Heart and Vessels
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ORIGINAL ARTICLE

The first multicenter, randomized, controlled trial of home telemonitoring for Japanese patients with heart failure: home telemonitoring study for patients with heart failure (HOMES-HF)

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Abstract
Home telemonitoring is becoming more important to home medical care for patients with heart failure. Since there are no data on home telemonitoring for Japanese patients with heart failure, we investigated its effect on cardiovascular outcomes. The HOMES-HF study was the first multicenter, open-label, randomized, controlled trial (RCT) to elucidate the effectiveness of home telemonitoring of physiological data, such as body weight, blood pressure, and pulse rate, for Japanese patients with heart failure (UMIN Clinical Trials Registry 000006839). The primary end-point was a composite of all-cause death or rehospitalization due to worsening heart failure. We analyzed 181 recently hospitalized patients with heart failure who were randomly assigned to a telemonitoring group ($n = 90$) or a usual care group ($n = 91$). The mean follow-up period was 15 (range 0–31) months. There was no statistically significant difference in the primary end-point between groups [hazard ratio (HR), 0.95; 95% confidence interval (CI), 0.548–1.648; $p = 0.572$]. Home telemonitoring for Japanese patients with heart failure was feasible; however, beneficial effects in addition to those of usual care were not demonstrated. Further investigation of more patients with severe heart failure, participation of home medical care providers, and use of a more integrated home telemonitoring system emphasizing communication as well as monitoring of symptoms and physiological data are required.

Keywords Heart failure · Disease management · Telemonitoring · Home healthcare · Multidisciplinary

Introduction

Since the prevalence of heart failure (HF) increases with age, it is estimated that the number of elderly patients with HF in Japan will peak in 2035 [1] and will decrease thereafter in association with a falling birth rate and depopulation. High rehospitalization rates, long hospital stays, and high medical costs impose an increasing burden on such patients, their families, health care providers, and society. Not only Japan, but also many developed countries face the same issues. As a countermeasure, the Japanese government has recently decided to shift the main healthcare environment from the hospital to the community by 2025. However, most patients with HF need intensive and specific care; so there are many obstacles to transferring patients with HF from cardiologists and hospitals to primary care physicians and home-healthcare providers. Home telemonitoring is a promising solution to reduce rehospitalization and mortality rates [2], despite the negative results of some multicenter, randomized, controlled trials (RCTs) [3, 4]. The existence of a subgroup of patients who might benefit from home telemonitoring has been suggested [5]. In that analysis, treatment effects were significant only for patients with a prior HF decompensation or an implantable cardioverter defibrillator (ICD) or a Patient Health Questionnaire-9 (PHQ-9) score

The members of HOMES-HF study investigators are listed in "Acknowledgements".

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of less than 10. However, there are no data regarding the effectiveness of home telemonitoring in Japanese patients with HF. Therefore, in this multicenter, prospective RCT, the Home Telemonitoring Study for Japanese Patients with Heart Failure (HOMES-HF), we planned that all participants were hospitalized or recently discharged due to HF decompensation, and screened with the PHQ-9.

Methods

Study population

The protocol of this trial was described previously [6]. In brief, eligible patients were randomly assigned via a website to either a telemonitoring group or a usual care group with a biased-coin minimization method balanced for age (≥ 65 vs < 65 years), left ventricular ejection fraction (LVEF; ≥ 30 vs < 30%), and history of ischemic heart disease (IHD; IHD vs non-IHD) [7]. The patients and treating physicians, but not the independent endpoint committee, were aware of group allocation. The participants were enrolled from December 2011 to August 2013 and were followed until August 2014. The intervention was continued to the end of the follow-up period. Eligible patients were aged 20 years or older with New York Heart Association (NYHA) functional class II–III HF and were discharged or scheduled to be discharged following admission for acute HF or acute decompensated chronic HF within 30 days of enrolment. The exclusion criteria were as follows: use of an implantable device [i.e., cardiac pacemaker, ICD/cardiac resynchronization therapy (CRT), because an alternating-current signal travels through the body when patients measure their body weight and body composition on an electronic scale]; hemodialysis requirement or serum creatinine level ≥ 3.0 mg/dl; severe liver dysfunction; planned percutaneous coronary intervention or coronary artery bypass grafting; unable to stand on a scale safely; limited life expectancy because of malignant diseases or other causes; high suspicion of severe depression (e.g., PHQ-9 score ≥ 20); severe dementia; pregnancy; and no access to a telephone line. All participants provided their written informed consent, and the study protocol was approved by the institutional review board of Saga University and each participating site. The trial was registered with the University Hospital Medical Information Network clinical trial registry (No. UMIN000006839; URL: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000007983&language=E).

Participating centers

A total of 27 centers participated in this study. The types of hospitals were as follows: 3 outpatient clinics, 4 provincial hospitals, 6 general hospitals in urban areas, 1 national center, and 13 university hospitals in Japan.

Home telemonitoring system

The home telemonitoring system consisted of an electronic scale with a body composition meter, a sphygmomanometer and a device called a "receiver," which received acquired physiological data, including blood pressure, pulse rate, body weight, and body composition, wirelessly and transmitted the data to the central web server via the internet. These were commercially available products for health maintenance (Karada Karte™ Tanita Health-link Co. Ltd, Tokyo, Japan), and were distributed to the participants assigned to the telemonitoring group when they were discharged from the hospital. The patients were shown how to use the monitoring devices after providing informed consent, and they were encouraged to measure their body weight and blood pressure by themselves at least once a day at approximately the same time to minimize daily variance caused by meals, micturition and bowel movement. The telemonitoring center was established at Saga University Hospital for the present study, and full-time nurses monitored the acquired data on the secure website from 9 a.m. to 5 p.m., 7 days a week. The monitoring nurses made contact with the patients by telephone and established internet communication with the monitoring devices as soon as the patient's physician ordered the home telemonitoring to start. Before the monitoring started, the patient's physician determined the warning threshold for body weight, blood pressure and pulse rate for each patient. If the acquired data exceeded the threshold, the monitoring nurses notified the patient's physician. There were no restrictions on the ability of the patient's physician to perform any intervention in response, such as providing telephone guidance, changing medications, modifying the warning threshold, and ordering hospital readmission.

Usual care

Patients assigned to the usual care group were treated by their physicians in accordance with the 2010 Japanese Circulation Society Guidelines for treatment of chronic HF. Clinicians provided discharge education and encouraged the patients to measure their body weight by themselves every day.

Adherence

The adherence of the patients randomized to the telemonitoring group to measurement of their daily weight and blood pressure was defined as follows:

Adherence = (days that each patient actually measured body weight and blood pressure in a month/days that body weight and blood pressure should be measured by the patient in a month)*100%.

Study endpoint

The primary endpoint was a composite of all-cause death or rehospitalization due to worsening HF. The secondary endpoints were as follows: all-cause death; death from cardiovascular causes; all-cause rehospitalization; rehospitalization due to cardiovascular causes; rehospitalization due to worsening HF; worsening of symptoms; cost of medical care; worsening of LVEF, the levels of N-terminal pro B-type natriuretic peptide (NT-pro BNP), high-sensitivity C-reactive protein (hs-CRP), pentraxin-3 (PTX3), high-sensitivity cardiac troponin T (hs-cTnT), or high-molecular weight adiponectin; changes in the Mini Mental State Examination (MMSE) score, the General Self-Efficacy Scale (GSES), the Minnesota Living With Heart Failure (MLWHF) score, or the PHQ-9 score; and adherence to medication. The MMSE is a commonly used paper-based test for the diagnosis of dementia, with a maximum score of 30. MMSE scores 25–30, 20–25, 10–20, and 0–10 represented questionably significant, mild, moderate, and severe dementia, respectively [8]. The GSES is a 16-item psychometric scale to assess optimistic self-beliefs to cope with a variety of difficult demands in life [9]. The maximum score of GSES is 16, and a higher GSES score indicates higher self-efficacy. The MLWHF is a 21-item disease-specific instrument with summary scores ranging from 0 to 105, with a higher score representing a worse HF-related quality of life [10]. The PHQ-9 is a 9-item self-administered tool for assessing the presence and severity of depression. A PHQ-9 score ≥ 10 had a sensitivity of 88% and a specificity of 88% for major depressive disorder. PHQ-9 scores of 5, 10, 15, and 20 represented mild, moderate, moderately severe, and severe depression, respectively [11]. All endpoints were assessed by the independent endpoint committee after the follow-up period.

Statistical analysis

We assumed that the Hazard Ratio (HR) of the primary endpoint (all-cause death or hospitalization for worsening HF) of the telemonitoring group to the control group would be 0.60 and that the cumulative annual event rate in the usual care group would be 0.30, based on the results of previous studies [12, 13]. This study was designed to have 80% power to detect a 40% relative reduction in the risk of the primary outcome in the telemonitoring group within 12 months as compared with the control group, based on an expected death rate at 12 months of 30% in the control group using a log-rank test with a two-sided α of 0.05. A total sample size of 420 patients was planned according to the Schoenfeld and Richter method [14], with a 2-year period for patient enrolment and a follow-up period of 1 year. All statistical analyses were pre-specified

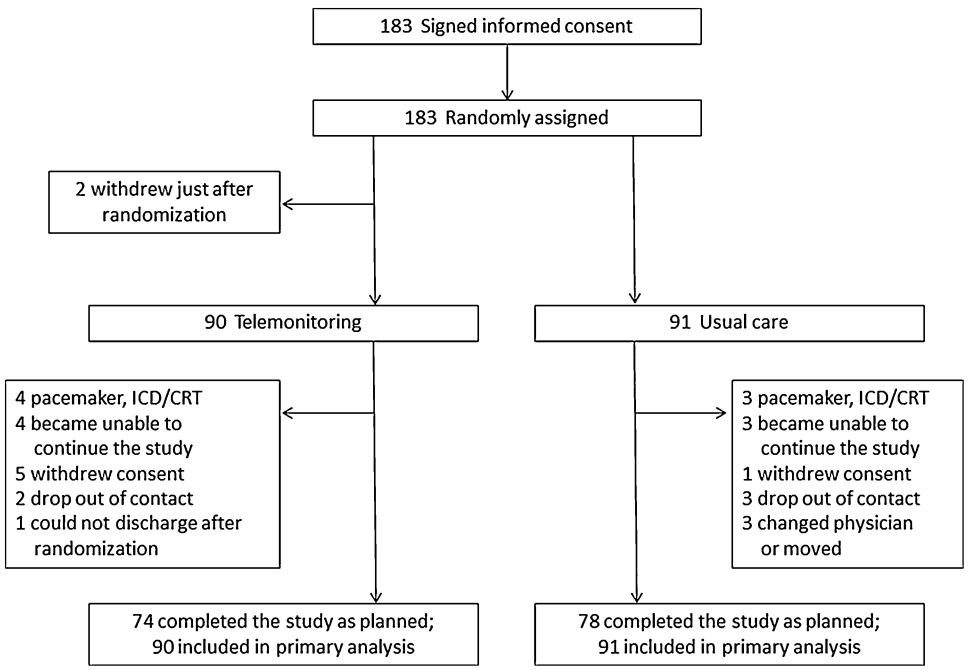


Fig. 1 The numbers of patients randomly assigned to the telemonitoring group and the usual care group and analyzed for the primary endpoint

Table 1 Baseline characteristics

Variables	Telemonitoring ($n = 90$)	Usual care ($n = 91$)	p value
Age, years, mean ± SD	67.1 ± 12.8	65.4 ± 15.6	0.425
Men/women, *n*	51/39	56/35	0.547
NYHA II/III, *n*	70/20	72/19	0.858
Prior ischemic heart disease, *n* (%)	28 (31.1)	27 (29.7)	0.873
Prior hospitalization, frequency, median (range)	1 (0–17)	1 (0–8)	0.548
Beta-blockers, *n* (%)	83 (92.2)	79 (86.8)	0.332
Angiotensin converting enzyme inhibitors, *n* (%)	49 (54.4)	51 (56.0)	0.882
Angiotensin II receptor blockers, *n* (%)	32 (35.6)	31 (34.1)	0.877
Aldosterone blockades, *n* (%)	53 (58.9)	58 (63.7)	0.543
Diuretics, *n* (%)	79 (87.8)	77 (84.6)	0.667
Hemoglobin, g/dl, mean ± SD	12.9 ± 2.2	12.8 ± 2.4	0.788
Albumin, g/dl, mean ± SD	3.7 ± 0.5	3.7 ± 0.6	0.642
Sodium, mEq/l, mean ± SD	139.3 ± 3.6	139.6 ± 3.1	0.545
Total cholesterol, mg/dl, mean ± SD	164.5 ± 44.9	166.5 ± 43.7	0.776
N-terminal pro-BNP, pg/ml, median, range	2024.5, 372–29225 ($N = 28$)	1247.0, 181–13183 ($N = 25$)	0.132
BNP, pg/ml, median, range	210.9, 26–2252 ($N = 62$)	238.6, 14–3260 ($N = 64$)	0.230
LVDd, mm, mean ± SD	55.1 ± 10.2	57.0 ± 10.8	0.229
LVDs, mm, mean ± SD	44.3 ± 11.4	45.9 ± 13.5	0.391
LVEF, %, mean ± SD	40.5 ± 14.8	39.2 ± 16.5	0.602

Values are mean ± SD, median and range, or number of subjects and percentage. A p value was calculated with Fisher's exact test for categorical outcomes, Wilcoxon rank sum test for ordinal variables, and t tests for continuous variables, as appropriate

BNP B-type natriuretic peptide, *LVDd* left ventricular end-diastolic diameter, *LVDs* left ventricular end-systolic diameter, *LVEF* left ventricular ejection fraction

Table 2 Adherence to daily measurement of the patients assigned into the telemonitoring group

Months	1	2	3	4	5	6	7	8	9	10	11	12
n	82	81	79	78	77	75	74	73	72	68	68	66
Adherence (%)	96.2	94.2	96.2	92.7	91.0	90.4	89.6	88.2	88.5	88.4	89.2	90.9
SD	9.6	15.1	8.7	18.6	17.9	18.6	19.2	18.6	21.1	22.4	17.9	15.6

Mean adherences of the patients who were randomized into the monitoring group to measurement of their daily weight at every months. Adherence = (days that a patient actually measured in a month/days should be measured for the patient in a month)*100 (%)

in a detailed statistical analysis plan and performed at the Department of Biostatistics, Chiba University Hospital. The analyses of the adjudicated primary and secondary outcomes were performed on the full analysis set. For the baseline variables, summary statistics were constructed employing frequencies and proportions for categorical data and means and SDs for continuous variables. Patient characteristics were compared with Fisher's exact test for categorical outcomes, the Wilcoxon rank sum test for ordinal variables, and t tests for continuous variables, as appropriate. The primary endpoint of the composite of all-cause death or rehospitalization for worsening HF was analyzed with the stratified log-rank test for eligible patients with age (65 vs < 65 years), LVEF (≥ 30 vs < 30%) and history of IHD (IHD vs non-IHD) as stratification factors. Time-to-event analyses were carried out with the Kaplan–Meier method, and adjusted HRs and 95% confidence intervals (CIs) were calculated with Cox proportional hazards models with stratification factors. For the aforementioned secondary endpoint analyses of time-to-event outcomes, competing risk analysis was performed with the Fine-Gray generalization of the proportional hazards model accounting for death as a competing risk [15, 16]. Fine-Gray makes use of the sub-distribution hazard to model cumulative incidence, thereby quantifying the overall benefit or harm of an exposure [17]. Death is a competing risk for loss to follow-up; therefore, patients who died could no longer become lost to follow-up. Competing risks are defined as events that prevent the outcome of interest from occurring. The standard Kaplan–Meier method assumes the follow-up of those developing a competing event to simply be censored. This assumption is invalid

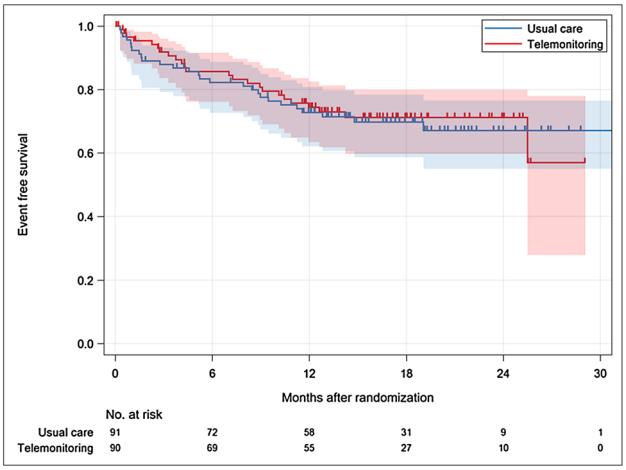


Fig. 2 Kaplan–Meier time-to-event (95% confidence interval) estimates for the primary endpoint (a composite of all-cause death and rehospitalization due to worsening HF) according to treatment group. Shaded areas represent 95% CIs

because the outcome of interest can no longer occur in those developing the competing event, and such analyses will therefore overestimate the probability of the outcome of interest [18]. All comparisons were planned, and all *p* values were two-sided. A *p* value of less than 0.05 was considered to be statistically significant. All statistical analyses were performed with SAS software V.9.4 (SAS Institute, Cary, NC, USA).

Results

We planned a total sample size of 420 patients before the study started. However, we could not reach this number within the pre-defined enrollment period. As a result, a total of 183 patients were randomly assigned to the telemonitoring group or the usual care group. One patient withdrew consent immediately after randomization and refused to allow use of any of his baseline data for analysis. Another patient never visited the outpatient clinic after discharge (both patients were in the telemonitoring group). Of the 181 patients (telemonitoring group, $n = 90$; usual care group, $n = 91$) who were assigned to the analysis, 29 patients (16 patients in the telemonitoring group and 13 patients in the usual care group) dropped out during the study period. Among these, 7 patients underwent placement of a cardiac pacemaker or ICD/CRT, 7 became unable to continue the study (for reasons including cognitive disorder, frailty, or malignant diseases), 6 withdrew consent during the follow-up period, 5 dropped contact, 3 changed their physician or moved, and the remaining patient was never discharged after randomization (Fig. 1).

Baseline characteristics

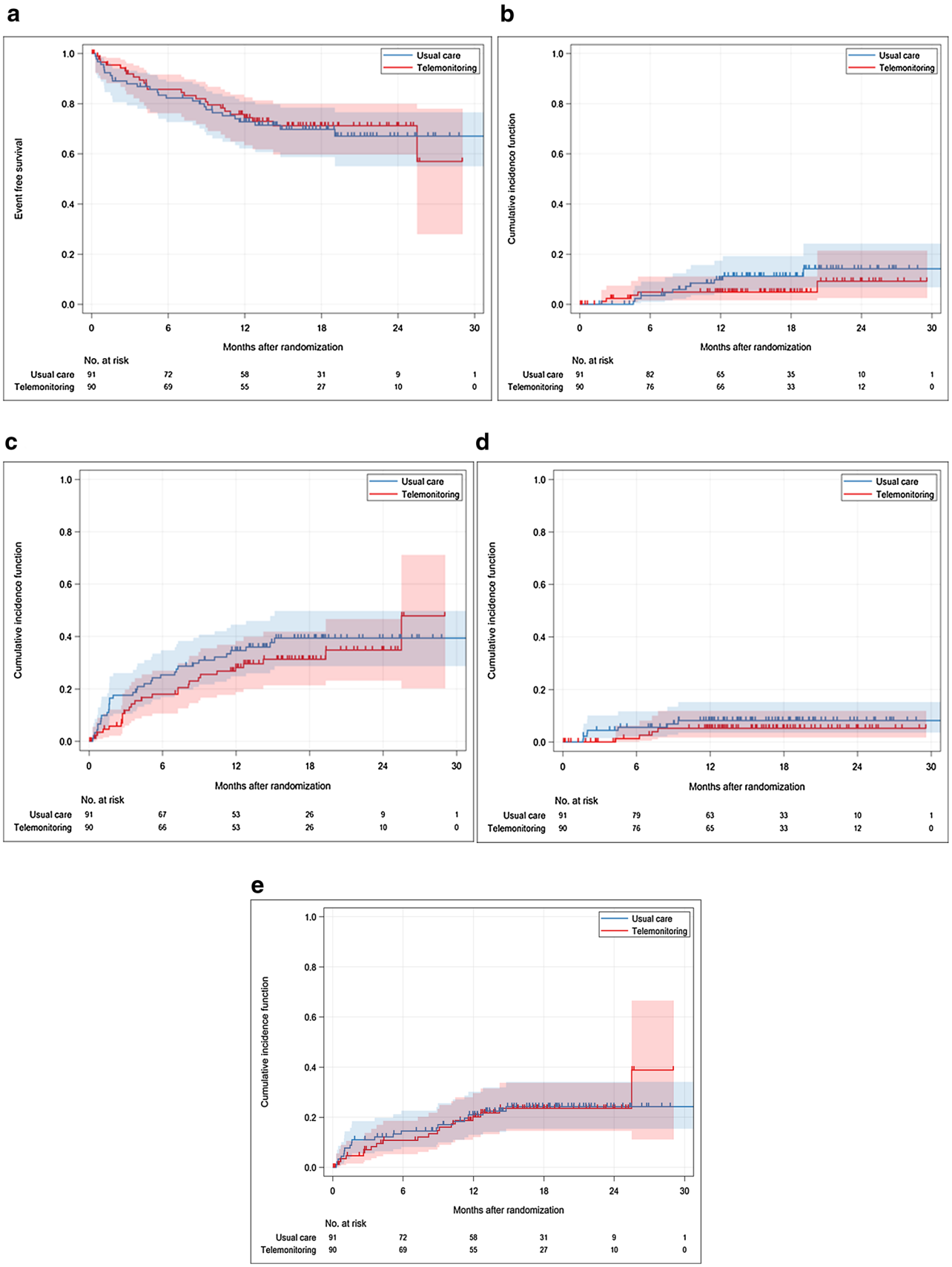
Both groups were similar with respect to a range of baseline characteristics, including age, gender, ratio of NYHA class II/III, number with IHD, and number of prior hospitalizations. Medications were balanced between the groups at baseline. In the telemonitoring group, 81 patients (90%) received angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 53 patients (58.9%) received aldosterone blockers, and 83 patients (92.2%) received beta-blockers with the use of guideline-directed dosages. In the usual care group, 82 (90.1%), 58 (63.7%), and 79 (86.8%) patients received these medications, respectively. Laboratory data, including hemoglobin, serum albumin, sodium concentration, total cholesterol levels, plasma NT-pro BNP levels, and plasma BNP levels were also similar in both groups. Left ventricular echocardiographic parameters, including left ventricular end-diastolic dimension (LVDd), left ventricular end-systolic dimension (LVDs), and LVEF, were also similar in both groups (Table 1).

Adherence

Adherence to daily measurements for the patients assigned to the telemonitoring group was maintained sufficiently

Table 3 Primary and secondary endpoints

Outcomes	Number of events		Hazard ratio (95% CI)	*p* value
	Telemonitoring ($n = 90$)	Usual care ($n = 91$)		
Primary endpoint				
All-cause death and rehospitalization due to worsening HF, *n* (%)	24 (26.7)	27 (29.7)	0.950 (0.548–1.648)	0.572
Secondary endpoints				
All-cause death, *n* (%)	10 (11.1)	13 (14.3)	0.809 (0.354–1.847)	0.614
Death from cardiovascular causes, *n* (%)	5 (5.6)	10 (11.0)	0.524 (0.176–1.557)	0.245
All-cause rehospitalization, *n* (%)	27 (30.0)	34 (37.4)	0.795 (0.479–1.320)	0.376
Rehospitalization due to cardiovascular causes, *n* (%)	4 (4.4)	7 (7.7)	0.595 (0.171–2.074)	0.415
Rehospitalization due to worsening HF, *n* (%)	19 (21.1)	20 (22.0)	1.007 (0.534–1.897)	0.983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◂**Fig. 3** Kaplan–Meier time-to-event (95% confidence interval) estimates for the secondary endpoint (**a** all-cause death) according to treatment group. The cumulative incidence (95% confidence interval) of the secondary endpoints (**b** death from cardiovascular causes, **c** all-cause rehospitalization, **d** rehospitalization due to cardiovascular causes, **e** rehospitalization due to worsening HF) according to treatment group. Shaded areas represent 95% CIs

high throughout the study period. The mean rates of adherence at 1, 6, and 12 months after randomization were 96.2, 90.4, and 90.9%, respectively (Table 2).

Primary endpoint

The median interval from discharge up to the start of the home telemonitoring was 9 (interquartile range 6–13) days, and the mean follow-up period was 15 (range 0–31) months. During the follow-up period, the composite of all-cause death or rehospitalization due to worsening HF occurred in 24 (26.7%) patients in the telemonitoring group and in 27 (29.7%) patients in the usual care group. As shown in Fig. 2 and Table 3, there was no significant difference in the primary endpoint between groups (HR 0.95; 95% CI 0.548–1.648; $p = 0.572$).

Secondary endpoints

There were no significant differences between groups with respect to the secondary endpoints, including all-cause death (Fig. 3a, Table 3; HR 0.809; 95% CI 0.354–1.847; $p = 0.614$), death from cardiovascular causes (Fig. 3b, Table 3; HR 0.524; 95% CI 0.176–1.557; $p = 0.245$), all-cause rehospitalization (Fig. 3c, Table 3; HR 0.795; 95% CI 0.479–1.320; $p = 0.376$), rehospitalization due to cardiovascular causes (Fig. 3d, Table 3; HR 0.595; 95% CI 0.171–2.074; $p = 0.415$), rehospitalization due to worsening HF (Fig. 3e, Table 3; HR 1.007; 95% CI 0.534–1.897; $p = 0.983$), changes in NT-pro BNP (ANCOVA 135.18; 95% CI − 1133.59 to 1403.95; $p = 0.829$), changes in BNP (ANCOVA 47.74; 95% CI − 58.71 to 154.19; $p = 0.375$), and changes in LVEF (ANCOVA − 0.24; 95% CI − 5.18 to 4.70; $p = 0.922$), (Table 4). The other secondary endpoints, including worsening of symptoms, cost of medical care, and changes in hs-CRP, PTX3, hs-cTnT, and high-molecular weight adiponectin could not be analyzed because of insufficient data collection. Improvements in the MMSE score (ANCOVA − 0.24; 95% CI − 1.07 to 0.59; $p = 0.568$), the GSES score (ANCOVA 0.03; 95% CI − 0.28 to 0.34; $p = 0.842$), the MLWHF score (ANCOVA − 0.27; 95% CI − 7.72 to 7.18; $p = 0.943$), and the PHQ-9 score (ANCOVA 0.49; 95% CI − 0.94 to 1.91; $p = 0.498$) were also similar between groups (Table 5).

Safety

There was no harmful event caused by the telemonitoring system.

Discussion

To the best of our knowledge, the present study is the first multicenter RCT to assess whether a home telemonitoring system has a benefit over usual care for reducing rehospitalization and mortality rates in Japanese patients with HF. Contrary to our expectation, the results showed that home telemonitoring of physiological data, including body weight, blood pressure, and pulse rate, in addition to usual care for recently hospitalized patients with HF did not reduce the rate of all-cause death or rehospitalization compared to usual care. Although several meta-analyses and systematic reviews have found beneficial effects of home telemonitoring on the management of patients with HF [2, 12, 13, 19, 20], two recently reported large-scale, multicenter RCTs showed negative results [3, 4]. In the Tele-HF study [3], Chaudhry and colleagues discussed that their negative results might have been explained by poor adherence, because 14.4% of the participants who were assigned to the telemonitoring group never used the monitoring system, and only 55.1% of the patients were using the system at least three times per week at week 26 of the study period. Regarding this point, Swedberg and coworkers suggested that patient-centered care (PCC) could increase the effectiveness of home telemonitoring, and discussed the importance of a partnership between patients and healthcare professionals [21]. Accordingly, we intended to maintain adherence by introducing the concept of PCC, referring to a 2012 policy statement by the American College of Cardiology Foundation [22]. For instance, in the outpatient clinic, mainly nurses (sometimes physicians) provided advice to the patients at every visit on the basis of their physiological data obtained from the daily monitoring, while showing patients the website on a tablet computer. However, our results did not show an additional benefit of home telemonitoring, despite the finding that the mean adherence rate of the present study participants was actually maintained at about 90% at 12 months. One of the potential reasons for that might be patient selection. In the present study, we excluded patients in whom a pacemaker or ICD/CRT was implanted, because a body composition scale using an alternating current for measurement was included in our home telemonitoring system. Therefore, there is a high probability that many patients in stage D of HF were excluded. We also excluded patients with severe renal dysfunction, severe liver dysfunction, and limited life expectancy because of malignant diseases or other causes; therefore, the Charlson Comorbidity Index

Table 4 Secondary endpoints

	Telemonitoring		Usual care		ANCOVA	95% CI	*p* value
	Baseline	12 months	Baseline	12 months			
NT-proBNP, pg/ml (SD) *n*	4374.85 (6165.28) 28	2035.29 (2820.21) 23	2540.51 (3040.24) 25	1161.71 (1235.77) 16	135.18	− 1133.59 to 1403.95	0.829
BNP, pg/ml (SD) *n*	332.72 (360.08) 62	193.95 (298.84) 44	526.77 (618.39) 64	183.90 (214.07) 47	47.74	− 58.71 to 154.19	0.375
LVEF, % (SD) *n*	40.46 (14.76) 90	51.81 (15.77) 61	39.24 (16.49) 89	52.43 (15.33) 60	− 0.24	− 5.18 to 4.70	0.922

Values are mean (SD). Changes from baseline are assessed using an analysis of covariance (ANCOVA) model with value of 12 months as the dependent variable and baseline as a covariate

NT-proBNP N-terminal pro-B-type natriuretic peptide, *BNP* B-type natriuretic peptide, *LVEF* left ventricular ejection fraction

Table 5 Secondary endpoints

	Telemonitoring		Usual care		ANCOVA	95% CI	*p* value
	Baseline	12 months	Baseline	12 months			
MMSE (SD) *n*	27.93 (2.42) 82	27.98 (2.24) 40	27.57 (3.82) 86	27.88 (3.10) 40	− 0.24	− 1.07 to 0.59	0.568
GSES (SD) *n*	3.02 (0.97) 82	3.14 (1.06) 51	3.18 (1.10) 82	3.26 (1.02) 53	0.03	− 0.28 to 0.34	0.842
MLWHF (SD) *n*	38.82 (25.14) 82	18.53 (16.93) 51	43.48 (23.21) 86	20.35 (21.50) 54	− 0.27	− 7.72 to 7.18	0.943
PHQ-9 (SD) *n*	5.02 (4.64) 82	3.52 (3.53) 46	5.04 (4.23) 85	3.20 (3.94) 50	0.49	− 0.94 to 1.91	0.498

Values are mean (SD). Changes from baseline are assessed using an analysis of covariance (ANCOVA) model with value of 12 months as the dependent variable and baseline as a covariate

MMSE mini mental state examination, *GSES* General Self-Efficacy Scale, *MLWHF* minnesota living with heart failure questionnaire, *PHQ-9* patient health questionnaire

[23] of the present study participants might be less than 1 point. As a result, rehospitalization rates for worsening HF were 21 and 22% for each group, respectively, during the mean follow-up period of 15 months, which is significantly lower compared with that in previous Japanese reports [24, 25]. DeBusk and colleagues showed that a specific nurse care management program for HF did not reduce rehospitalization rates in patients with low-risk HF compared with usual care [26], suggesting that such specific care might not be effective in patients with a low risk for rehospitalization [12]. In another recently reported large-scale, multicenter RCT, the Telemedical Interventional Monitoring in Heart Failure (TIM-HF) trial [4], the authors suggested that when telemonitoring is applied to stable, optimally treated, ambulatory patients with chronic HF, a reduction in mortality is not present. The second potential reason might be the quality of usual care. Goldberg and coworkers demonstrated that specific care using a technology-based daily weight and symptom-monitoring system also did not reduce rehospitalization rates, even in patients with advanced HF, compared with usual care [27]. In their study, all enrolled patients were followed at HF specialty clinics, and they reported that it was possible that the high quality of usual care left little room for improvement by the additional specific care. In the present study, most of the patients visited the same hospital from which they were recently discharged, and were provided ambulatory treatment by cardiologists. Pandor and colleagues stated that structured telephone support (STS) delivered via human–human contact and home telemonitoring with medical support showed beneficial effects compared to STS delivered via a human–machine (interactive response system) interface in their latest systematic review and meta-analysis [2]; therefore, it may be that human–human communication plays a key role in home telemonitoring for HF to prevent rehospitalization [28]. The home telemonitoring system in the present study did not have an interactive communication function, and the monitoring nurses were prohibited from having direct conversations with the patient, excluding a response to malfunction of the home telemonitoring devices, because of a limitation by a national medical

practitioners' act. Furthermore, no home-healthcare professionals participated in this study.

Our study has several limitations. First, the number of study participants was smaller than we initially planned in the study protocol. We were unable to extend the registration period of the study due to insufficient funds. Therefore, the study may have been statistically underpowered to detect the primary endpoint. Second, the open-label design may have introduced bias, especially for occasionally subjective outcomes, such as rehospitalization [29]. In addition, there were no existing home telemonitoring services for patients with HF in either the public or private sector, and home telemonitoring has not been covered by the national health insurance program in Japan. Therefore, all of the healthcare professionals who participated in the present study were inexperienced in the telemonitoring process, and the monitoring system was handmade by a physician with commercially available devices.

In conclusion, home telemonitoring of physiological data for patients with HF was feasible under the current Japanese healthcare environment; however, its effects in addition to the benefit of usual care were not demonstrated for the present study participants. In the near future, more patients with HF will be treated by home-healthcare providers in Japan and many developed countries because of the growth of the aging population. Frenneaux et al. stated in their recent editorial comment, "It is likely that the greatest promise lies with next generation home-monitoring systems, provided that strategies are implemented for integrating them effectively into the healthcare framework to close the loop between patients and healthcare providers" [30]. Further investigation of more patients with severe heart failure, participation of home medical care providers, and use of a more integrated home telemonitoring system emphasizing communication as well as monitoring of symptoms and physiological data are required.

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Compliance with ethical standards

Conflict of interest Dr. Kotooka and Dr. Asaka have an endowed chair from Sumitomo Electric Industries Ltd., since 2014, and from Asahi Kasei Corporation since 2017. None of the authors has any relationship with industry or any financial associations within the past 2 years that might pose a conflict of interest in connection with the submitted article.

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