Impact of Remote Telemedical Management on Mortality and Hospitalizations in Ambulatory Patients With Chronic Heart Failure

The Telemedical Interventional Monitoring in Heart Failure Study

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Background—This study was designed to determine whether physician-led remote telemedical management (RTM) compared with usual care would result in reduced mortality in ambulatory patients with chronic heart failure (HF).

Methods and Results—We enrolled 710 stable chronic HF patients in New York Heart Association functional class II or III with a left ventricular ejection fraction ≤35% and a history of HF decompensation within the previous 2 years or with a left ventricular ejection fraction ≤25%. Patients were randomly assigned (1:1) to RTM or usual care. Remote telemedical management used portable devices for ECG, blood pressure, and body weight measurements connected to a personal digital assistant that sent automated encrypted transmission via cell phones to the telemedical centers. The primary end point was death from any cause. The first secondary end point was a composite of cardiovascular death and hospitalization for HF. Baseline characteristics were similar between the RTM (n=354) and control (n=356) groups. Of the patients assigned to RTM, 287 (81%) were at least 70% compliant with daily data transfers and no break for >30 days (except during hospitalizations). The median follow-up was 26 months (minimum 12), and was 99.9% complete. Compared with usual care, RTM had no significant effect on all-cause mortality (hazard ratio, 0.97; 95% confidence interval, 0.67 to 1.41; $P=0.87$) or on cardiovascular death or HF hospitalization (hazard ratio, 0.89; 95% confidence interval, 0.67 to 1.19; $P=0.44$).

Conclusions—In ambulatory patients with chronic HF, RTM compared with usual care was not associated with a reduction in all-cause mortality.

Clinical Trial Registration:—URL: http://www.ClinicalTrials.gov. Unique identifier: NCT00543881.

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Key Words: heart failure ■ hospitalization ■ managed care programs ■ mortality ■ telemedicine

Chronic heart failure (HF) results in poor life expectancy, impaired quality of life, and repeated hospitalizations, and represents a considerable economic burden to society.[1] Over the past years, the combination of an aging population and an escalation in healthcare costs has amplified the need for alternative care strategies for these patients. Disease management programs provided via HF clinics have been shown to reduce healthcare utilization and improve outcomes.[2] In the last decade, for patients with chronic HF, the focus has shifted as developments in modern telecommunication technologies have created new options to deliver remote telemedical care.

Clinical Perspective on p 1880

In chronic HF, remote telemedical management (RTM) can be used to optimize therapy, improve compliance, and enable early detection of cardiac decompensation. In the last decade, several clinical trials have been performed to assess the

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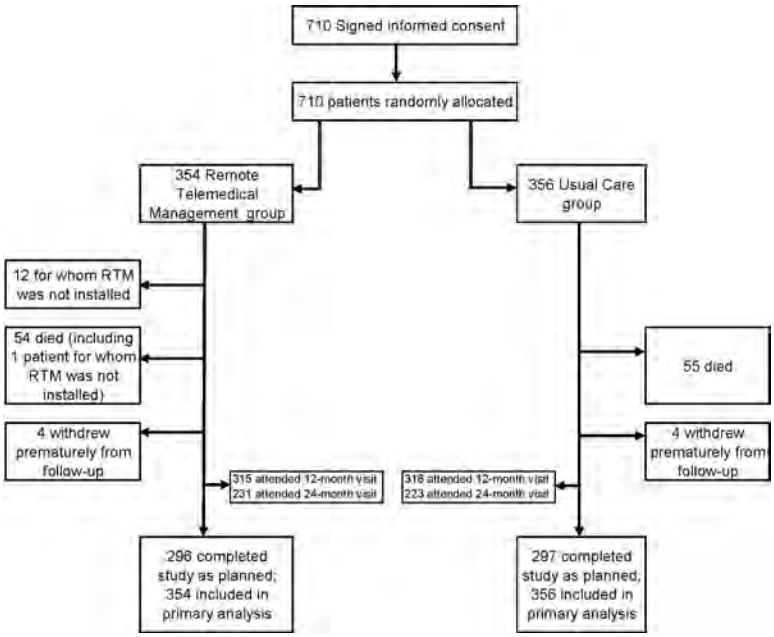

Figure 1. The numbers of patients for each group who were randomly assigned to remote telemedical management (RTM) or usual care, and who were analyzed for the primary outcome.

efficacy of telemedical monitoring to improve symptoms or quality of life. Two recent meta-analyses suggest that telemedical monitoring of chronic HF patients can improve overall survival by 17% to 47% during 6 to 12 months of follow-up.[3,4] In these studies, rates and duration of hospitalization for cardiovascular reasons or HF were reduced in the telemedical intervention groups. This needs prospective testing.

In the majority of reported telemedical studies, telemedical support was restricted to office hours. This could limit efficacy, and therefore we used telemedical centers with 24-hour physician availability. The Telemedical Interventional Monitoring in Heart Failure (TIM-HF) trial was a randomized, multicenter, controlled intervention study designed to investigate whether RTM would reduce mortality and hospitalizations in ambulatory chronic HF patients compared with usual care.

Methods

Trial Design and Oversight

Between January 10, 2008, and June 22, 2009, 710 eligible patients with chronic HF were enrolled from 165 cardiology, internal medicine, or general medicine practices (Figure 1). The protocol was approved by the institutional review board at each participating center and conducted in accordance with the principles of the Declaration of Helsinki (1996), International Conference on Harmonization Good Clinical Practice, and local and national regulations. The primary hypothesis was that RTM would be associated with a reduced risk of death compared with usual care.

A description of the study design has been published previously.[5] All patients provided written informed consent. The trial was designed, implemented, and overseen by the Steering Committee. The Clinical Trial Center Leipzig (University Leipzig, Leipzig, Germany) acted as the coordinating center, which included data management and on-site monitoring in addition to performing the sample size calculations for the trial. SOCAR Research, Nyon, Switzerland, was responsible for data analysis. Clinical Trial Center Leipzig performed the same analyses, separately, with identical results. The manuscript was prepared and submitted for publication by the Steering Committee. An independent Data Safety Monitoring Board reviewed safety data on an ongoing basis. The Clinical End Point Committee, blinded to study group assignment, classified all deaths and hospitalizations using the prospectively defined criteria detailed in the Clinical End Point Committee charter.[5] The authors had access to the study data and vouch for the accuracy and completeness of the reported analyses.

Patient Recruitment and Follow-Up

Stable, ambulatory patients of either sex with chronic HF who had signed informed consent were eligible to participate if they were at least 18 years of age, were in New York Heart Association (NYHA) class II or III, and had a left ventricular ejection fraction of ≤35%. Eligible patients with a left ventricular ejection fraction >25% must have had at least 1 HF decompensation episode that resulted in hospitalization or treatment with intravenous loop diuretics (>40 mg furosemide per day) in the 24 months before randomization. All patients had to be optimally treated for HF according to current guidelines. The inclusion and exclusion criteria are provided in Table I in the online-only Data Supplement.

Patients were followed for a minimum of 12 months, with outpatient visits at 3, 6, 9, and 12 months during the first year and at 18 and 24 months in the second year. Clinical evaluation and blood testing were performed during the follow-up visits, and were documented on paper case report forms. Two self-administered questionnaires, the depression model of the Patient Health Questionnaire (PHQ-9)[6] and the 36-item Short Form health survey of the Medical Outcome Study (SF-36), were completed by patients at baseline and at months 12 and 24.

Data Collection for Hospitalizations

A decision was made early in the trial to implement a quality control system to ensure the accurate and complete reporting of hospitalizations. This process required the cooperation of patients, investigators, and the patients' respective medical insurance companies. Patients were asked to sign an additional informed consent giving their permission for the coordinating center to contact their medical insurance company in order to cross-check the hospitalizations reported by the investigators with those on file in the medical insurance records. This process was approved by the Data Protection Office of the German Federal Social Insurance Office.

Randomization

During screening, a clinical history, physical examination, and 12-lead ECG were obtained for each patient in addition to assess-

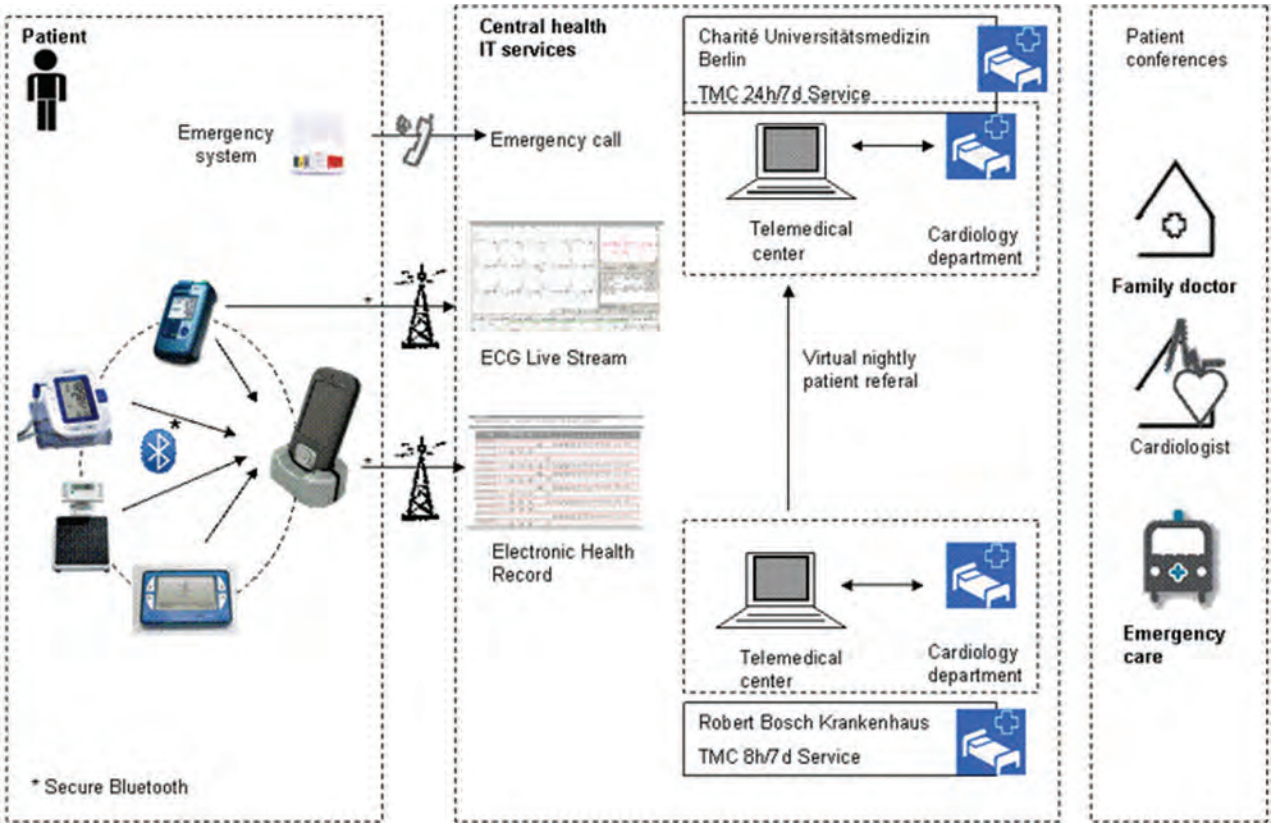

Figure 2. Overview of telemedical system and service structure. Devices for ECG, blood pressure, and body weight measurements are connected via Bluetooth at the patient's home. A personal digital assistant transmits the data via its integrated cell phone module to the central servers. In the Telemedical Interventional Monitoring in Heart Failure trial, there were 2 telemedical centers, the first located in Berlin and the second in Stuttgart, that communicated via electronic patient records. A home emergency call system enables the patient to have direct contact with the healthcare specialist. IT indicates information technology; TMC, telemedical center.

ment of quality of life and depression. Eligible patients were then randomly assigned in a 1:1 ratio to receive either RTM or usual care. As described previously,[5] Pocock's minimization algorithm,[7] with 20% residual randomness, was used to ensure balance of important clinical characteristics.

Treatment

The RTM system used was described previously.[5,8,9] Briefly, the system is based on a wireless Bluetooth device, together with a personal digital assistant, as the central structural element (Figure 2). Data transfer was performed with the use of cell phone technologies. The following devices were part of the integrated sensor network: a 3-lead ECG, a blood pressure device, and a weighing scale with 50-g precision. The patient performed a daily self-assessment with these devices, and the data were transferred to the responsible telemedical center. Data privacy was ensured with dynamic encryption.

The RTM equipment was installed, and training was given to patients within a maximum of 5 working days after randomization. The 2 telemedical centers provided physician-led medical support 24 hours per day, 7 days per week for the entire study period with the use of standard operating procedures. The patient was contacted by the telemedical center physician in accordance with the standard operating procedures in place or when requested by the patient to verify measurements, to give consultation, or to institute treatment. The telemedical center contacted the patient's local physician at least every 3 months. The general responsibility for the patient's care remained with the local physician.

Other than RTM support, patients assigned to the usual care group were followed and treated in the same manner as patients assigned to RTM. At the study start, all investigators were instructed to treat patients in accordance with the current guidelines for the management of HF, irrespective of group assignment.

Outcome Measures

The primary end point was all-cause mortality. The first secondary end point was a composite of cardiovascular mortality and hospitalization for HF.

Other secondary end points included days lost because of death or Clinical End Point Committee–adjudicated HF hospitalization, duration of hospitalization for HF, rate of hospitalization for a cardiovascular reason, and rate of hospitalization for HF at 6, 12, and 24 months, respectively, as well as NYHA functional classification, SF-36 physical functioning score, and PHQ-9 depression score at 12 and 24 months, all adjusted for baseline results.

Statistical Analysis

We predefined all data analysis in a formal statistical analysis plan. Data analysis was performed according to the intention-to-treat principle by assigned study group. The sample size calculation was done with the use of PASW 2002 (NCSS, Kaysville, UT). The initial sample size of 600 patients (300 patients per study group) had a 90% power to detect a hazard ratio of 0.59 at a 2-sided type I error level of 0.05.[5] Following a recommendation by the Data Safety Monitoring Board at the end of 2008, the sample size was increased to 710 patients (355 patients per study group), and the follow-up was extended by 12 months because, at that time, there was a lower than anticipated event rate after 1 year of follow-up.

Cumulative survival curves for the time-to-event analyses were constructed according to the Kaplan-Meier method, and the differences between curves were examined by the log-rank statistic. The Cox proportional hazards regression (SAS PROC PHREG procedure)[10] was used to estimate the hazard ratios, with treatment as the only covariate. Event rates are expressed as the percentage of events per 100 patient-years of follow-up, taking into account the censoring

of follow-up data. New York Heart Association functional class during follow-up was compared by means of logistic regression with ordinal polytomous response adjusted for baseline functional NYHA class. The repeated-measures analysis for categorical variables was done with the SAS PROC logistic procedure, including terms for treatment and baseline value. For hospitalized patients, a missing NYHA functional class value was ranked as class IV, and for patients who had died, the value was ranked as class V (died). For continuous variables like the SF-36 questionnaire scores, group means of RTM and usual care groups at 12 and 24 months were compared by repeated-measures models with the SAS PROC MIXED procedure, including terms for treatment, visit, baseline value, and treatment by visit with an unstructured matrix of covariance.

For the analysis of days lost because of death or HF hospitalization, the fraction of follow-up time lost because of death or HF hospitalization was defined as the number of days lost divided by the intended follow-up. For patients who died, the number of days lost between the date of death and the date of intended follow-up plus the number of days spent in hospital for HF was counted. For patients who completed the study as planned or who withdrew prematurely from follow-up, the fraction of follow-up time was defined as number of days lost (because of HF hospitalization) divided by the follow-up time realized (ie, up to the censoring date). A t test was used to compare the treatment groups. The significance level for tests was 2-sided α of 0.05. All analyses were conducted with SAS software, version 9.2 (SAS Institute).

Results

A total of 710 patients with chronic HF were enrolled in the TIM-HF study, with 354 patients randomly assigned to the RTM group and 356 to the usual care group. Baseline clinical and laboratory characteristics, in addition to the use of cardiovascular medications, were similar between the 2 groups (Table 1).

Follow-Up and Disposition of Patients

The median follow-up was 26 months. All patients were followed until a common stopping date, which was minimally 12 months and maximally 28 months after randomization. Of the 354 patients randomly assigned to receive RTM, 287 (81%) were at least 70% compliant with the daily transfer of data to the telemedicine centers and had no break in information transfer for >30 days (except during hospitalizations). Overall, patient follow-up was 99.7% complete.

Primary Outcome

The rate per 100 person-years of follow-up for the primary outcome of death for any cause was 8.4% in the RTM group compared with 8.7% in the usual care group (hazard ratio in the RTM group, 0.97; 95% confidence interval, 0.67 to 1.41; $P=0.87$) (Table 2 and Figure 3A).

Secondary Outcomes

For the composite secondary outcome, cardiovascular death and hospitalization for HF, the rate per 100 person-years of follow-up was 14.7% in the RTM group compared with 16.5% in the usual care group (hazard ratio in the RTM group, 0.89; 95% confidence interval, 0.67 to 1.19; $P=0.44$) (Table 2 and Figure 2B). Other secondary event–based outcomes are reported in Tables 2 through 4.

Table 1. Baseline Demographics and Clinical Characteristics of the Study Patients in the Intention-to-Treat Population, According to Study Group

Variable	RTM (n=354)	Usual Care (n=356)
Age, y	66.9±10.8	66.9±10.5
Male sex, No. (%)	285 (80.5)	292 (82.0)
Living alone, No. (%)	75 (21.2)	77 (21.6)
NYHA class, No. (%)		
II	176 (49.7)	180 (50.6)
III	178 (50.3)	176 (49.4)
Left ventricular ejection fraction, %	26.9±5.7	27.0±5.9
Body weight, kg	84.7±18.9	84.7±18.3
Body mass index, kg/m^2*	28.4±5.4	28.2±5.3
Blood pressure, mm Hg		
Systolic	121±16	122±17
Diastolic	74±10	74±10
Pulse, bpm	71±13	71±13
Duration of heart failure, y	6.7±6.6	6.8±6.4
Ischemic cause of heart failure, No. (%)	202 (57.1)	194 (54.5)
Cardiovascular risk factor, No. (%)		
Hypertension	241 (68.1)	235 (66.0)
Hyperlipidemia	262 (74.0)	266 (74.7)
Diabetes mellitus	141 (39.8)	140 (39.3)
Medical history, No. (%)		
Hyperuricemia	121 (34.2)	144 (40.4)
Myocardial infarction	176 (49.7)	176 (49.4)
Coronary revascularization†	189 (53.4)	184 (51.7)
Implantable cardioverter-defibrillator	164 (46.3)	160 (44.9)
Cardiac resynchronization therapy	54 (15.3)	60 (16.9)
Laboratory measurements		
Hemoglobin, g/L	138±17	140±15
Uric acid, μmol/L	448.09±128.05	441.98±113.49
C-reactive protein, mg/L	7.58±12.54	5.99±7.01
Serum sodium, mmol/L	140±3	139±3
Potassium, mmol/L	4.63±0.62	4.59±0.57
Serum creatinine, μmol/L	115±37	111±31
Estimated glomerular filtration rate, mL/min per 1.73 m^2 of body surface area‡	62.5±21.9	64.0±20.2
Total cholesterol, mmol/L	4.79±1.25	4.91±1.20
N-terminal pro-B-type natriuretic peptide, pg/mL	2478±3266	2319±3641
Midregional pro-adrenomedullin, nmol/L	1.00±0.50	0.97±0.51
Midregional pro-atrial natriuretic peptide, pmol/L	334±237	320±228

(Continued)

Table 1. Continued

Variable	RTM (n=354)	Usual Care (n=356)
Concomitant treatment, No. (%)		
Diuretic	332 (93.8)	333 (93.5)
ACE inhibitor or ARB	342 (96.6)	335 (94.1)
Digitalis glycoside	108 (30.5)	112 (31.5)
β-blocker	326 (92.1)	331 (93.0)
Antiplatelet therapy/anticoagulant therapy	315 (89.0)	326 (91.6)
Allopurinol	73 (20.6)	87 (24.4)
Lipid-lowering	228 (64.4)	240 (67.4)
Insulin	63 (17.8)	56 (15.7)
Oral hypoglycemic	58 (16.4)	64 (18.0)
Aldosterone antagonist	231 (65.3)	225 (63.2)
Calcium antagonist	21 (5.9)	26 (7.3)
Nitrate	41 (11.6)	36 (10.1)
Antiarrhythmic	52 (14.7)	66 (18.5)

Plus-minus values are mean±SD. Percentages are based on the number of patients who underwent randomization. RTM indicates remote telemedical management; NYHA, New York Heart Association; ACE, angiotensin-converting enzyme; and ARB, angiotensin receptor blocker.

*The body mass index is the weight in kilograms divided by the square of the height in meters.

†Coronary revascularization includes coronary artery bypass grafting and percutaneous coronary intervention.

‡Estimated glomerular filtration rate was calculated by using the Modification of Diet in Renal Disease formula: 186×[serum creatinine (μmol/L)/88.4]−1.154 ×age−0.203×(1.21 if black)×(0.742 if female). To convert the values for creatinine to milligrams per deciliter, divide by 88.4.

Symptoms and Quality of Life

The likelihood of being in a better NYHA functional class and having an improved PHQ-9 depression score at months 12 and 24 was similar between the assigned groups ($P>0.5$; Figures I and II in the online-only Data Supplement). Patients randomly allocated to the RTM group compared with the usual care group showed an improved score for SF-36 physical functioning over the entire study period ($P<0.05$): Mean score at month 12 was 54.3±1.2 versus 49.9±1.2 ($P=0.01$); mean score at month 24 was 53.8±1.4 versus 51.7±1.4 ($P=0.30$).

Discussion

The TIM-HF trial was designed to evaluate the effect of RTM compared with usual care on all-cause mortality in ambulatory chronic HF patients. The results of TIM-HF suggest that when RTM is applied to stable, optimally treated, ambulatory chronic HF patients, a reduction in mortality is not present.

Another recently reported study, Telemonitoring to Improve Heart Failure Outcomes (Tele-HF),[11] found that, compared with the usual care group, there was no reduction in the risk of hospital readmission (for any reason) or all-cause mortality in HF patients assigned to telemonitoring who had been recently hospitalized for worsening HF. Although the outcomes of TIM-HF and Tele-HF are similar, important differences in the design of these studies need to be addressed. First, the HF populations investigated had different disease severities. Second, the follow-up times differed substantially between the 2 studies; the mean follow-up was 6 months in Tele-HF, whereas the median follow-up in TIM-HF was 26 months. Third, the RTM intervention implemented and the compliance associated with that differed between these 2 studies. Another important reason why these 2 trials cannot be compared is that because of the low statistical power in TIM-HF, we cannot exclude a more modest yet clinically important treatment effect on mortality, whereas Tele-HF was more sufficiently powered to provide a robust answer.

Another study that investigated the impact of telemonitoring in HF patients was the Trans-European Network–Home-Care Management System (TEN-HMS) study.[12] Investigating a total of 426 patients with HF in 3 intervention groups, TEN-HMS reported that home telemonitoring for patients with HF reduced the days lost because of death or hospitalization during 240 days of follow-up. Patients in the usual care group had a higher mortality rate at 240 days of follow-up than patients with home telemonitoring (24% versus 17%), and after 450 days of follow-up, the percentage of patients who had died in the usual care and home telemonitoring group was 51% and 34%, respectively. The mortality rate in TIM-HF was lower than in TEN-HMS. We speculate that the main reason for the higher absolute event rates in TEN-HMS is that patients were recruited more

Table 2. Prespecified Primary and Secondary Outcomes

Outcomes	RTM (n=354) Total No. of Events	RTM (n=354) No. of Patients With Event (Incidence per 100 Patient-Years at Risk)	Usual Care (n=356) Total No. of Events	Usual Care (n=356) No. of Patients With Event (Incidence per 100 Patient-Years at Risk)	Hazard Ratio (95% CI)	P
Primary outcomes						
Death from any cause	54	54 (8.43)	55	55 (8.68)	0.97 (0.67–1.41)	0.87
Death due to cardiovascular cause	40	40 (6.24)	46	46 (7.26)	0.86 (0.56–1.31)	0.49
Secondary outcomes						
Hospitalization for heart failure or death due to cardiovascular cause	153	87 (14.70)	160	95 (16.51)	0.89 (0.67–1.19)	0.44
Any hospitalization	486	192 (44.09)	394	179 (39.19)	1.12 (0.91–1.37)	0.29
Hospitalization for any cardiovascular cause	290	141 (27.79)	248	132 (26.05)	1.07 (0.84–1.35)	0.58
Hospitalization for heart failure	113	64 (10.81)	114	74 (12.86)	0.84 (0.60–1.18)	0.32

RTM indicates remote telemedical management; CI, confidence interval. Hazard ratio=comparison of RTM with usual care.

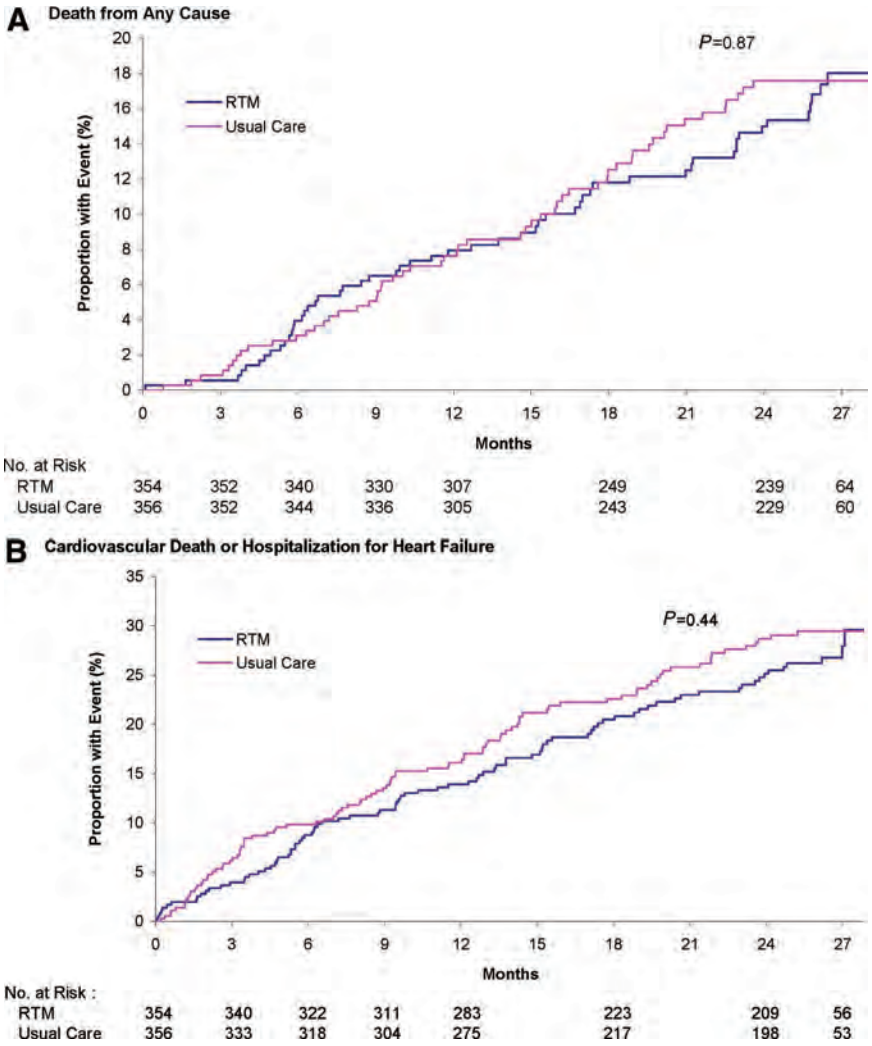

Figure 3. Shown are the cumulative incidence of the primary outcome (death from any cause) (**A**) and the composite secondary outcome (hospitalization for heart failure or cardiovascular death) (**B**) during follow-up. RTM indicates remote telemedical management.

immediately after a recent hospitalization, as is also evident from Tele-HF,[11] and this may possibly explain the lower rate of guideline-mandated medication, including angiotensin-converting enzyme inhibitors, β-blockers, and aldosterone receptor antagonists. TIM-HF is the first RTM trial to prospectively investigate clinical outcomes in chronic HF patients over a median follow-up of 26 months. Whether this prolonged period of RTM is required remains uncertain.

The results of TIM-HF and Tele-HF are in clear contrast to those presented in 2 prior meta-analyses,[3,4] which reported that telemedical monitoring in chronic HF patients improved overall survival by 17% to 47% during 6 to 12 months of follow-up. The reason for such contrasting results may be explained by the fact that the meta-analyses combined many small dissimilar telemonitoring studies that investigated HF patients with varying risk profiles who were followed for different durations and for which the intervention used was different between studies. In addition, the majority of these small studies were not prospectively designed to collect events or to show this reduction in mortality. Before the

Table 3. Hospitalization Rates at 6 and 12 Months

	RTM (n=354)		Usual Care (n=356)			
	Total No. of Hospitalizations	No. of Patients With Event (Incidence per 100 Patient-Years at Risk)	Total No. of Hospitalizations	No. of Patients With Event (Incidence per 100 Patient-Years at Risk)	Hazard Ratio (95% CI)	*P*
Cardiovascular hospitalizations	290	141 (27.79)	248	132 (26.05)	1.07 (0.84–1.35)	0.58
6 mo	75	56 (34.78)	80	58 (36.19)	0.96 (0.67–1.39)	0.84
12 mo	144	96 (32.60)	145	87 (29.52)	1.10 (0.83–1.47)	0.51
Hospitalization for heart failure	113	64 (10.81)	114	74 (12.86)	0.84 (0.60–1.18)	0.32
6 mo	31	23 (13.53)	36	29 (17.32)	0.78 (0.45–1.35)	0.38
12 mo	56	35 (10.82)	63	44 (13.82)	0.78 (0.50–1.22)	0.28

RTM indicates remote telemedical management; CI, confidence interval. Hazard ratio=comparison of RTM with usual care.

Table 4. Duration of Hospitalizations and Days Lost Because of Death or Heart Failure Hospitalization

	RTM (n=354)	Usual Care (n=356)	*P* (*t* Test)
Any hospitalization			
No. of days in hospital	16.7±32.3	13.7±22.7	0.15
Percentage of follow-up time spent in hospital	3.4±7.3	3.1±6.5	0.53
Heart failure hospitalization			
No. of days in hospital for heart failure	5.3±18.1	4.9±13.2	0.71
Percentage of follow-up time spent in hospital for heart failure	1.3±5.7	1.1±3.3	0.49
Days lost because of death or heart failure hospitalization			
No. of days lost because of death or heart failure hospitalization	32.8±82.1	38.9±97.0	0.37
Percentage of follow-up time lost because of death or heart failure hospitalization	6.3±16.5	6.9±17.1	0.66

Plus-minus values are mean±SD. RTM indicates remote telemedical management. *P*=comparison of RTM with usual care.

results of the TIM-HF and Tele-HF trials, the bulk of the evidence concerning the utility and benefit of telemedicine with respect to a reduction in mortality in HF patients originated from meta-analyses. The results of the TIM-HF and Tele-HF trials emphasize the importance and need for well-conducted randomized and clearly reported clinical trials to draw rightful conclusions, because meta-analyses may not always provide accurate clinical evidence.

A limitation of our analysis is that we had low statistical power to detect a clinically relevant difference in mortality between the compared patient groups, as is evidenced by the wide 95% confidence intervals. However, we still consider our findings to be of scientific value because they can be combined with other relevant data obtained from similar clinical studies to lead to more accurate conclusions. Another limitation of our study is that no information is available concerning the number of patients who were prescreened and who were not enrolled in the trial. In essence, investigators prescreened all their patients (on paper), and only contacted those who met the inclusion/exclusion criteria. To our knowledge, all patients who were asked to participate in this trial agreed to participate and subsequently signed the informed consent.

Another issue that needs careful consideration in the interpretation and applicability of telemedicine clinical trial and meta-analyses results is a clear understanding of the telemonitoring procedures and processes implemented for each trial concerned, because these may differ greatly between studies. For instance, in the TIM-HF study, the telemonitoring management was a 24 hours per day, 7 days per week, physician-led intervention in which patients were contacted regularly by a physician, whereas in the Tele-HF study, patients used a toll-free telephone system in which an automated voice asked them a series of questions about general health and HF symptoms, and patients entered responses using the telephone keypad.

Future randomized clinical trials in telemedical management of HF patients should focus on the identification of the target population most likely to respond to this intervention. As suggested by exploratory subgroup analyses in TIM-HF, profiling of such patient groups may be possible.

The results of the TIM-HF study suggest that RTM compared with usual care does not improve survival in stable, optimally treated patients with chronic HF. Given the lack of power in our trial, the lack of benefit from RTM as seen in the TIM-HF trial on the prespecified end point does not rule out the potential role of RTM as an addition to the management of HF. Rather, it emphasizes the need to identify the HF population that could benefit from using this intervention.

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CLINICAL PERSPECTIVE

The Telemedical Interventional Monitoring in Heart Failure (TIM-HF) trial was designed to determine whether physician-led remote telemedical management (RTM) compared with usual care would positively affect total mortality in ambulatory, stable chronic heart failure patients. Eligible patients were in New York Heart Association class II or III, with a left ventricular ejection fraction ≤35% who had a history of heart failure decompensation within the previous 2 years or with a left ventricular ejection fraction ≤25%. Patients were randomly assigned (1:1) to RTM (n=354) or usual care (n=356). Remote telemedical management used portable devices for ECG, blood pressure, and body weight measurements. Data were transferred daily via a personal digital assistant to physician-led telemedical centers that were active on a 24 hours per day, 7 days per week basis. Of the patients assigned to RTM, 81% were ≥70% compliant with daily data transfers and no break for >30 days (except during hospitalizations). Over a median follow-up of 26 months, compared with usual care, RTM had no significant effect on total mortality (hazard ratio, 0.97; 95% confidence interval, 0.67 to 1.41; $P=0.87$) or on cardiovascular death or heart failure hospitalization (hazard ratio, 0.89; 95% confidence interval, 0.67 to 1.19; $P=0.44$), the first secondary outcome. In conclusion, in stable ambulatory patients with chronic heart failure, RTM compared with usual care was not associated with a reduction in all-cause mortality. Our results do not concur with the recently published meta-analysis. However, the latter need to be interpreted with caution, because not all telemedical approaches are the same. Telemedicine may not be appropriate for all heart failure patients. Future research needs to document which patients with chronic heart failure could benefit from certain types of telemedical support/management.