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The value of telemonitoring and ICT-guided disease management in heart failure: Results from the IN TOUCH study

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ABSTRACT

Aim: It is still unclear whether telemonitoring reduces hospitalization and mortality in heart failure (HF) patients and whether adding an Information and Computing Technology-guided-disease-management-system (ICT-guided-DMS) improves clinical and patient reported outcomes or reduces healthcare costs.
Methods: A multicenter randomized controlled trial was performed testing the effects of INnovative ICT-guided-DMS combined with Telemonitoring in OUtpatient clinics for Chronic HF patients (IN TOUCH) with in total 179 patients (mean age 69 years; 72% male; 77% in New York Heart Association Classification (NYHA) III–IV; mean left ventricular ejection fraction was 28%). Patients were randomized to ICT-guided-DMS or to ICT-guided-DMS + telemonitoring with a follow-up of nine months. The composite endpoint included mortality, HF-readmission and change in health-related quality of life (HR-QoL).
Results: In total 177 patients were eligible for analyses. The mean score of the primary composite endpoint was −0.63 in ICT-guided-DMS vs. −0.73 in ICT-guided-DMS + telemonitoring (mean difference 0.1, 95% CI: −0.67 +0.82, $p = 0.39$). All-cause mortality in ICT-guided-DMS was 12% versus 15% in ICT-guided-DMS + telemonitoring ($p = 0.27$); HF-readmission 28% vs. 27% $p = 0.87$; all-cause readmission was 49% vs. 51% ($p = 0.78$). HR-QoL improved in most patients and was equal in both groups. Incremental costs were €1360 in favor of ICT-guided-DMS. ICT-guided-DMS + telemonitoring had significantly fewer HF-outpatient-clinic visits ($p < 0.01$).
Conclusion: ICT-guided-DMS + telemonitoring for the management of HF patients did not affect the primary and secondary endpoints. However, we did find a reduction in visits to the HF-outpatient clinic in this group suggesting that telemonitoring might be safe to use in reorganizing HF-care with relatively low costs.

1. Introduction

Increasing shortage of resources, growing costs, increase in expensive treatments and downwards pressure on healthcare budgets, necessitates a thorough review of management of patients with heart failure (HF). Heart failure is a chronic debilitating condition with a poor prognosis and can be defined as an abnormality of the cardiac structure or function leading to failure of the heart to deliver oxygen and causes a cascade of syndromes, symptoms and complaints [1]. A first step in efficiently organizing HF-care was taken by implementing specialized HF-outpatient clinics, with a strong collaboration between HF-nurses and cardiologists [2,3]. In these HF-outpatient clinics, Disease Management Programs (DMP) were introduced [4,5] and over the last decade, these clinics became 'care as usual' in several European countries [6]. The effect on quality of care and clinical outcomes in HF-clinics in the Netherlands was investigated by two randomized studies [7,8]. Although both studies have contributed to the quality of DMP in HF-outpatient

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clinics led by specialized HF-nurses, the key characteristics of patients who benefits most from a DMP remained unclear [9].

Although tele cardiology seems to be a large success for the management of pace-makers and defibrillators, the use of tele cardiology in the follow-up of technological functioning of pacemakers and defibrillators is quite different from the use in the monitoring of symptoms of deterioration in patients. Guidelines suggest to include careful monitoring of HF patients in addition to regular outpatient clinic visits by means of telephonic assessments or telemonitoring [1]. On a caregiver level, cardiologists and HF-nurses have high expectations of telemonitoring by expecting it to improve quality of care, reduce costs and improves patients' Health-Related Quality of Life (HR-QoL) by increasing feelings of control and empowerment of the patient [10]. On the other side, the misalignment between patients expectations regarding the continuously monitoring of the data and the actually non-continuously monitoring activities from the professionals providing the service is a cause of concern. On a patient level, patients experience by using telemonitoring an increase in their self-care activities [11], an increase in their understanding of HF symptoms and an improvement in their feeling of safety [12]. Furthermore, patients experience a high level of satisfaction with telemonitoring and have the feeling that care-givers continuously monitor the transmitted parameters (despite the knowledge that monitoring by care-givers is non-continuously) [13]. On a population level, results regarding reduction in hospitalization and mortality rates by the use of telemonitoring in HF patients compared to usual care are ambiguous [14–19]. It is suggested that the development of tools to automatically analyze the data and provide advice to patients and caregivers regarding the treatment of the patient would be a revolution [18]. However, until now it is not clear whether telemonitoring, when delivered as an integrated approach added to an information and communication technology guided disease management system (ICT-guided-DMS), improves clinical and patient reported outcomes or reduces healthcare costs. The value of a Computer Decision Support System (CDSS) incorporated into an ICT-guided-DMS to facilitate healthcare professionals into optimizing treatment and care is also not known. Therefore, the aim of this study is to assess the effect of telemonitoring on top of an ICT-guided-DMS with an CDSS in patients with worsening HF on the combined endpoint of death, readmission and HR-QoL, compared to patients treated with ICT-guided-DMS and CDSS alone.

2. Methods

2.1. IN TOUCH study

The IN TOUCH (the value of INnovative ICT-guided disease management combined with Telemonitoring in OUt patient clinics for Chronic Heart failure patients) was a multicenter, randomized controlled study designed to investigate the effects and costs of ICT-guided-DMS with CDSS, versus ICT-guided-DMS with CDSS and telemonitoring in HF-patients on a composite endpoint of mortality, HF-readmission and change in HR-QoL. The rational and design have been described elsewhere [20]. In short, the study consisted of one control group and two intervention groups. The control group consisted of separate hospitals in which patients received usual care without any use of telemonitoring devices for the entire study. The intervention group consisted of one group receiving ICT-guided-DMS with CDSS without telemonitoring, the other group received ICT-guided-DMS with CDSS and telemonitoring, from now on described as ICT-guided-DMS group and telemonitoring group respectively. In December 2010, adjustments to the study protocol were necessary for two reasons. It was impossible to recruit hospitals for the usual care part of the study (the control group) because using any form of telemonitoring in the control group during the complete study period was an exclusion criterion to participate as a control hospital in this study. The second reason for the adjustment of the study protocol was the low inclusion rate of patients with an HF-admission in the intervention hospitals. The adjustments to the study protocol were (1) to have a randomized intervention study without control group and (2) broadening of the inclusion criteria to inclusion of patients with HF-deterioration visiting the HF clinic and outpatient HF clinic and needed to be treated with extra diuretics. In addition, the inclusion period was extended with nine months. As a result of this the study design changed from a study with 3 arms (a control group and two intervention groups) to a study with 2 intervention arms and no control group. Patients were recruited in ten Dutch hospitals during a period of in total 25 months (December 2009–January 2012). The medical ethical committee approved the protocol and the adjustments to the protocol which had no consequences for the feasibility of the ongoing study (ABR:NL26271.042.08). All patients provided written informed consent and our study conforms to the principles outlined in the Declaration of Helsinki.

2.2. Patient population

All included patients had worsening HF based on typical signs and symptoms of fluid retention. Inclusion criteria were: admission to the intensive care/ coronary care unit or cardiology ward or visiting the outpatient HF-clinic and in need of treatment or adjustment with oral or intravenous diuretics, aged 18 years or older, evidence of structural underlying heart disease, documented reduced left ventricular ejection fraction (LVEF) $\leq$45%. Exclusion criteria were: myocardial infarction in the last month, cardiac invasive intervention in the past 6 months or planned in the next 3 months, hemodialysis, use of other telemonitoring systems, inability or unwillingness to give informed consent.

2.3. Randomization

Randomization to one of the intervention groups was performed within 2 weeks after inclusion. One group received ICT-guided-DMS, the other group received telemonitoring. The computer-generated randomization scheme used random permuted blocks of 2:1 (original protocol) and 1:1 (adjusted protocol December 2010) stratified by centre to ensure balanced assignment of patients to each group in the ten participating centres.

2.4. Intervention

2.4.1. ICT-guided-DMS

All patients in both groups. The function of the CDSS in the DMS was to provided advice to the healthcare providers according to the actual ESC-HF guidelines, regarding the up-titration of HF-medication to optimal individual doses. The ESC-HF guidelines were programmed into the DMS as workable digital flow-charts. The advice of the CDSS was based on the input of data from nursing assessment, physical examination, medical history, laboratory and questionnaires; if for example the vital signs and laboratory values of the patient were within the pre-defined ranges of the digital flow-chart, the CDSS generated an advice to further up-titrate the medication to optimal doses according to the HF-guidelines. The data regarding the nursing assessment, physical examination and medical history was added manually to the system by the nurse. The data regarding the laboratory system was loaded into the CDSS automatically. The questionnaires could be presented to the patient electronically or on paper. If the questionnaire was filled in by the patient electronically, the data was loaded into the CDSS automatically. If the questionnaire was filled in by the patient on paper, the

data was entered into the CDSS manually by the nurse. Furthermore, the data from the health-monitor loaded automatically into the CDSS. Both groups received counselling on HF-symptom management and improvement of the non-pharmacological regimen based on protocols and recent HF-guidelines [20]. Patients allocated to the telemonitoring group were only allowed to visit the cardiologist or HF-nurse in case of an absolute need for intervention. The ICT-guided-DSM group followed the normal HF-routine of the individual hospitals, like any other HF-patient, without limitations to the visits.

2.4.2. Telemonitoring

Patients in the telemonitoring group received telemonitoring devices at home consisting of a weighing scale, blood pressure equipment, an ECG-device and a health-monitor. The instruction was to record weight and blood pressure once a day and an ECG in case of starting or up-titration of Beta-blockers. The health-monitor was an interactive monitor which received the data from the weighing scale, blood pressure equipment and if applicable the ECG-device automatically at the end of the measurement by means of a wireless bluetooth connection. After receiving the data from the above mentioned devices, the health-monitor generated standard health-related questions regarding the patients' health status. The HF-nurse could add pre-defined and individual ranges of weight, blood pressure or heart rhythm in the CDSS. In case of deviation of the pre-defined ranges the health-monitor at home generated automatically supplementary questions to evaluate the actual health situation. The data of the weighing scale, blood pressure equipment and if applicable the ECG-device and the answers on the health-related questions were directly transmitted by the health-monitor through the GPRS network to the DMS system located in the hospital and loaded in the CDSS. In case of deviation of the pre-defined ranges the HF-nurse was informed automatically by mobile phone and email (according to the study protocol). To prevent an increased workload for the HF-nurse and to prevent an incorrect perception of the patient that the telemonitoring measurements were continuously monitored, the patients were informed that they had to perform the measurement every morning (including the weekends) before a certain time. If there was a deviation of the pre-defined ranges, the HF-nurse contacted the patient within two hours and discussed the symptoms and treatment with the patient [21].

2.5. Data collection

The change in HR-QoL between baseline and the end of the study was assessed by the Minnesota Living with HF Questionnaire (MLHFQ). The MLHFQ is a 21-item disease-specific HR-QoL instrument with scores for each item ranging from 0 to 5, a summary score ranging from 0 to 105 and 2 subscales. Higher scores represents worse HR-QoL [22].

Data on hospitalizations and mortality were collected from the medical records during the 9 months of follow-up. The reason of hospital readmission or death and the date of the event were adjudicated by an independent endpoint committee blinded for the group assignment. The days lost to death were defined as the number of days lost because of death during the 9 months of follow-up.

Data on costs; for the cost minimization analyses a distinction was made between intervention costs and resource utilization costs. Data on resource use were collected from medical records and questionnaires. The cost of the intervention was defined as the costs of the ICT-guided-DMS with CDSS, the costs of the telemonitoring devices and handling of the alarms (personnel) and were calculated as a fixed price over the follow-up period. Resource utilization costs were calculated by collecting data on scheduled and non-scheduled outpatient clinic visits and hospital admissions (HF and non-HF-related). In addition, a patient MTA-questionnaire adapted from the iMTA/TiC-P [23] was administered at 4.5 and 9 months follow-up to collect complementary data (e.g., GP, dietician, physiotherapist visits, home care, and nursing home [day care, and admissions]). Unit costs were estimated by using the Dutch guidelines for cost studies [24] and inflated to the price level of 2012 using a general consumer price index (http://www.CBS.nl). The time horizon of the cost analysis was 9 months. Indirect costs, such as productivity losses, were not calculated.

Table 1
Scoring system for the primary composite endpoint [25].

End point	Score
Death (at any time during study)	−3
Survival to end of study	0
First readmission for heart failure during the study period	−1
No readmission for heart failure during the study period	0
Change in quality of life at 9 months:	
• Improvement ≥20 units	+2
• Improvement by 10 until 19 units	+1
• No improvement by −9 until +4 units	0
• Worsening by +5 until +9 units	−1
•Worsening by ≥10 units	−2
Possible score	−6 to +2

2.6. Endpoints

The primary endpoint was a composite weighted score consisting of a value for mortality, HF-readmission and change in HR-QoL between baseline and end of study measured with the MLHFQ with a possible range of –6 to +2. A HF-readmission was defined as an unplanned overnight hospital stay due to progression of HF or directly related to HF. The scoring system of the primary composite endpoint was adapted from the A-HeFT study [25] (Table 1). The endpoint has been used in several other studies and is also recommended in a recent statement by the Heart Failure Association [26]. In case of missing data for the primary composite endpoint, the worst-case scenario was used for the analyses. Patients lost to follow-up were assumed to have died (−3), and patients without a HR-QoL score received the worst score for that component (−2). Secondary endpoints of the study were the separate components of the primary endpoint (mortality, HF-readmission and change in HR-QoL). Other major secondary endpoints were the total number and duration of all hospital admissions, number of visits to the outpatient HF-clinic and cost analyses.

2.7. Sample size

We expect with 80% power to detect superiority for telemonitoring using a one-sided, two-sample *t*-test, when 130 patients are included in the telemonitoring group and 90 patients in the ICT-guided-DMS group. The true difference between both groups was assumed to be 0.8 regarding the primary composite endpoint score. The largest difference between both groups was expected to be observed in the HR-QoL domain.

2.8. Statistical analyses

All analyses were conducted according to the intention-to-treat principle ($n = 177$). Descriptive statistics, independent *t*-tests in case of normal distributions, Mann–Whitney *U*-tests in case of skewed distributions for continuous variables and Chi-square tests for categorical variables were used to compare the demographic and clinical characteristics between both groups. To compare the primary composite endpoint score between both groups a

one-sided two-sample *t*-test was performed and 95% confidence intervals were constructed to describe the treatment differences. Kaplan Meier curves were constructed for the differences in time to mortality between both groups. Costs per category were calculated by multiplying resource use with the cost per item. Means per group and incremental costs were calculated based on the trial data. Bootstrap simulations (5000 replications of the trial data) were performed to estimate the confidence intervals surrounding the incremental costs (2.5th and 97.5th percentile). The cost data for hospital admissions were highly skewed due to one patient with an extreme admission duration (126 days) therefore, we performed this analysis whereby the mean admission duration for this patient was replaced with the group mean value. Analyses were performed using PASW-version 18.0, Excel-version 2003 and R-version 2.15.1.

3. Results

Overall, 179 patients were randomized into the study. Two patients did not fulfil the inclusion criterion of worsening HF and were therefore not part of the analysis. In total, 177HF-patients were analyzed, of which 83 patients were randomized into the ICT-guided-DMS group and 94 patients to the telemonitoring group. Twenty-three patients (13%) were included from the outpatient HF-clinic, the others from a hospital admission for HF. The distribution of the number of patients in both groups was not equal, due to the design of the study (see power analysis) and the forced adjustment of the study protocol (change in randomization blocks).

3.1. Patient characteristics

Overall, the mean age of the patients was 69 (±12) years, 72% was male ($n = 128$) and the mean LVEF was 28% (±9%). During inclusion most patients (77%, $n = 133$) were classified as NYHA III–IV while 23% ($n = 39$) were in NYHA II. In total 31% of the patients ($n = 54$) were newly diagnosed with HF (diagnosis <6 months), the average period diagnosed with HF was 4.6 years for the ICT-guided-DMS group and 5.5 years for the telemonitoring group ($p = 0.41$). Other baseline characteristics such as co morbidity and prescribed medication were comparable between both groups (Table 2). The adherence of the patients to telemonitoring (assessed by daily weighing and measuring of blood pressure) had a median of 95% with a range from 87 to 99% for the total study period (not shown).

3.2. Primary endpoint

The mean composite endpoint score in the ICT-guided-DMS group of −0.63 was not significantly different from the score of −0.73 in the telemonitoring group (mean difference 0.1; 95% CI: −0.67 +0.82, $p = 0.39$) (Table 3). In total, 8% of the patients ($n = 14$) had the worst possible score of −6 (6 patients in the ICT-guided-DMS group and 8 patients in the telemonitoring group). In total, 27% of the patients ($n = 47$) had the best possible score of +2 (19 patients in the ICT-guided-DMS group and 28 patients in the telemonitoring group), with no statistical differences between the groups ($p = 0.39$).

3.3. Secondary endpoints

3.3.1. Mortality

All-cause mortality in the ICT-guided-DMS group was 12% ($n = 10$) and in the telemonitoring group 15% ($n = 14$), $p = 0.27$ (Table 3). The analyses of time to death showed a hazard-ratio (HR) of 1.25 (95% CI 0.52–3.00, $p = 0.62$). At the end of the follow-up, the total number of days lost to death was 156 days (range 114–206) for the ICT-guided-DMS group and 128 days (range 84–217) for the telemonitoring group ($p = 0.52$). Kaplan Meier survival analy-

Table 2
Baseline characteristics of the patients according to the assigned treatment ($n = 177$).

	ICT DMS $n = 83$	ICT DMS with TM $n = 94$	*p*-Value
Demographics			
Age (yrs)	69 ± 11	69 ± 12	0.98
Male sex	62 (75)	66 (70)	0.51
LVEF%	28 ± 9.0	27 ± 9.9	0.57
Duration of diagnosis HF (yrs)	4.6 ± 5.6	5.5 ± 6.5	0.41
New diagnosis of HF	25 (30)	29 (31)	0.92
Etiology			
Ischemic	35 (42)	45 (48)	0.45
History of myocardial infarction	25 (30)	35 (37)	0.32
Co-morbidities			
Hypertension	29 (35)	26 (28)	0.30
COPD	17 (21)	21 (22)	0.76
Atrial fibrillation	32 (40)	47 (48)	0.13
Diabetes	29 (35)	32 (34)	0.26
Stroke	6 (7)	12 (13)	0.22
Oncology	12 (15)	12 (13)	0.74
Clinical variables			
NYHA classification			0.92
II	18 (22)	21 (23)	
III	49 (60)	51 (57)	
IV	15 (18)	18 (20)	
Heart rate (bpm)	84 ± 20	81 ± 19	0.42
Weight (kg)	84 ± 18	81 ± 17	0.40
LBTB	16 (19)	31 (33)	0.04
SBP (mmHg)	123 ± 21	117 ± 20	0.09
DBP (mmHg)	74 ± 13	71 ± 11	0.06
Cardiovascular interventions			
CABG	15 (18)	22 (23)	0.38
PCI	13 (16)	18 (19)	0.54
ICD (CRT not included)	10 (12)	16 (17)	0.35
Laboratory			
Hemoglobin, mmol/L	8.36 ± 0.98	8.24 ± 1.16	0.52
Sodium, mmol/L	141 ± 3.07	141 ± 4.33	0.94
Creatinine, μmol/L	135 ± 70.4	134 ± 64.7	0.90
Nt-pro BNP, ng/L	3672 (384–22929)	4394 (598–28887)	0.34
Mean Egfr, mL/min/1.73 m^2	66.3 ± 26.6	65.3 ± 29.8	0.82
Medication			
Diuretica	69 (89)	72 (87)	0.74
ACE-inhibitor	46 (59)	50 (60)	0.87
Angiotensin receptor blocker	21 (27)	20 (24)	0.68
Beta blocker	54 (69)	53 (64)	0.47
Aldosteron antagonist	45 (58)	49 (59)	0.86

Note: values are given as mean ± SD, number (percentage), or median (25–75 percentiles).
Variables were tested two-sided.
ICT DMS = ICT-guided-disease management system with computer decision support.
ICT DMS with TM = ICT-guided-disease management system with computer decision support and telemonitoring.
yrs = years; LVEF = left ventricular ejection fraction; HF = heart failure; NYHA = New York Heart Association; bpm = beats per minute; kg = kilograms; LBTB = left bundle branch block; SBP = systolic blood pressure; DBP = diastolic blood pressure; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; ICD = internal cardiac defibrillator; NT-pro-BNP = N-terminal prohormone of brain natriuretic peptide; eGFR = estimated globular filtration rate: ACE-inhibitor = angiotensine converting enzyme inhibitor.

Table 3
Primary and secondary outcomes: composite endpoint score and the separate components of the composite endpoint ($n = 177$).

	ICT DMS $n = 83$	ICT DMS with TM $n = 94$	CI 95%	p-Value
Primary endpoint				
Composite endpoint	−0.63 ± 2.37	−0.73 ± 2.59	-0.67 +0.82	0.39
Secondary endpoints				
Mortality	10 (12)	14 (15)	−0.14 +0.07	0.27
Re-admission HF	23 (28)	25 (27)	−0.12 +0.14	0.87
Change in HR-QoL	−14.63 ± 25.14	−13.97 ± 22.31	−8.68 +7.36	0.63

Note: variables were tested one-sided.
Values are given as mean ± SD or number (percentage).
ICT DMS = ICT-guided-disease management system with computer decision support.
ICT DMS with TM = ICT-guided-disease management system with computer decision support and telemonitoring.

Table 4
Number of patients with hospitalizations, number of hospitalizations, number of outpatient visits and change in HR-QoL ($n = 177$).

	ICT DMS $n = 83$	ICT DMS with TM $n = 94$	p-Value
Number of patients with hospitalizations n(%)			
All-cause hospitalization	41 (49)	48 (51)	0.78
Cardiovascular-related hospitalizations	15 (18)	17 (18)	0.90
Heart failure-related hospitalizations	23 (28)	25 (27)	0.87
Total number of hospitalizations			
All cause	76	96	0.58
Cardiovascular-related	23	19	0.87
Heart failure-related	35	37	0.93
Total number of visits to outpatient clinics (median, IQR)			
All-cause	7 (4–12)	6.5 (4–9)	0.28
Heart failure-related	4 (0–6)	2 (0–5)	0.02
Change in HR-QoL			0.71
Improvement ≥20 units	21 (25)	30 (32)	
Improvement 10–19 units	14 (17)	7 (7)	
No improvement	13 (16)	18 (19)	
Worsening	14 (17)	1 (15)	
Not available[a]	21 (25)	25 (27)	

Note: values are given as number (percentage) or median (25–75th percentiles).
Variables were tested two-sided.
ICT DMS = ICT-guided-disease management system with computer decision support.
ICT DMS with TM = ICT-guided-disease management system with computer decision support and telemonitoring.
HR-QoL: health-related quality of life.
IQR= interquartile range.
[a] Of $n = 46$, in total 24 patients have died.

sis did not show a statistically significant difference between both interventions (log rank $\chi^2 = 0.025$, $p = 0.88$).

3.3.2. Readmission

Readmission for HF in the ICT-guided-DMS group was 28% ($n = 23$) versus 27% ($n = 25$) in the telemonitoring group. All-cause readmission was 49% ($n = 41$) in the ICT-guided-DMS group and 51% ($n = 48$) for the telemonitoring group. The differences were non-significant between both groups (Tables 3 and 4).

3.3.3. Change in HR-QoL

At 9 months the mean change in score was −15 units in the ICT-guided-DMS group versus −14 units in the telemonitoring group (95% CI: −8.7 +7.4, $p = 0.63$) (Table 3). The HR-QoL was improved with ≥20 units in 29% ($n = 51$) of the patients (21 patients in the ICT-guided-DMS group and 30 patients in the telemonitoring group). In total 12% ($n = 21$) improved between 10 and 19 units (14 patients in the ICT-guided-DMS group versus 7 patients in the telemonitoring group). In total 35% of the patients did not improve or had worse HR-QoL at the end of the study, with no differences between both groups (Table 4). Regarding both sub-scores of the MLHFQ, no significant differences were seen between the groups.

Table 5
Bootstrap simulations (5000 replications of the trial data) to estimate the confidence intervals surrounding the incremental costs (2.5th and 97.5th percentile) of the interventions.

Costs	ICT-DMS	ICT-DMS with TM	Difference	CI 95%
Intervention	€37[a]	€1766[b]	€1729	Constant
Re-admission	€3213	€2427	€786	−2875 +1525
Out-of-hospital care	€1152	€1642	€490	−1297 +2880
Outpatient clinic	€603	€530	€73	−261 +110
Total	€5006	€6366	€1360	−2263 +5221

Note: ICT-DMS = ICT-guided-disease management system with computer decision support.
ICT-DMS with TM = ICT-guided-disease management system with computer decision support and telemonitoring.
[a] Software.
[b] Software, telemonitoring devices and the handling of incoming data.

3.3.4. HF-outpatient clinic visits

The median number of visits to the HF-outpatient clinic was 4 for the ICT-guided-DMS group versus 2 for the telemonitoring group ($p < 0.02$) (Table 4). To any outpatient clinic a median of approximately 7 visits for both groups was observed ($p = 0.28$).

3.3.5. Cost analysis

The mean total costs was €5006 per patient for the ICT-guided-DMS group and €6366 per patient for the telemonitoring group (Table 5). Incremental costs were €1360 in favour of patients in the ICT-guided-DMS group. In this scenario the costs for outpatient visits were €530 for the telemonitoring group versus €603 for the ICT-guided-DMS. Hospital admissions were €3213 for ICT-guided-DMS and €2427 for the telemonitoring group. In both groups, the highest proportion of costs consisted of costs for admissions to a hospital ward. Costs made outside the hospital (GP, dietician, physiotherapist visits, home care and nursing home [day care, and admissions]) were €1152 in the ICT-guided-DSM group and €1642 in the telemonitoring group. The major cost driver in this category was nursing home admissions. The handling of the incoming telemonitoring data (alerts, viewing the ICT-guided-DMS, making telephone calls to patients, reporting the action/intervention and performing follow-up) was estimated at 12 h for each patient for the total study period, which was calculated to be €364 based on salary of the nurses.

4. Discussion

In this study we found no additional benefit from adding telemonitoring to an ICT-guided-DMS with CDSS with regard to the composite endpoint score; all-cause mortality, HF-readmission and change in HR-QoL. We expected to find a difference of 0.8, however we found a difference of only 0.1. An explanation for this absence of effect could be that the study population was relatively "healthy" compared to other HF-studies with a comparable patient population [27], making a significant or clinical difference for

further improvement in outcome rather difficult. Only 16 patients had more than 1HF-readmission (9%), and a relative large number of patients (31%) was newly diagnosed with HF and therefore did not have a history of frequent readmissions. Frequent readmissions are known as unfavourable for outcome [28,29], and it is known that newly diagnosed patients stay in a stable condition for a period after they receiving diagnosis and care. Also the mortality rate in our study was relatively low (13%) and almost all patients (96%) received only scheduled visits to the HF-clinic, indicating that there was no need for acute care for worsening HF. Although in both groups the HR-QoL increased, no differences in score between baseline and 9 months was seen between both groups. Moreover, it might be possible that the effect of the intervention was not large enough to be able to discriminate.

To find an effect of telemonitoring on mortality, readmissions and, HR-QoL probably requires a more defined and coherent group of patients that could benefit from this new intervention [30]. It seems reasonable to assume that other variables such as age, socio-economic status or severity of the disease in terms of frequent readmissions before starting with telemonitoring might affect the benefit of telemonitoring, perhaps more than we initially calculated and defined in the study protocol. However, previous studies do not show specific profiles of patients who could benefit more from telemonitoring, with the exception for patients with depressive symptoms [30].

We found a very high adherence among patients with the telemonitoring system during the entire study period, which shows that our telemonitoring system was well tolerated by the patient in comparison with systems used in other studies [19,30]. Furthermore there were issues with adherence by nurses, especially regarding to the up-titration of HF-medication during the follow-up period in both groups. The CDSS functionality for up-titrating HF-medication was experienced as difficult, which might be reflected by the relatively low percentage of prescribed ACE-inhibitor used at the end of the follow-up period. Although the percentage of Beta-blockers and Mineralocorticoid receptor antagonists are conform the observed percentages in the EURO Heart survey II study [31], the percentage of ACE-inhibitors at the end of the study (59% vs. 60%) is lower than the observed 80% in the EURO Heart survey II. The main reason for the lack of use of the CDSS was that the usability and acceptability were considered poor, primarily due to organization- and system-related barriers, which are known as major obstacles in applying CDSS in healthcare [32–34].

A known personal-related barrier to use a CDSS is a lack of trust, which was also observed in some participating hospitals where HF nurses were not allowed to titrate medication themselves due to hesitations of the cardiologists. Finally, the lack of use was also attributed to the fact that the CDSS was not integrated into the existing electronic patient record and therefore caused additional work.

Despite the fact that we could not find a difference in outcome in favour of the telemonitoring group, we found that the number of HF-related visits to the outpatient HF-clinic was statistically significant lower compared to patients who did not use telemonitoring. This difference in HF-related outpatient HF-clinic visits was partly protocol-driven; patients in the telemonitoring group were only allowed to visit the cardiologist of HF nurse in case of an absolute need for intervention. Moreover, this indicates also that it was not necessary to schedule more HF-related visits when telemonitoring is being used. The outcome in terms of readmission and mortality was similar in both groups. Importantly in this context, the overall patient adherence of using telemonitoring at home was very high (the telemonitoring devices were used in 95% of the patients during the whole study period) compared to other studies [19,30] in which patient adherence of using telemonitoring overall was not higher than 30–40% or that patient adherence compliance rates decreased after adding blood pressure measurement to daily weighing [35]. This indicates that the devices used for this study, combined with the protocol of daily measurements, were very well accepted by patients. Furthermore, it was explained to the patients that the telemonitoring measurements would only be reviewed once a day by the HF nurse, namely in the morning after a certain time and in case of a deviation of the predefined ranges the HF nurse would contact the patient within 2 h. This defined time-range for the use of telemonitoring prevented that the HF nurse needed to be available during the whole day and outside office hours. This time-range was also applicable in the weekends. Therefore the HF nurse could schedule the contacts (if necessary) with the patients in the morning during their normal work routine and it was not too much of a workload in the weekends. This prevented an increased work load for the HF-nurse and the perception of the patient that the telemonitoring measurements were continuously monitored [13].

4.1. Practical implications

Taking into consideration the advances and possibilities of telemonitoring and the limited increase in costs (€1360), an intervention with telemonitoring might be an option for caregivers. For patients who do not have direct or difficult access to a HF-outpatient clinic (e.g., long distance to travel, the inability of a patient to visit the HF outpatient clinic) or in case of preventing regular HF-related visits to the HF-outpatients clinic just for up-titration of medication or assessment of physical condition, telemonitoring could be a safe and efficient alternative for visiting the HF-outpatient clinic. Telemonitoring could be a significant tool for re-organizing HF-care to be more efficient, a necessity due to the understaffed care of a growing and aging population.

4.2. Limitations

Despite an extended inclusion period combined with an adjustment of the study protocol, we were not able to include the number of patients needed as calculated. This could have influenced the outcome in terms of a lack of sample strength. However, the calculated *p*-values did not show a trend or 'near' significance. In addition there were no numerical differences between both groups indicating that a larger population would probably not make a difference in outcome. In the design of the study, a cost effectiveness analysis and/or cost consequence analysis was planned. The planned analyses were not performed since no difference in primary and secondary clinical endpoints were found, therefore we only performed a cost minimization analysis. This study was designed as a clinical study, therefore some technical aspects might be underexposed. Finally, we have no information on how many patients were not eligible for this study because this was not part of the protocol.

5. Conclusions

ICT-guided disease management in combination with telemonitoring, used in the follow-up of HF-patients, did not affect the primary (composite) endpoint of mortality, HF-readmission and HR-QoL, nor the separated individual outcomes of this composite endpoint. However, we demonstrated that telemonitoring is safe and can reduce HF-related visits to the HF-outpatient clinic, keeping HF-care accessible. Costs however were €1360,- higher with telemonitoring. The adherence of patients in using telemonitoring was very high, indicating that the devices used for this study, in combination with daily measurements, were well accepted

Summary points

What was already known on the topic of the study:

- On a caregiver level, cardiologists and HF-nurses have high expectations of telemonitoring by expecting it to improve quality of care, reduce costs and to improve patients' Health-Related Quality of Life (HR-QoL) by increasing feelings of control and empowerment of the patient.
- On a population level, results regarding reduction in hospitalization and mortality rates by using telemonitoring in HF patients compared to usual care, are ambiguous.

What this study added to our knowledge:

- It is safe to use telemonitoring and it can reduce HF-related visits to the HF-outpatient clinic, keeping HF-care accessible. However the costs were &z.euro;1360,- higher with telemonitoring.
- The adherence of patients using telemonitoring was very high indicating that the devices used in combination with daily measurements were well accepted by patients.
- We found no additional benefit from adding telemonitoring to an ICT-guided-DMS with CDSS with regard to the composite endpoint score; all-cause mortality, HF-readmission and change in HR-QoL.

by patients and therefore acceptable when implementing regular care.

Authors' contributions

Imke Kraai, Arjen de Vries, Hans Hillege, and Ivonne Lesman: designing, conducting, analyzing and interpreting data and drafting the article. Vincent van Deursen: conducting survival analyses. Karin Vermeulen: analyzing and conducting cost analyses. All other authors made substantial contributions to the design of the study, interpreting data, drafting the article to revising it critically for important intellectual content.

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Conflicts of interest

René van Dijk: Medical advisor CURIT. All other authors: none declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijmedinf.2015.10.001.

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