related hospitalization was 16.0% and 10.0%, respectively (log-rank *P*=0.006) (Figure S1 and Table S7).

Consistent with the nonpharmacological nature of the intervention, no intervention-related adverse events or unintended harms were reported in either the TCI or usual care group during the follow-up period.

DISCUSSION

In this multicenter randomized clinical trial of 982 patients with AHF, although the simplified TCI did not increase the achievement of a high GAI in the mITT analysis, per-intervention analysis revealed that actual delivery of intervention components was associated with improved guideline adherence. Moreover, each component independently contributed to improved guideline adherence: discharge checklist, education, and telephone monitoring. These findings suggest that improving implementation fidelity may be a key factor in optimizing HF care.

In patients with HF with reduced ejection fraction, early initiation and maintenance of GDMT are strongly recommended to improve HF outcomes.[7–9] Transitional care aims to bridge the gap between hospital discharge and home-based care. A recent HF guideline recommends home-based programs to reduce the risk of HF-related hospitalization and mortality, with a class I recommendation.[26] In a meta-analysis of TCIs in HF, home visits and disease management clinics were shown to reduce all-cause mortality; however, telephone monitoring or education interventions did not improve clinical outcomes.[12] Our findings align with this evidence, highlighting that a structured but simplified approach may be beneficial but only when fully implemented. A recent randomized controlled trial, where the TCI comprised patient education, a discharge summary, short-term follow-up, and home visits for high-risk patients, did not improve clinical outcomes.[15]

Despite previous inconsistencies in TCI effectiveness, our study suggests that adherence to all intervention components—rather than just assignment to the TCI group—was associated with improved medication adherence. This emphasizes the need for strategies to enhance adherence to prescribed interventions in real-world practice. We specifically included the per-intervention analysis in our study design to address a critical gap in transitional care research: understanding the impact of implementation fidelity on outcomes. Although mITT analysis provides the most conservative estimate of intervention effectiveness in real-world settings, per-intervention analysis offers insights into the potential efficacy of interventions when optimally delivered. This is particularly relevant in our study context, where some components of the intervention were already implemented as part of usual care in several centers (discharge checklist in 10.5% and education in 43.1% of the usual care group), which could not be restricted for ethical reasons, potentially diluting the contrast between groups. In addition, incomplete implementation of telephone monitoring (81.3%) in the TCI group may have further reduced the intervention's effectiveness. Our findings from this prespecified per-intervention analysis highlight that simply offering an intervention may not be sufficient; ensuring its full execution is crucial for achieving intended benefits.

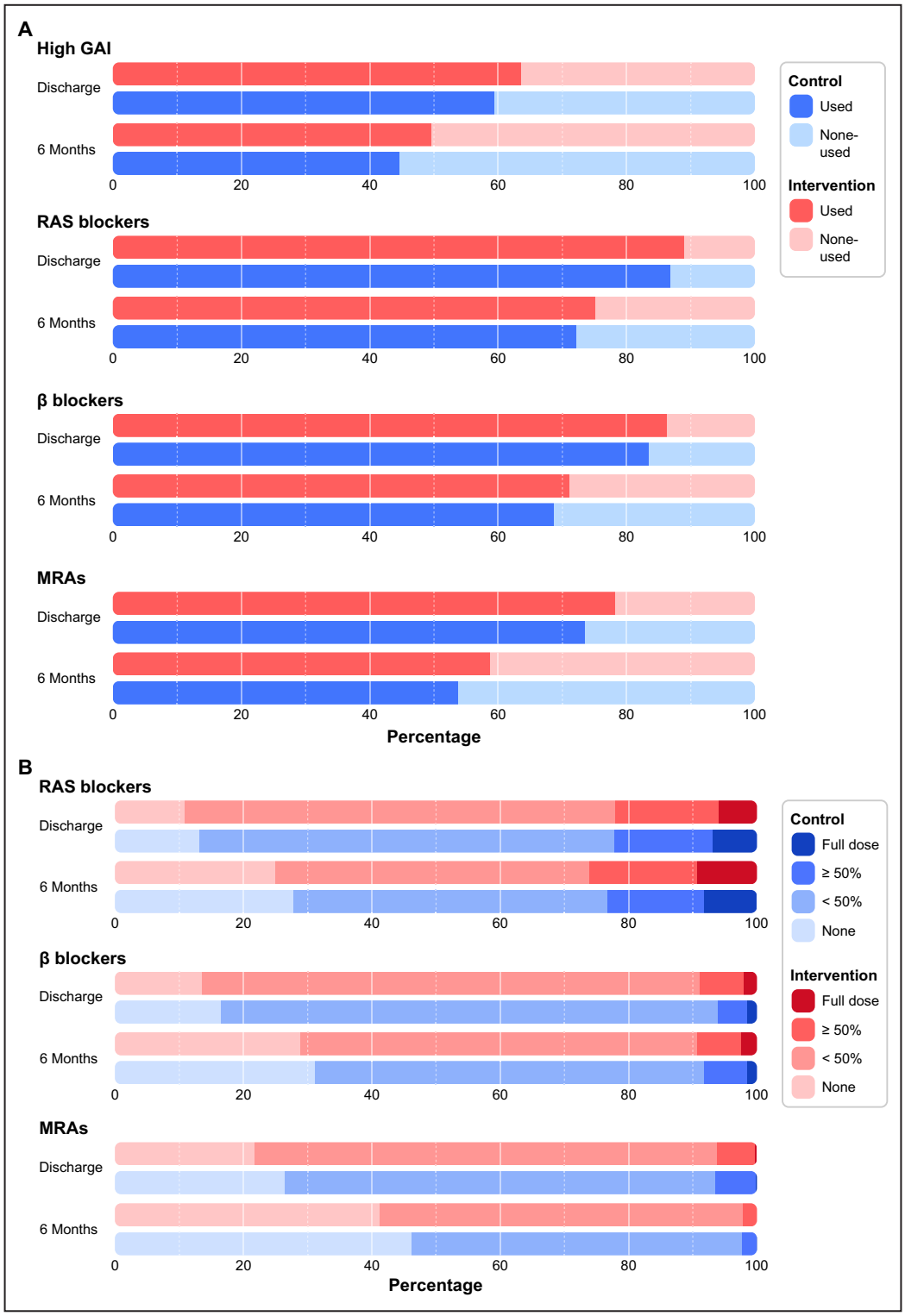

Figure 2. Change in (A) use and (B) dose of guideline-directed medical therapy between baseline and 6 months follow-up.
GAI indicates guideline adherence indicator; MRA, mineralocorticoid receptor antagonists; RAS, renin-angiotensin-system; and TCI, transitional care intervention.

In our study, the 3 components of the transitional care intervention likely contributed to improving GDMT prescription through both direct and indirect mechanisms. The discharge checklist provided structured reminders to clinicians, thereby directly reducing therapeutic inertia and ensuring that evidence-based therapies were

Table 3. Primary End Point (High GAI Achievement) According to Individual Components of TCI (Discharge Checklist, HF Education, and Telephone Monitoring)

	No (Reference)		Yes		Crude odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)	*P* value
	No.	Event (%)	No.	Event (%)				
Discharge checklist	451	204 (45.2%)	531	258 (48.6%)	1.14 (0.89–1.47)	0.29	1.55 (1.13–2.11)*	0.006
Education	287	142 (49.5%)	695	320 (46.0%)	0.87 (0.66–1.15)	0.33	1.59 (1.09–2.30)†	0.02
Telephone	593	262 (44.2%)	389	200 (51.4%)	1.34 (1.03–1.73)	0.03	1.38 (1.03–1.83)‡	0.03

Odds ratio and *P* value estimated from multivariable logistic regression model. GAI indicates guideline adherence indicator; HF, heart failure; and TCI, transitional care intervention.

*adjusting diastolic blood pressure, left ventricular ejection fraction, sodium, number of hospitalization (de novo or not), and cause of HF.

†Adjusting sodium, and cause of HF.

‡Adjusting age, diabetes, and cause of HF.

systematically considered at the time of discharge.[27] The HF education program, although not focused on prescribing itself, likely improved patients' understanding of their disease and the importance of evidence-based therapy, which may have enhanced adherence and facilitated subsequent treatment optimization.[21] Similarly, structured telephone consultations did not include direct medication-related questions but may have promoted patient engagement, timely reporting of symptoms, and adherence to follow-up visits, thereby creating more opportunities for clinicians to optimize GDMT.[28] However, it is also possible that patients who responded to telephone calls were a self-selecting group with higher health literacy and stronger motivation and that these baseline characteristics, rather than the telephone intervention itself, contributed to the observed association. This limitation highlights the need to develop future interventions that can effectively reach patients with lower health literacy or less engagement in their care.

The lack of overall effect in the mITT analysis might be explained by several factors. First, some control group centers already implemented certain components such as discharge checklist (10.5%) and education (43.1%) as part of their routine care, potentially diminishing the observable difference between groups. This partial adoption of intervention elements in the usual care group could have diluted the contrast between groups. Second, incomplete implementation of telephone monitoring (81.3%) in the TCI group may have reduced the intervention's effectiveness. This suggest that simply offering an intervention may not be sufficient; ensuring its full execution is crucial for achieving intended benefits.

Importantly, the study set medication adherence to essential HF medications as the primary outcome, which is a critical indicator of quality of care.[21,22,26] In a study based on Korean nationwide multicenter registry data with AHF between 2011 and 2014, the use of RAS inhibitors, beta blockers, and MRAs at discharge was 64.9%, 49.9%, and 44.9%, respectively.[29] Another study demonstrated that intervention increased the GDMT drug dose and reduced clinical events in patients with AHF. In that study, the baseline GDMT use was relatively low, except for MRAs (RAS inhibitors, 64%; beta blockers, 36%; and MRAs, 94%), leaving considerable room for improvement in adherence to GDMT.[30] Our study focused on patients in tertiary hospitals at the contemporary period, where the use of GDMT was already high at discharge (RAS inhibitors, 86.9%; beta blockers, 83.5%; and MRAs, 73.6%), making it more challenging to achieve further improvements in adherence. These findings also suggest that contemporary HF practice has significantly improved the use of GDMT. Additionally, the mere participation in a study aiming to achieve a high GAI may have increased physician adherence owing to the Hawthorne effect, which is when individuals modify an aspect of their behavior in response to their awareness of being observed.[31]

Our findings have important implications for improving HF care. First, future interventions should focus not only on designing structured transitional care programs but also on ensuring their full execution in clinical settings. Second, each component of TCI—checklists, education, and follow-up monitoring—plays a distinct role in improving guideline adherence, suggesting that multifaceted approaches may be more effective than single-component interventions. Lastly, health care providers and policymakers should consider strategies to enhance patient engagement and provider adherence to intervention protocols to maximize real-world impact.

Although no significant difference in KCCQ-CSS was observed between groups, this finding should be interpreted with caution. Patient-reported outcomes often require longer follow-up to capture meaningful changes, and the KCCQ is influenced by multiple factors beyond pharmacological treatment, including comorbidities and psychosocial status.[24] Moreover, partial implementation of intervention components in the control group, together with an overall increase in GDMT prescription in both groups during follow-up, may have attenuated between-group differences. These findings suggest that future strategies should place greater emphasis on interventions directly targeting patient-reported outcomes, such as symptom management, self-care support, and psychosocial interventions.

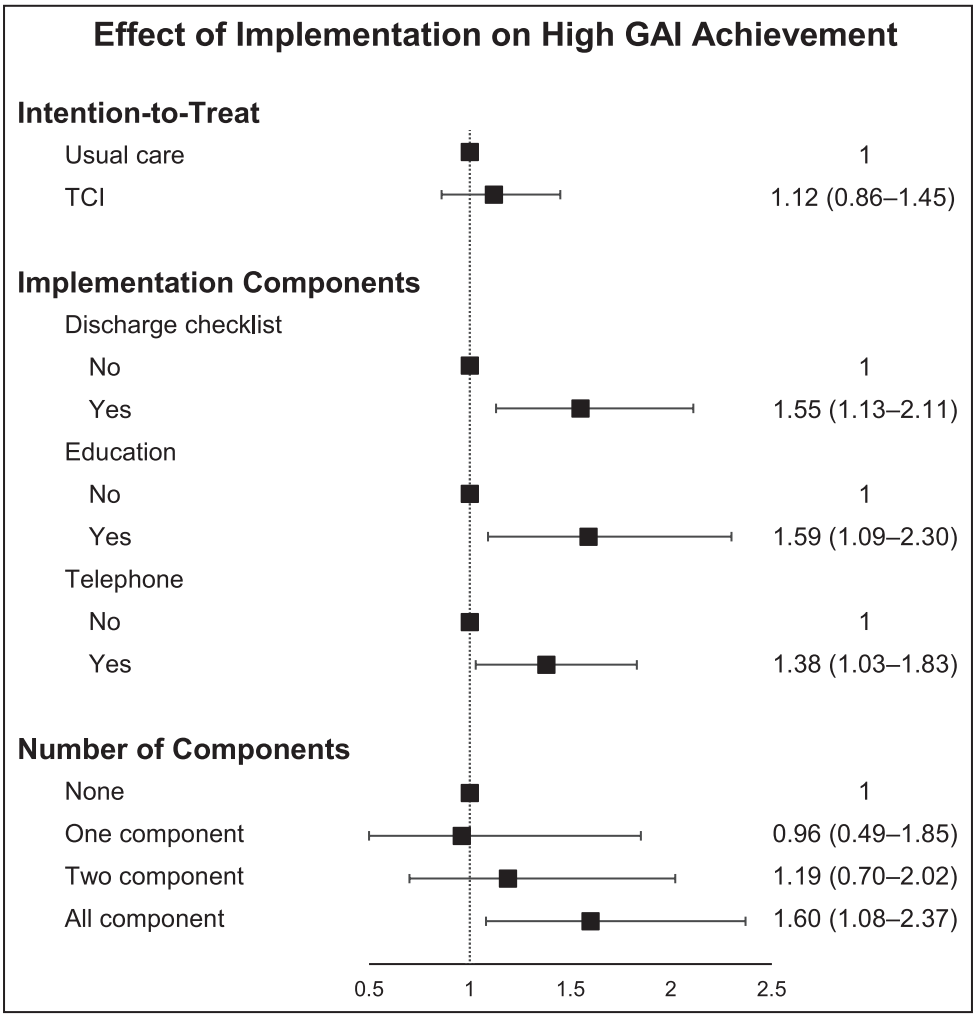

Figure 3. Effects of transitional care implementation on high guideline adherence indicator achievement.
Forest plot showing the odds ratios with 95% CIs for achieving high guideline adherence indicator. The analysis includes intention-to-treat analysis of the overall intervention effect and per-intervention analysis by individual components and number of components received. For per intervention analysis, odds ratios were calculated comparing those who received each component (or number of components) vs those who did not. Adjusted odds ratios were obtained from multivariable logistic regression models adjusting for baseline characteristics including age, diabetes, systolic blood pressure, heart rate, and cause of heart failure. Vertical dashed line represents an odds ratio of 1.0. GAI indicates guideline adherence indicator; OR, odds ratio; and TCI, transitional care intervention.

Limitations

This study had several limitations. First, our analysis of guideline adherence did not include SGLT2 (sodium-glucose cotransporter-2) inhibitors, which are now a key component of GDMT. Future studies should incorporate newer therapeutic agents to ensure contemporary relevance. Second, there is a possibility of type II error, as the study may have been underpowered to detect smaller differences in outcomes. The sample size calculation was based on an expected 20% improvement in the proportion of patients achieving high GAI, whereas the observed difference between groups was substantially smaller, suggesting that the trial may not have been sufficiently powered to detect the true effect size. Third, the findings may not be generalizable to nontertiary hospitals, where resources and patient profiles differ. Finally, contamination in the control group could not be fully excluded, given that some components of transitional care were already implemented as part of usual care in certain centers.

CONCLUSIONS

In this multicenter randomized clinical trial of 982 patients with AHF, whereas the simplified TCI did not

Table 4. Primary End Point (High GAI Achievement) According to Number of TCI Components Received

	No.	Event (%)	Crude odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)*	*P* value
No. of interventions						
0	287	142 (49.5%)	1 (Reference)		1 (Reference)	
1	164	62 (37.8%)	0.62 (0.42–0.92)	0.02	0.96 (0.49–1.85)	0.89
2	142	58 (40.8%)	0.71 (0.47–1.06)	0.09	1.19 (0.70–2.02)	0.53
3	389	200 (51.4%)	1.08 (0.80–1.47)	0.62	1.60 (1.08–2.37)	0.02

1, education only; 2, education and discharge checklist; 3, education, discharge checklist, and telephone. Odds ratio and *P* value estimated from multivariable logistic regression model. GAI indicates guideline adherence indicator; and TCI, transitional care intervention.

*adjusting age, New York Heart Association class, left ventricular ejection fraction, sodium, and number of hospitalization (de novo or not).

increase the achievement of a high GAI in the mITT, per-intervention analysis revealed that actual delivery of intervention components was associated with improved guideline adherence. These findings highlight that implementation fidelity of TCI is the critical determinant for optimizing heart failure care during the vulnerable period after hospitalization.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Figure S1
Tables S1–S7

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