HSR Health Services Research

DOI: 10.1111/1475-6773.12661
RESEARCH ARTICLE

Telemedical Care and Monitoring for Patients with Chronic Heart Failure Has a Positive Effect on Survival

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Background. Telemedical care and monitoring programs for patients with chronic heart failure have shown beneficial effects on survival in several small studies. The utility in routine care remains unclear.

Methods. We evaluated a large-sized telemedicine program in a routine care setting, enrolling in total 2,622 patients (54.7 percent male, mean age: 73.7 years) with chronic heart failure. We used reimbursement data from a large statutory health insurance and approached a matched control analysis. In a complex propensity score matching procedure, 3,719 suitable controls (54.2 percent male, mean age: 74.5 years) were matched to 1,943 intervention patients (54.1 percent male, mean age: 74.4 years). The primary endpoint of our analysis was survival after 1 year.

Results. Analyses revealed a higher survival probability among subjects of the intervention group compared to controls group after 1 year (adjusted OR: 1.47, CI 95 percent: 1.21–1.80, $p < .001$) and 2 years (adjusted OR: 1.51, CI 95 percent: 1.28–1.77, $p < .001$), respectively.

Conclusions. The probabilities to survive after 1 and 2 years were significantly increased in the intervention group. Our findings confirm previous results of controlled trials and importantly indicate that patients with chronic heart failure may benefit from telemonitoring programs in routine care.

Key Words. Chronic heart failure, telemedical care, telemedical monitoring, reimbursement data, routine data, propensity score matching

Chronic heart failure (CHF) is a main cause of morbidity, hospital admission, and death in Germany (Statistisches Bundesamt 2014, 2015). Both the prevalence and incidence rate of CHF are continuously increasing because of the strong positive correlation with increasing age (Bleumink et al. 2004) and improved treatment options for patients with acute myocardial infarction, heart valves diseases, and cardiomyopathies resulting in elevated survival rates (Roger 2013).

However, the prognosis of CHF is still poor. Thus, a large-scale European population-based prospective cohort study in the elderly population concludes that heart failure continues to be a fatal disease, with only 35 percent surviving patients 5 years after the first diagnosis (Bleumink et al. 2004).

Telemedicine programs were developed to improve monitoring and therapy adherence of patients with chronic diseases (Inglis et al. 2010). Telemonitoring of patients with CHF can potentially facilitate early detection warning signs of impending decompensation and thereby prevent hospitalization. A recent review of van den Berg et al. shows that telemedical measures can be implemented also in an older population. In particular, intervention measures that are based on personal contact with the patient seem to be successful (van den Berg et al. 2012). Chaudhry et al. (2007) review telemonitoring programs especially for patients with CHF and conclude that telemonitoring may be an effective strategy for disease management in high-risk heart failure patients with respect to reduction in hospitalizations (all-cause and heart failure-related hospitalizations) and mortality.

In this study, we evaluate the telemonitoring program "AOK-Curaplan Herz Plus" for patients with CHF, comprising the provision of information leaflets about heart failure, a modem-connected scale, and telephone coaching by special trained nurses (Gesellschaft für Patientenhilfe DGP mbH 2009). Primary outcome of this investigation is survival 1 year after enrollment into the intervention program. The secondary outcomes are survival after 2 years and hospitalization. Further, an analysis of survival after 1 year is conducted in the patient group with a documented beginning of the intervention (treated group).

METHODS

Intervention Program

AOK-Curaplan Herz Plus is a telemedicine program for CHF patients, offered by the statutory health insurance AOK Nordost in Germany. The

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AOK Nordost is a statutory health insurance with insured persons living in the German federal states of Berlin, Brandenburg, and Mecklenburg-Western Pomerania in northeastern Germany.

The program consists of regular telephone coaching and counseling, information leaflets about disease-related themes, and a digital scale for weight control. Telephone coaching and counseling is conducted by trained nurses in a telemedicine service center, specialized on medical services. Telephone contacts are conducted every 4 to 12 weeks, dependent on the patients' individual needs. If needed, patients can contact the telemedicine service center any time. In case of a deteriorating health situation, the nurses give concrete recommendations or contact the treating physician. AOK-Curaplan Herz Plus started in 2006 and is still running in the German federal states of Berlin and Brandenburg.

Participants

The intervention was implemented in a regular care setting. Patients with a diagnosis of CHF (ICD-10 diagnosis codes I50.12, I50.13, or I50.14 and NYHA class > I) with a high risk for a heart failure–related hospitalization were included. High risk was defined as a prior hospitalization due to heart failure. Exclusion criterion was the presence of any diagnosed mental disorder (ICD-10 F00-F99) at the time of recruitment. The recruitment of patients was divided into two phases: From 2006 to 2009, eligible patients, insured with the statutory health insurance, were included by general practitioners and cardiologists in private practices. Since 2009, possible participants were retrieved from the database from the statutory health insurance AOK Nordost. All patients, included in the telemedicine program, provided written informed consent.

Study Design

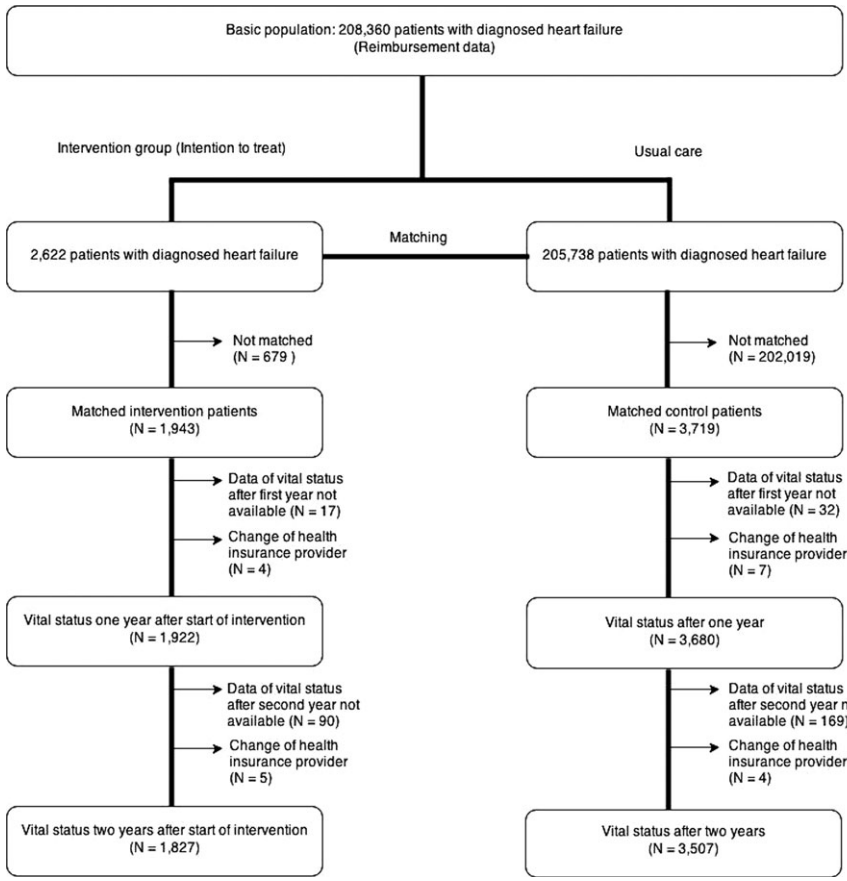
To analyze the effect of the intervention on the survival of all participating patients (intention-to-treat) compared to an appropriate control group, we implemented a matched control analysis (Stuart and Rubin 2007). The control group was compiled using a combination of propensity score and exact matching (see section "matching" for further details). The control patients were retrieved from the database of the statutory health insurance. For patients of the intervention group, the quarter year of enrollment served as baseline. The baseline for patients of the control group was set as the quarter year of matching.

Multivariate regression models were performed to analyze the effects of the intervention (Ho et al. 2007). Figure 1 shows the study flow from baseline to the analysis.

Variable Definitions

Matching procedure and statistical analyses were based on routine data (reimbursement data) only. Most baseline variables refer to the quarter year of enrollment, because reimbursement is carried out on the basis of quarter

Figure 1: Consort Diagram Showing the Selection of Patients to Be Included in the Analysis (Intention-to-Treat Analysis)



years. Exceptions are hospital admissions (all causes and related to CHF) and emergency hospitalizations, which refer to the quarter of enrollment and three prior quarter years (hereafter denoted as "baseline year"). Total health costs refer to a quarter mean of total health costs during the baseline year. We defined baseline NYHA class as the measure of NYHA stage which was identified temporally closest prior to the quarter of enrollment. In the German health care system, NYHA is collected in the administrative database and reimbursement data as part of every CHF diagnosis, usually in case of CHF-specific diagnostic or therapeutic activities. The most recent diagnosed NYHA class was in average 1.50 quarter years before enrollment in the intervention group (range 0–18, median 1.0) and 1.51 quarter years in the control group (range 0–18, median 1.0).

For patients' residential area, level of care, and retirement home status, information was only available for the time of data acquisition (July 2012). Survival was measured as the absence of death. Insured persons who changed the health insurance provider within the first year after enrollment were excluded from the analysis.

Matching Procedure

The control group was retrieved from the database of the statutory health insurance. The initial sample consisted of all patients with a diagnosis of CHF registered in the database. We combined exact and propensity score matching using a nearest neighbor method (greedy algorithm) with restrictions in chosen covariates (matching without replace, two controls per case at the maximum) (Rubin 1973; Ho et al. 2007).

Intervention patients were matched at their quarter year of enrollment (respectively the quarter of starting the intervention in the sensitivity analysis), and controls were drawn dynamically. Dynamically means that controls could be matched to intervention patients every quarter year as long as they were insured, still alive, and not matched in a prior quarter year.

The following variables were considered for the exact matching procedure: sex, 5-year-age group, NYHA class, the number of hospital admissions in the 12 months prior to inclusion, cost category (23 categories of various ranges, representing the medical costs of the patients/quarter year), and the presence of any mental or behavioral disorders (ICD-10: F00–F99). In addition, medication in six groups of active agents used for treatment of CHF (angiotensin-converting enzymes, beta-blockers, renin inhibitors, glycosides, diuretics, and AT1 receptor blockers) and mental and behavioral disorders in

11 diagnoses groups (organic, including symptomatic, mental disorders [F00–F09], mental and behavioral disorders due to psychoactive substance use [F10–F19], schizophrenia, schizotypal, and delusional disorders [F20–F29], mood [affective] disorders [F30–F39], neurotic, stress-related, and somatoform disorders [F40–F49], behavioral syndromes associated with physiological disturbances and physical factors [F50–F59], disorders of adult personality and behavior [F60–F69], mental retardation [F70–F79], disorders of psychological development [F80–F89], behavioral and emotional disorders with onset usually occurring in childhood and adolescence [F90–F98], and unspecified mental disorders [F99–F99]) were included as further propensity score matching criteria. The reason for including mental disorders in the matching procedure was that, although the existence of any mental disorder was an exclusion criterion, a high number of patients with these diagnoses were included in the intervention program.

All matched patients received a statistical weight (1 for 1,943 matched intervention patients, 0.957 for 3,552 patients of the control group who were matched to two partners in the intervention group, and 1.914 for 167 control patients for whom only one matching partner could be identified). The statistical weighting was described by the authors of the used matching software (Ho et al. 2011).

Statistical Analysis

The main analysis was performed according to an intention-to-treat approach, including all matched patients. In the descriptive baseline analysis, group differences between the matched intervention and the matched control group in continuous variables were compared using unpaired two-sample *t*-tests, while chi-square tests were used to compare categorical variables.

Analysis of the primary endpoint (survival after 1 year) was conducted by logistic regression models. All models were adjusted by age, sex, NYHA class, CHF-related hospitalization, medication, mental disorders, and the dichotomized residential area (urban = Berlin vs. rural = Brandenburg, Mecklenburg-Western Pomerania, and other). Age was modeled as a continuous variable. As a secondary endpoint, we examined the number of hospitalizations per patient. We determined the mean numbers of total hospital admissions and CHF-related hospital admission per year 1 and 2 years after baseline, respectively. We only considered years where the patient was (at least 1 day) alive. Group differences in negative binomial regression models were expressed by incidence risk ratios (IRRs).

We considered a *p*-value <.05 to show statistically significant differences in all comparisons. Statistics were calculated using *R* statistical software, version 3.0 (R Foundation for Statistical Computing, Vienna, Austria). We used the *R* packages "MatchIt" (Ho et al. 2011) for data matching, "Survey" (Lumley 2004) for weighted descriptive analyses, and "base" (R Core Team 2015) for fitting the regression models.

To examine the impact of the dropouts on the results of the intervention, a sensitivity analysis under the assumption that all patients missing from follow-up died was performed.

Furthermore, the intervention program was run by a third-party supplier. Detailed information on the individual patients' treatment was not known. Hence, another sensitivity analysis was performed with the subgroup of 1,835 patients with a documented start of the intervention program (treated group). Because of a high variation in time between enrollment and start of the intervention program among the patients, a separate matching was performed. The quarter year of the start of the intervention served as baseline. In the treated analysis, the odds ratios were fitted in the same regression models as the intention-to-treat models.

RESULTS

Intention-to-Treat Analysis

Overall, 1,943 intervention patients (74.1 percent of the entire intervention group) could be matched to 3,719 control patients. Information on the vital status for the 12-month follow-up was available for 1,922 patients in the intervention group (98.9 percent of matched intervention group) and 3,680 patients in the control group (99.0 percent). At the 2-year follow-up, the vital status was known for 1,827 patients in the intervention (94.0 percent) and 3,507 patients in the control group (94.3 percent), respectively.

Baseline Characteristics

Table 1 shows the distribution of parameters at baseline, defined as the quarter year of enrolment in the intervention program for patients of the intervention group, and the quarter year of matching for patients of the control group.

The overall and the matched intervention group showed only slight differences in most variables. Comparing the matched and the unmatched intervention group, statistically significant differences can be seen in the variables

Table 1: Baseline Characteristics of the Intervention Patients and Controls

	*Mean (SD)/N (%)**					
Variable	*Overall Intervention Group (N = 2,622)*	*Unmatched Intervention Group (N = 679)*	*Matched Intervention Group (N = 1,943)*	*Matched Control Group (N = 3,719)*	*p-value (Intervention Groups)*	*p-value (Matched Groups)*
Sex						
Male	1,439 (54.88)	387 (57.00)	1,052 (54.14)	2,014 (54.15)	.2146	–
Female	1,183 (45.12)	292 (43.00)	891 (45.86)	1,705 (45.85)		
Age groups						
≤40 years	7 (0.27)	7 (1.03)	–	–	<.0001	–
41–45 years	18 (0.69)	10 (1.47)	8 (0.41)	15 (0.41)		
46–50 years	42 (1.60)	20 (2.95)	22 (1.13)	42 (1.12)		
51–55 years	72 (2.75)	26 (3.83)	46 (2.37)	88 (2.36)		
56–60 years	110 (4.20)	41 (6.04)	69 (3.55)	132 (3.54)		
61–65 years	176 (6.71)	49 (7.22)	127 (6.54)	243 (6.52)		
66–70 years	414 (15.79)	109 (16.05)	305 (15.70)	585 (15.72)		
71–75 years	561 (21.40)	135 (19.88)	426 (21.92)	816 (21.93)		
76–80 years	595 (22.69)	154 (22.68)	441 (22.70)	845 (22.73)		
81–85 years	390 (14.87)	76 (11.19)	314 (16.16)	601 (16.16)		
86–90 years	200 (7.63)	41 (6.04)	159 (8.18)	304 (8.18)		
91–95 years	37 (1.41)	11 (1.62)	26 (1.34)	49 (1.33)		
Age [years]	73.73 (SD 9.64)	71.70 (SD 11.09)	74.44 (SD 8.97)	74.48 (SD 9.04)	<.0001	.9004
NYHA class						
NYHA I	32 (1.45)	13 (4.91)	19 (0.98)	36 (0.98)	<.0001	–
NYHA II	675 (30.57)	61 (23.02)	614 (31.60)	1,175 (31.60)		
NYHA III	877 (39.72)	98 (36.98)	779 (40.09)	1,491 (40.09)		
NYHA IV	624 (28.26)	93 (35.09)	531 (27.33)	1,016 (27.33)		
Missing	414	414	-	–		

continued

Table 1: *Continued*

Variable	Mean (SD)/N (%)* Overall Intervention Group (N = 2,622)	Unmatched Intervention Group (N = 679)	Matched Intervention Group (N = 1,943)	Matched Control Group (N = 3,719)	p-value (Intervention Groups)	p-value (Matched Groups)
Hospital admissions (baseline year)						
All causes	2.55 (SD 2.14)	2.57 (SD 3.04)	2.54 (SD 1.73)	2.53 (SD 1.88)	.7672	.9283
Related to CHF	1.38 (SD 1.28)	1.39 (SD 2.05)	1.37 (SD 0,86)	1.37 (SD 0.86)	.8744	–
Emergency hospitalizations (baseline year)						
All causes	0.64 (SD 1.27)	0.60 (SD 1.24)	0.65 (SD 1.27)	0.55 (SD 1.30)	.3967	.0059
Total health costs [Euros] (quarterly mean in baseline year)						
All regions	3,918.40 (SD 3,904.32)	4,421.21 (SD 5,754.73)	3,746.80 (SD 3,007.20)	3,750.10 (SD 3,021.40)	.0040	.9705
Urban	3,748.43 (SD 3,670.68)	3,815.41 (SD 5,175.95)	3,722.90 (SD 2,899.90)	3,958.60 (SD 3,502.80)	.6903	.1201
Rural	4,501.74 (SD 4,572.86)	7,604.49 (SD 7,399.72)	3,819.40 (SD 3,313.30)	3,676.60 (SD 2,829.30)	<.0001	.3777
Health costs [Euros] (quarterly mean in baseline year)						
Inpatient	2,604.70 (SD 3,162.30)	3,016.13 (SD 4,750.57)	2,464.30 (SD 2,375.60)	2,403.00 (SD 2,322.30)	.0042	.3702
Outpatient	317.22 (SD 744.13)	379.22 (SD 996.14)	296.06 (SD 634.63)	293.53 (SD 763.82)	.0443	.9000
Drugs	562.47 (SD 910.85)	608.59 (SD 1,200.42)	546.74 (SD 787.84)	563.50 (SD 751.29)	.2158	.4523
Remedy	44.76 (SD 121.90)	31.57 (SD 87.54)	49.26 (SD131.30)	39.43 (SD 125.86)	<.0001	.0068
Adjuvant	98.47 (SD 224.12)	103.78 (SD 254.59)	96.66 (SD 212.76)	109.62 (SD 225.80)	.5179	.0358
Home health care	117.91 (SD 490.44)	91.40 (SD 368.55)	126.95 (SD 525.38)	140.06 (SD 425.66)	.0565	.3583
Travel costs	166.01 (SD 305.45)	183.34 (SD 389.37)	160.09 (SD 270.80)	198.21 (SD 304.08)	.1547	<.0001
Rehabilitation	6.87 (SD 44.45)	7.18 (SD 46.32)	6.76 (SD 43.81)	2.71 (SD 26.82)	.8371	.0002
Medication (percentage "yes" per active agent in baseline quarter year)						
Angiotensin-converting enzymes	1,119 (42.94)	274 (41.33)	845 (43.49)	1,637 (44.01)	.3546	.7301
Beta-blockers	1,643 (63.05)	382 (57.62)	1,261 (64.90)	2,340 (62.93)	.0009	.1515

continued

Table 1: *Continued*

	*Mean (SD)/N (%)**					
Variable	*Overall Intervention Group (N = 2,622)*	*Unmatched Intervention Group (N = 679)*	*Matched Intervention Group (N = 1,943)*	*Matched Control Group (N = 3,719)*	*p-value (Intervention Groups)*	*p-value (Matched Groups)*
Renin inhibitors	45 (1.73)	9 (1.36)	36 (1.85)	51 (1.36)	.5011	.1853
Cardiac glycosides	372 (14.27)	93 (14.03)	279 (14.36)	548 (14.73)	.8833	.7388
Diuretics	1,643 (63.05)	345 (52.04)	1,298 (66.80)	2,507 (67.40)	<.0001	.6727
AT1 receptor blocker	532 (20.41)	147 (22.17)	385 (19.81)	651 (17.51)	.2133	.0360
Mental and behavioral disorders (baseline quarter year)						
Yes	983 (37.72)	240 (36.1)	743 (38.24)	1,421 (38.20)	.3736	–
No	1,623 (62.28)	423 (63.8)	1,200 (61.76)	2,298 (61.80)		
Missing	16	16	–	–		
Residential area						
Berlin	2,032 (77.50)	571 (84.09)	1,461 (75.19)	969 (26.06)	<.0001	<.0001
Brandenburg	524 (19.98)	88 (12.96)	436 (22.44)	1,482 (39.84)		
Mecklenburg-Western Pomerania	40 (1.53)	13 (1.91)	27 (1.39)	1,235 (33.20)		
Other	26 (0.99)	7 (1.03)	19 (0.98)	34 (0.90)		
Comorbidities, stationary diagnoses						
Diabetes (E10–E14)	1,198 (45.69)	248 (36.52)	950 (48.89)	1,944 (52.27)	<.0001	.0172
Cancer (C00–C97)	315 (12.01)	67 (9.87)	248 (12.76)	481 (12.95)	.0536	.8788
Kidney disease (N17–N19)	1,153 (43.97)	223 (32.84)	930 (47.86)	1,862 (50.08)	<.0001	.1204
COPD (J44)	635 (24.22)	118 (17.38)	517 (26.61)	1,002 (26.94)	<.0001	.8144

*Matched patients received a statistical weight: 1 for 1,943 matched intervention patients, 0.957 for 3,552 patients of the control group who were matched to two partners in the intervention group, and 1.914 for 167 control patients for whom only one matching partner could be identified.

age, NYHA class, total health costs, three cost sections (inpatient, outpatient, and remedy), medication (beta-blockers and diuretics), residential area, and level of care.

Around 54 percent of the patients in both matched groups were male. The mean of age was approximately 74 years in both groups (intervention group: 74.44 years, SD 8.97, control group: 74.48 years, SD 9.04). NYHA II and III were the most frequent NYHA classes. The mean number of hospital admissions (all causes) was 2.54 per year (SD 1.73) during the baseline quarter year and three previous quarter years for the intervention group (control group: 2.53, SD 1.88), while 1.37 (SD 0.86) hospital admissions were related to CHF in both groups. The total health costs per quarter year in the baseline year averaged 3,746.80 euros (SD: 3,007.20) in the intervention group and 3,750.10 euros (SD: 3,021.40) in the control group. In the intervention group, 743 patients (38.24 percent) had at least one diagnosed mental disorder (ICD-10 Chapter V) in the baseline quarter year.

With respect to comorbidities, the prevalence of cancer, kidney disease, and COPD was similar between the matched intervention and control group. Only the prevalence for diabetes differs (48.89 percent in the intervention group vs. 52.27 percent in the control group; $p = .017$).

The intervention and control group differed significantly with respect to the frequencies of AT1 receptor blocker medication, the number of emergency hospitalizations, the residential area, the level of care, and the rate of patients living in retirement houses.

Survival

Table 2 shows the weighted number of patients who were alive at the 1-year follow-up. Of 1,922 patients of the intervention group, 1,711 (89.02 percent) were still alive compared to 3,179 of 3,680 (86.37 percent) in the control group. The survival rates among the sexes were similar in the control group (male: 86.44 percent, female: 86.30 percent), whereas 90.27 percent of all females in the intervention but only 87.96 percent of all males survived the first year.

At the 2-year follow-up, the probability to survive was increased by 5.7 percentage points in the intervention group compared to the control group (79.4 percent vs. 73.7 percent). In the intervention group, the rate of surviving patients converged among the sexes (male: 79.03 percent, female: 79.76 percent). Again, in the control group, the likelihood to survive did not differ among the sexes (Table 2).

Table 2: Survival and Hospitalization after 1 and 2 years

		*N (%)**			*Logistic Regression Models (matched patients only)*	
Survival		*Total Intervention Group*	*Matched Intervention Group*	*Matched Control Group*	*OR of Study Group (adjusted, reference: control group)*	*p-value*
1-year follow-up						
Group size		2,574	1,922	3,680		
All patients	Alive	2,261 (87.84)	1,711 (89.02)	3,179 (86.37)	1.47 (CI 95%: 1.21–1.80)	.0002
	Dead	313 (12.16)	211 (10.98)	501 (13.63)		
Male	Alive	1,213 (86.33)	913 (87.96)	1,719 (86.44)	1.26 (CI 95%: 0.97–1.65)	.0906
	Dead	192 (13.67)	125 (12.04)	270 (13.56)		
Female	Alive	1,048 (89.65)	798 (90.27)	1,460 (86.30)	1.75 (CI 95%: 1.29–2.38)	.0003
	Dead	121 (10.35)	86 (9.73)	232 (13.70)		
2-year follow-up						
Group size		2,450	1,837	3,507		
All patients	Alive	1,935 (78.98)	1,450 (79.37)	2,584 (73.67)	1.51 (CI 95%: 1.28–1.77)	<.0001
	Dead	515 (21.02)	377 (20.63)	924 (26.33)		
Male	Alive	1,044 (77.91)	780 (79.03)	1,399 (73.89)	1.43 (CI 95%: 1.15–1.79)	.0016
	Dead	296 (22.09)	207 (20.97)	494 (26.11)		
Female	Alive	891 (80.27)	670 (79.76)	1,185 (73.41)	1.59 (CI 95%: 1.25–2.02)	.0002
	Dead	219 (19.73)	170 (20.24)	429 (26.59)		

continued

Table 2: *Continued*

Hospitalizations per Patient and Year		*Mean (SD)*			*Negative Binomial Regression Models (Matched Patients Only)*	
		Total Intervention Group	*Matched Intervention Group*	*Matched Control Group*	*IRR of Study Group (Adjusted, Reference: Control Group)*	*p-value*
1-year follow-up						
All patients	All causes	1.55 (SD 2.00)	1.56 (SD 1.93)	1.57 (SD 2.03)	1.01 (CI 95%: 0.93–1.09)	.8939
	Related to CHF†	0.60 (SD 1.15)	0.61 (SD 1.10)	0.61 (SD 1.13)	1.10 (CI 95%: 0.98–1.23)	.0932
2-year follow-up						
All patients	All causes	1.33 (SD 1.86)	1.53 (SD 1.96)	1.38 (SD 1.92)	1.17 (CI 95%: 0.98–1.40)	.0767
	Related to CHF	0.48 (SD 1.04)	0.56 (SD 1.09)	1.52 (SD 1.05)	1.32 (CI 95%: 1.01–1.73)	.0411

*Matched patients received a statistical weight: 1 for 1,943 matched intervention patients, 0.957 for 3,552 patients of the control group who were matched to two partners in the intervention group, and 1.914 for 167 control patients for whom only one matching partner could be identified.
†CHF is principal or secondary diagnosis of the hospitalization.

Table 3 shows the logistic regression model of survival after 1-year follow-up. The dichotomous outcome (survived/dead) was adjusted for the values of all matching criteria at baseline. Being in the intervention group increased the probability to survive significantly (OR = 1.47, $p = .0002$). Moreover, further determinates that were positive significantly associated with survival were female sex (OR = 1.23, $p = .020$), medication with angiotensin-converting enzyme inhibitors (OR = 1.24, $p = .013$), beta-blockers (OR = 1.31, $p = .002$) or AT1 receptor blockers (1.84, $p < .001$), or a diagnosis of neurotic, stress-related, and somatoform disorders (F40–F49, OR = 1.36, $p = .023$). In contrast, the following determinants were negatively associated with survival: living in a urban residential area (OR = 0.72, $p < .001$), older age (OR = 0.96, $p < .001$), higher number of hospitalizations related to CHF during the year before intervention (OR = 0.86, $p = .001$), medication with diuretics (OR = 0.74, $p = .002$) as well as a diagnosis of organic, including symptomatic, mental disorders (F00–F09, OR = 0.51, $p < .001$).

In addition, the probability of being alive after 1-year follow-up decreased with increasing age and NYHA class, except for patients with NYHA I. The matched dataset includes 48 patients with NYHA I (19 in intervention group and 29 in control group).

Table 4 shows the logistic regression model on survival after 2 years. The probability to survive was still significantly higher in the intervention group compared to the control group (OR = 1.51, $p < .001$). Determinants for survival were approximately the same as for the 1-year follow-up survival analysis with exception of the difference between NYHA classes I (reference) and II (OR = 2.27, $p = .010$) as an additional determinant.

Gender-Specific Survival

The interaction between study group and sex (completely adjusted logistic regression) was not significant neither after 1 ($p = .131$) nor after 2 years ($p = .508$). Nevertheless, we examined gender-specific survival results. The odds ratio for survival (completely adjusted logistic regression) after the first year for the female intervention subgroup is considerable greater (OR = 1.75, CI 95 percent: 1.29–2.38) than for the male intervention group (OR = 1.26, CI 95 percent: 0.97–1.65), both in relation to correspondent control groups. The difference between males and females is smaller after 2 years: OR = 1.59 for female subgroup, OR = 1.43 for male subgroup (Table 2).

Table 3: Logistic Regression Model Showing Survival after First Year (Intervention Group: $N = 1{,}922$, Control Group: $N = 3{,}680$)

			CI 95%		
	Reference	*Odds Ratio*	*2.5%*	*97.5%*	*p-value*
Study group	Control group	1.47	1.21	1.80	.0002
Residential area (Berlin vs. rural)	Rural	0.72	0.60	0.87	.0006
Age (in years)	(continuous)	0.96	0.95	0.97	<.0001
Sex	Male	1.23	1.03	1.46	.0197
NYHA class					
NYHA II	NYHA I	1.89	0.79	3.97	.1182
NYHA III	NYHA I	1.50	0.63	3.13	.3187
NYHA IV	NYHA I	1.06	0.44	2.23	.8787
CHF-related hospitalization	(continuous)	0.77	0.71	0.84	<.0001
Intake of medication related to CHF (yes/no by groups of agents)					
ACE inhibitors	No	1.24	1.05	1.48	.0133
Beta-blockers	No	1.31	1.11	1.56	.0016
Renin inhibitors	No	0.83	0.45	1.66	.5637
Glycosides	No	0.73	0.59	0.91	.0050
Diuretics	No	0.74	0.61	0.90	.0024
AT1 receptor blockers	No	1.84	1.44	2.38	<.0001
Mental and behavioral disorders (yes/no by blocks of ICD-10 Chapter V)					
F00–F09 (Organic, including symptomatic, mental disorders)	No	0.51	0.41	0.65	<.0001
F10–F19 (Mental and behavioral disorders due to psychoactive substance use)	No	0.83	0.62	1.13	.2323
F20–F29 (Schizophrenia, schizotypal, and delusional disorders)	No	1.09	0.47	3.02	.8567
F30–F39 (Mood [affective] disorders)	No	0.98	0.78	1.24	.8860
F40–F49 (Neurotic, stress-related, and somatoform disorders)	No	1.36	1.05	1.79	.0225
F50–F59 (Behavioral syndromes associated with physiological disturbances and physical factors)	No	0.95	0.60	1.58	.8396
F60–F69 (Disorders of adult personality and behavior)	No	1.07	0.52	2.46	.8670
F70–F79 (Mental retardation)	No	0.50	0.19	1.61	.1988
F80–F89 (Disorders of psychological development)	No	–	–	–	–
F90–F98 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	No	1.29	0.23	26.28	.8136
F99–F99 (Unspecified mental disorders)	No	0.54	0.15	2.70	.3891
Intercept	–	193.58	64.16	630.67	<.0001

Table 4: Logistic Regression Model on Survival after 2-Year Follow-Up (Intervention Group: $N = 1{,}827$, Control Group: $N = 3{,}507$)

			CI 95%		
	Reference	*Odds Ratio*	*2.5%*	*97.5%*	*p-value*
Study group	Control group	1.51	1.28	1.77	<.0001
Residential area (Berlin vs. rural).	Rural	0.82	0.70	0.96	.0114
Age (in years)	(continuous)	0.95	0.94	0.96	<.0001
Sex	Male	1.18	1.03	1.36	.0197
NYHA class					
NYHA II	NYHA I	2.27	1.19	4.14	.0098
NYHA III	NYHA I	1.69	0.89	3.08	.0943
NYHA IV	NYHA I	1.23	0.64	2.24	.5217
CHF-related hospitalization	(Continuous)	0.75	0.70	0.81	<.0001
Intake of medication related to CHF (yes/no by groups of agents)					
ACE inhibitors	No	1.25	1.09	1.44	.0020
Beta-blockers	No	1.37	1.19	1.57	<.0001
Renin inhibitors	No	1.19	0.69	2.14	.5528
Glycosides	No	0.75	0.63	0.90	.0014
Diuretics	No	0.59	0.51	0.69	<.0001
AT1 receptor blockers	No	1.48	1.22	1.79	.0001
Mental and behavioral disorders (yes/no by blocks of ICD-10 Chapter V)					
F00–F09 (Organic, including symptomatic, mental disorders)	No	0.58	0.47	0.72	<.0001
F10–F19 (Mental and behavioral disorders due to psychoactive substance use)	No	0.72	0.57	0.92	.0081
F20–F29 (Schizophrenia, schizotypal, and delusional disorders)	No	1.41	0.66	3.32	.4031
F30–F39 (Mood [affective] disorders)	No	1.02	0.85	1.23	.8399
F40–F49 (Neurotic, stress-related, and somatoform disorders)	No	1.10	0.90	1.36	.3424
F50–F59 (Behavioral syndromes associated with physiological disturbances and physical factors)	No	1.03	0.70	1.54	.8930
F60–F69 (Disorders of adult personality and behavior)	No	0.94	0.52	1.79	.8450
F70–F79 (Mental retardation)	No	0.96	0.35	3.11	.9373
F80–F89 (Disorders of psychological development)	No	–	–	–	–
F90–F98 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	No	1.30	0.33	8.90	.7428
F99–F99 (Unspecified mental disorders)	No	0.58	0.17	2.46	.4162
Intercept	–	122.76	50.43	308.19	<.0001

Hospitalization

The number of total hospital admissions per year amounted to 1.56 for the matched intervention group and 1.57 for the matched control group after the first year. Compared to the baseline number (2.54 and 2.53 per year, respectively), we observe a reduction in both groups. The number of CHF-related hospital admissions of both matched groups accounted to 0.61 per quarter year. Again, this is a reduction compared to the baseline number of 1.37 for both groups. Interestingly, we observed no further reduction during the second year, but rather a stable level of the number of hospital admissions for both groups.

Overall, weighted descriptive analyses revealed no remarkable group differences, neither with respect of follow-up time nor in type of hospitalization (all causes or CHF-related). Multivariable negative binomial regression suggested a slightly higher of total hospital admissions in the intervention group after 1 year compared to the control group (IRR = 1.01, CI 95 percent: 0.93–1.09, $p = .894$) and a higher number of CHF-related hospital admissions (IRR = 1.10, CI 95 percent: 0.98–1.23, $p = .093$).

The intervention group showed a greater number of total (IRR = 1.17, CI 95 percent: 0.98–1.40 $p = .077$) and CHF-related hospital admissions (IRR = 1.32, CI 95 percent: 1.01–1.73, $p = .041$) during the second year.

Sensitivity Analysis

In the sensitivity analysis, we assumed that all patients missing at follow-up died. If we fit regression models under this assumption according to our primary analysis, we observe lower, but still significant, odds ratios for survival after 1 year (OR = 1.42, CI 95 percent: 1.17–1.72, $p < .001$) and 2 years (OR = 1.40, CI 95 percent: 1.21–1.62, $p < .001$), respectively (results not shown).

Treated Analysis

Via propensity score matching, 1,381 intervention patients (thereof 56.1 percent male, mean age 73.8 years) and 2,678 control patients (thereof 56.1 percent male, mean age 73.8 years) were selected. The follow-up analysis after 1 year included information of 1,376 intervention patients (thereof 56.0 percent male) and 2,668 matched control patients (thereof 56.1 percent male).

The effects of the intervention for the treated group were larger than in the intention-to-treat analysis. In this analysis, compared to the control group the intervention group had a greater probability to survive 1 year (OR = 1.70, CI 95 percent: 1.31–2.21). Subgroup analyses stratified to men and women showed similar results for both sexes. For male intervention patients, the odds ratio for survival was 1.77 (CI 95 percent: 1.26–2.52) after 1 year. The odds ratio for survival for female intervention patients was 1.57 (CI 95 percent: 1.05–2.37) compared to the matched female control group.

DISCUSSION

AOK-Curaplan Herz Plus is a telemedicine program in a regular care setting for patients with a CHF diagnosis. Based on an analysis with routine data collected for reimbursement purposes, we could show that patients in the intervention program benefitted from this telemedicine intervention with regard to higher survival rates as compared to matched control patients. Beside sex, age, baseline number of CHF-related hospitalizations, and baseline health costs per quarter year, the place of residence of the patients (urban or rural) was a significant determinant for survival (with better survival for patients living in a rural area). There is no obvious explanation for this effect. There could be some selection effect, which cannot be further analyzed and explained because of the structure of the reimbursement data used.

To assess sensitivity, we calculated a Cox proportional hazards model to compare survival rates between the study arms using the same predictors as in the logistic model. The results (hazard ratio for study group (ref.: control group): 0.78; CI 95 percent: 0.69–0.88; $p < .001$) were consistent with the logistic model.

Our finding of an increased probability to survive for the intervention group as compared to appropriately matched controls was even more pronounced when the analyses were repeated for the treated population only (treated analysis). The findings were observed for both men and women. One-year survival rates were 88.0 percent for male and 90.3 percent for female intervention patients. In the treated intervention group, 775 of 1,381 patients (56.1 percent) were men. For patients of that group, 1-year survival rates were 92.0 percent for male and 92.5 percent for female intervention patients.

A Cochrane review on telephone support for patients with CHF summarized 25 studies and five published abstracts on structured telephone support

or telemonitoring programs and concluded that most of these programs were beneficial (Inglis et al. 2010).

Furthermore, survival benefits were found in the telephone-based structured monitoring HeartNetCare-HF (Angermann et al. 2012), in TEN-HMS (Cleland et al. 2005) and in a home-based telemanagement program with a portable device for measuring a one-lead ECG and additional nurses, available for teleconsultation (Giordano et al. 2009) and in The Whole System (Steventon et al. 2012).

Other studies determined no survival benefits. In TIM-HF (Telemedical Interventional Monitoring in Heart Failure), no significant improvement on mortality for the telemedicine management group could be shown (Koehler et al. 2011, 2012). No significant effect is present in a telephone-based interactive voice response system that collected daily information about symptoms and weight (Chaudhry et al. 2010). Although these studies are not directly comparable with the present study because of differences in setting, participating patients, and type and duration of the intervention, the results suggest that telemedicine interventions may have positive effects on survival, especially in studies with a longer duration of the intervention. Intervention studies are typically based on relatively small numbers of patients and a high intensity of the intervention, partially with active participation of hospitals. In contrast, our study is characterized by a low-threshold telemedicine intervention in an ambulant real care setting.

Our study suggests that women are more likely to benefit from the intervention in the first year. This effect is reduced in the second year. Differences exist between women and men in the syndrome of heart CHF with respect to risk factors (Regitz-Zagrosek and Lehmkuhl 2005), age of diagnosis, and prognosis (Regitz-Zagrosek et al. 2010). Adherence to guidelines in the diagnosis and treatment of CHF is less strict in women than in men, leading to undertreatment with medication (Johansson et al. 2015) and the underuse of expensive and invasive therapies (Regitz-Zagrosek and Lehmkuhl 2005). The participation in the program may improve the medical care, especially of the women.

We observed no remarkable differences in the number of hospital admissions per patient and year during follow-up time. Compared to baseline, the analysis revealed a reduction in the number of hospital admissions for both groups after 1 year. In the CHAMPION Trial, the treatment group had a significant 37 percent reduction in CHF hospitalization rates (Krahnke et al. 2015). The drop in readmissions for both intervention and control is remarkable. The early detection of decompensation may have caused patients to be

admitted to the hospital prior to worsening condition and thus had an impact on survival without reducing hospitalizations.

The impact on hospitalizations in other telemedicine interventions is variable (Inglis Sally et al. 2015; Kotb et al. 2015; Pandor et al. 2013a, b).

Strengths and Limitations

The AOK-Curaplan Herz Plus telemedicine program was conducted in a routine care setting. A broad range of patients was included with respect to age, degree of severity of CHF, and comorbidities. Also, formal exclusion criteria as the existence of mental health disorders and NYHA I and IV were not consequently adhered to by the recruiting general practitioners. On the other hand, this resulted in a typical group of patients and results might therefore be more likely to be transferable to the general population. Unfortunately, the proportion of patients that declined to participate in the program is unknown. If participants and nonparticipants systematically differed from the control group with respect to adherence, this could cause a bias.

The matching procedure is a trade-off between the similarity between the matched intervention and control group and the proportion of matched subjects of the total intervention group. Given the chosen matching algorithm, we could match 74.1 percent of the overall intervention group. Due to the large range of different comorbidities in this routine health care setting, it was not possible to match on a patient individual level for comorbidity directly. We assumed that patients with the same NYHA cause similar costs, and differences in cost classes probably reflect comorbidity. Therefore, we used the cost category as a proxy for comorbidity.

With the exception of diabetes, the prevalence of the comorbidities after the matching process was similar between the intervention and control group. However, the prevalence in the overall intervention group before matching was considerably lower. Hence, the prevalence of the comorbidities was balanced due to the matching process.

The matched groups are very similar at baseline. Nevertheless, there might be some selection bias. The matched intervention group tends to be older, overrepresented in the NYHA classes II and III, and related to lower health costs. This may limit the external validity of the analysis.

However, all patients in both groups had the same access to all providers of medical care. Therefore, it is unlikely that socioeconomic factors differentially between the groups influenced the kind or quality of care and, associated with that, the mortality rate.

Routine data of the statutory health insurance were available to perform the analysis. These data were primarily collected for reimbursement reasons. This means that the data may not always reflect real medical care.

Another problem was that data for some variables in this kind of datasets were only available if it is relevant for reimbursement. For example, if a patient did not see a doctor in some quarter year, no data about diagnoses were available in this quarter year. A limitation of the analysis is that some known independent predictors of our outcome (e.g., renal function or the presence of an implantable cardioverter-defibrillator) could not be included in the logistic regression model because these data were not available in the dataset of the statutory health insurance. The logistic models were calculated without adjusting for costs, because of a moderate correlation ($r = 0.40$) between hospitalizations and costs at baseline. Including costs at baseline in the model changes the results only slightly.

With respect to our analysis, we had to search for the NYHA class in quarter years prior to inclusion of the patients in many cases and, if available, used these as best imputations for the situation at the time of recruitment. A further limitation of using routine data was a lack of information about the dose and duration of the intervention.

Strength of our study was the completeness of the data and the sample size. By the combination of exact and propensity score matching algorithms, we achieved a high similarity between the groups in most variables. Despite the huge database from which the controls could be drawn, we could not identify two control patients for all intervention patients: two controls were found for 1,776 of 2,622 intervention patients (67.7 percent) and one control for 167 (6.4 percent) of the intervention patients. A total of 679 (25.9 percent) of the intervention patients could not be matched.

CONCLUSION

This evaluation shows that patients with CHF benefit from the telemedicine program AOK-Curaplan Herz Plus. The probability to survive is significantly increased in the intervention group (1- and 2-year follow-up). Results were even better for the intervention subgroup with documented start of treatment (treated group).

ACKNOWLEDGMENTS

Joint Acknowledgments/Disclaimer Statement: Mr. Herold reports grants from Graduiertenförderung Universität Greifswald during the conduct of the study. Prof. Dr. Hoffmann reports grants from AOK Nordost – Die Gesundheitskasse during the conduct of the study. PD Dr. van den Berg and Prof. Dr. Dörr have nothing to disclose.

Disclosure: None.

Disclaimer: None.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Appendix SA1: Author Matrix.