Clinical Trials

A Randomized Clinical Trial of the Clinical Effects of Enhanced Heart Failure Monitoring Using a Computer-Based Telephonic Monitoring System in Older Minorities and Women

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ABSTRACT

Background: Prior studies suggest that disease management programs may be effective in improving clinical outcomes in patients with heart failure (HF). However, the use of these programs in settings with limited resources and among diverse population is not known. Thus the present study was designed to assess the impact of a computer-based home disease management program (Alere DayLink HF Monitoring System [HFMS]) on the clinical outcomes of Medicare beneficiaries with HF who were elderly, women, and non-white males who received the care from a community-based primary care practitioner.

Methods and Results: The Heart Failure Home Care (HFHC) trial was a multicenter, randomized, controlled trial of HFMS versus standard heart failure care (SC: enhanced patient education, education to clinicians, and follow-up). The primary study end point was treatment failure, defined as a composite of cardiovascular death or rehospitalization for heart failure within 6 months of enrollment. Among patients rehospitalized for HF, length of hospital stay was also considered a primary end point. A total of 315 patients were randomized: 160 to HFMS and 155 to SC. Although the incidence of the primary outcome was somewhat higher in the SC arm (28.8% versus 21.2%, \( P = .15 \)), the difference was not statistically different. The length of hospital stay was also similar in both groups.

Conclusions: Our study results suggest that enhanced patient education and follow-up is as successful as a sophisticated home monitoring device with an interactive program in patients with HF who are elderly, women and non-Caucasian males and receive the care from a community-based primary care practitioner.

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Key Words: Clinical outcomes, disease management program, heart failure.

Heart failure is a syndrome of epidemic proportions in the United States affecting more than 5 million patients. The syndrome is the end result of multiple etiologies, including coronary artery disease, among others.1 Heart failure disproportionately affects the aged, and between 5% to 10% of people older than age 75 have heart failure, resulting in frequent hospitalizations at an enormous cost to the health care system.2 Furthermore, the burden of heart failure among the Medicare beneficiary population is best demonstrated by the fact that heart failure is the most common diagnosis-related group for people older than age 65.2 Between 1985 and 1995, Haldeman et al reported that hospitalizations for a first-listed heart failure diagnosis increased by 51% and 53% for any diagnosis of heart failure.3 Given an aging population, the present and future clinical and economic burden of heart failure is large.
Although chronic medical therapies can improve outcomes and reduce the number of hospitalizations in patients with heart failure, disease management programs provide substantive benefit especially for patients cared for by cardiologists at academic or community-based tertiary care facilities.\textsuperscript{4-9} However, the typical heart failure patient is not treated by a cardiologist or by a chronic care team, but instead by a primary care physician in a community setting.\textsuperscript{10} Furthermore, information is even more limited regarding the success of home care disease management programs among elderly, women, and non-Caucasian men, compared with Caucasian men.\textsuperscript{11,12}

Limitations of disease management programs need to be addressed and overcome so that care of patients with heart failure can be successful.\textsuperscript{11-13} Among the studies to date, the limitations include: 1) patients drawn from large academic medical centers; 2) patients more often in the upper socioeconomic strata; and 3) patients less likely to be minorities and women. As stated by the American College of Cardiology/American Heart Association Guidelines for the treatment of patients with Chronic Heart Failure, “it is not known whether such interventions are feasible in settings with limited resources and personnel and among diverse patient populations.”\textsuperscript{11} The overall goal of the Heart Failure Home Care clinical trial (HFHC) was to determine if a heart failure disease management program using a computer-based telephonic system for home monitoring, in addition to targeted and consistent physician/patient education, coupled to assiduous efforts to use optimal medical therapy, would be successful in improving outcomes and lower costs in a Medicare population of elderly patients representing the understudied—women, and non-Caucasian males (African Americans, Hispanics)—who are cared for by primary care physicians in a community setting when compared with standard heart failure care.

Methods

The HFHC Trial was a multicenter, randomized controlled clinical trial with blinded end point evaluation designed to compare a computer-based telephonic heart failure monitoring system (HFMS: Alere Day Link Heart Failure Monitoring System, Alere Medical, Reno, NV) in Medicare-eligible patients with a control group receiving standard heart failure care (SC).

Eligible patients were randomized between April 2002 and September 2005. Data were collected, compiled, and analyzed at the University of Pittsburgh. The trial used an independent adjudication event committee to classify deaths, hospitalizations, and adverse events and was monitored by an independent data safety monitoring board. The trial was approved by the institutional review boards of the University of Pittsburgh, Case Western University, and Mount Sinai Medical Center in Miami Beach, FL. Informed consent was obtained from all patients before study enrollment.

Study Population

The study population was elderly, women, and non-Caucasian males, primarily African Americans and Hispanics, with a diagnosis of heart failure secondary to predominantly systolic dysfunction. The trial was conducted at 3 sites with affiliations to a major academic medical center: Pittsburgh, PA (University of Pittsburgh), Cleveland, OH (Case Western Reserve University), and Miami Beach, FL (Mount Sinai Medical Center). However, a unique aspect of this trial was that patients were recruited through the development of cooperative networks that had been established with primary care groups in each of these cities. Thus this trial assessed the utility of the HFMS in a “real-world setting” rather than within the confines of the academic medical center.

Inclusion criteria included 1) Medicare beneficiary; 2) ≤65 years of age; 3) discharged from hospital with a primary (diagnosis-related group 127) or secondary diagnosis of heart failure within 6 months of randomization; 4) evidence of systolic dysfunction via a left ventricular ejection fraction of ≤40% documented by echocardiography, radionuclide ventriculography, or a contrast ventricular angiogram; (5) current symptoms of heart failure including dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, fatigue, abdominal or lower extremity edema or swelling; and (6) receiving optimal medical care consistent with recent guidelines published by the Heart Failure Society of America and by the American College of Cardiology/American Heart Association Task Force. Intolerance of standard medications was documented among patients not receiving optimal medical therapy. Additionally, study participants also had to be able to stand for 20 seconds without holding the wall, weigh <400 pounds, and speak either English or Spanish (requirements for use of the HFMS).

Patients were excluded from the study if they met any of the following criteria: 1) participation in another heart failure study; (2) prior experience with HFMS for the inability to activate the system; (3) significant symptomatic ischemic heart disease; (4) renal failure requiring dialysis or a serum creatinine >2.5; (5) chronic or intermittent inotropic therapy; (6) uncorrected primary stenotic valvular disease, pericardial disease, amyloidosis, active myocarditis, or malfunctioning prosthetic heart valve; (7) uncorrected thyroid disease; (8) chronic obstructive pulmonary disease with a forced expiratory volume in 1 second <50%; (9) a life expectancy less than 6 months; or (10) Medicare+Choice subscribers; or (11) white non-Hispanic men.

Procedures

After eligibility was assessed patients were randomized in a 1:1 ratio to either SC, which included patient 1-on-1 education, availability of education to clinicians, an effort to use evidenced-based optimal medical treatment, and a commercially available digital home scale with management by primary physician; or the intervention group (SC plus HFMS).

HFMS consists of a home-based disease management program to monitor and to detect early signs and symptoms of heart failure using telecommunication equipment; such early detection could allow practitioners to focus their clinical resources on patients needing interventions. Patients assigned to HFMS were contacted to arrange the delivery and setup of the device.

The system includes an electronic scale and an individualized symptom response system (DayLink monitor) linked via a standard phone line to a computerized database staffed by trained nurses. Patients were instructed to weigh themselves and respond to heart failure symptom questions daily. Each patient’s primary care physician was responsible for selecting the monitoring parameters according to their patients’ disease status. The patients were asked questions such as: did you wake up with shortness of breath during the night; did you use an extra pillow last night, are your feet more swollen than usual, are you more tired than usual, are you coughing more
than usual. The HFMS nurses reviewed the transmitted data daily (7 days/week, 365 days/year) and contacted the patient to verify any changes observed in heart failure symptoms or weight. Changes in weight beyond a prespecified amount or changes in symptoms were reported to the attending primary care physician.

There was a standardized alert in which physicians individually choose the parameters for their patients. If, on review by the HFMS nurse, benchmarks were met for weight alerts or symptom alerts, the HFMS nurse immediately contacted the patient to ensure that the alerts had been met. After nurse–patient interactions, the primary physician was immediately notified of the change in either weight or symptoms by a fax report. Comments by an HFMS nurse were added when data were sent; however, medical recommendations were not made to the physicians. This report also graphically demonstrated trends in both weight and symptoms. A follow-up call was made to the physician’s office to ensure that the information was received. During periods of clinical stability, reports were faxed to the physician’s office at predetermined points as requested by the physician. Physicians were then able to adjust medications, schedule an office visit, or initiate other therapeutic changes with the goal being to prevent further deterioration and to stave off the need for a hospitalization.

Patients randomized to SC were provided a digital home scale and instructed to weigh themselves daily and record heart failure symptoms. All participants were provided with educational materials and information as to when they should seek medical attention related to the worsening of their heart failure.

All patients were seen in clinic or in their primary care physician’s office by the study nurse coordinator during their baseline and 6-month end-of-study visits. During this initial visit, the study nurse coordinator conducted a 1-to-1 educational session with the patient, which included the “Living with Heart Failure Booklet” (University Hospital of Cleveland). Patients were also contacted by telephone 30 days and 3 months after randomization by non-medical personnel assigned to treatment assignment to collect clinical data, including vital status, the type and date of cardiovascular-related hospital visits, and the administration of 2 quality of life instruments, the Medical Outcome Study 12 Item Short Form (SF-12),14 and the Kansas City Quality of Life Questionnaire (KCCQ).15

End Points

The primary study end point was treatment failure, defined as cardiovascular death or rehospitalization for heart failure within 6 months of enrollment. Among patients rehospitalized for heart failure, length of hospital stay was also considered a primary end point.

Secondary end points included 6-month all cause hospitalization, 6-month heart failure hospitalization, and number of emergency room visits. In addition to these secondary end points, economic end points, which included Medicare expenditure (assessed by Medicare data) and total patient costs and quality of life measurements SF-12 and the KCCQ, were also measured. (A detailed quality of life and cost outcome data will be published separately.)

Sample Size

We assumed a 40% event rate for the primary end points (cardiovascular death or rehospitalization; among patients rehospitalized for heart failure, length of hospital stay was also considered a primary end point) in the control group and 25% in the intervention group within the 6 months of enrollment. With a power of 80% and a 2-sided alpha level of 0.05, 315 patients were required.

Statistical Analysis

The intention to treat principle was used to compare HFMS to SC. Continuous data were compared with the t-test where appropriate; otherwise, the Wilcoxon rank sum test was used. Categorical data were compared using the chi-square test or the Fisher exact test. The Kaplan-Meier method was used to estimate 6-month cumulative event rates for cardiac mortality, all-cause mortality, heart failure rehospitalizations, all-cause hospitalizations, and the composite end point cardiac death and heart failure rehospitalization. The Kaplan-Meier curves were compared using the log-rank test. Cox proportional hazards methodology was used to estimate the independent risk (hazard) for 6-month outcomes.

Change in quality of life was evaluated 2 ways: among patients with both 6-month and baseline evaluations and among all patients with their last known value carried forward and baseline values. Mean scores and mean change scores were compared using the Wilcoxon rank sum test. Additionally, adjusted mean 6-month physical and mental functioning scores (SF-12) were calculated using general linear modeling techniques. Statistical significance for all comparisons was defined when $P < .05$.

The Wilcoxon nonparametric test was used to analyze the difference in costs between the 2 study arms. The t-test was used to check the effect of gender, race, heart failure classification, and path into the study separately. Analysis of variance was used to check the effect of the center. Multivariate regression was used to determine the effect of treatment assignment and other variables on total costs and total Medicare costs.

Results

A total of 315 patients were randomized: 160 to HFMS and 155 to SC. Eight patients refused to be recontacted after randomization and were considered lost to follow-up. The mean follow-up period was 171 ± 30 days (range 4–184 days). The mean age of all patients was 76 ± 7 years. Given that non-Hispanic white men were not enrolled, the participants were predominantly women (65%) with New York Heart Association Class II or Class III heart failure symptoms and who had a mean ejection fraction of 23 ± 9%.

As shown in Table 1 and 2, baseline characteristics including age, race/ethnicity, sex, and laboratory evaluations were equivalent in both treatment groups. The proportion of patients taking selected cardiac medications at baseline was also similar. Mean values for quality of life, as measured by the KCCQ and the SF-12, were also similar by treatment arm (Table 3).

Compliance with the monitoring system in the HFMS arm was 97%. A total of 839 alerts were sent to the physicians managing the 160 patients in the HFMS arm over the course of the study.

The incidence of the primary outcome, 6-month cardiac mortality or rehospitalization for heart failure, was not statistically different (28.8% versus 21.2%, $P = .15$) (Tables 4 and 5).

The incidence of heart failure hospital admissions, hospitalizations for other cardiovascular indications, as well as for all causes was similar by treatment assignment. Emergency room visits were common in both groups and the
number of visits was comparable across groups. Among only patients with at least 1 adjudicated hospital admission for heart failure, the mean number of heart failure hospitalizations during follow-up was <2 (SC 1.6 versus HFMS 1.8) and the mean total length of hospital stay for these admission was approximately 9.5 days (SC: 9.3 days versus HFMS 10.0 days, \( P = .22 \)). No statistically significant differences were observed between the groups with respect to the need for invasive procedures or intravenous inotrope use over the course of the study. There were no significant differences between the groups in any medication and at any time point.

Over the course of the 6-month follow-up, there were 28 (cumulative incidence 9.1\%) deaths from any cause, 17 (11.2\%) in the SC arm and 11 (7.0\%) deaths in the HFMS group, representing no statistically significant difference in mortality (\( P = 0.24, \) Fig. 1 Kaplan-Meier curve). There were 11 (7.3\%) adjudicated cardiovascular deaths in the SC arm and 6 (3.9\%) in the HFMS group, representing no statistically significant difference in cardiovascular mortality (\( P = .21 \)).

As shown in Table 4, there were no statistically significant differences in the cumulative incidence of the composite end points of cardiovascular deaths or heart failure hospitalization, all-cause hospitalization, or all-cause mortality.

### Discussion

Disease management programs for the treatment of patients with heart failure have been advocated by both managed care plans and society guidelines to improve patient compliance and decrease hospitalizations.4,9,16–19 However, the use of these programs in settings with limited sources and among diverse population is not known. Although many programs have been carried out in the context of heart failure programs at academic health centers, there is a paucity of information regarding the utility of disease management programs in the outpatient setting and a lack of information regarding the utility of these programs in the elderly, women, and non-Caucasians. Thus the present study was undertaken to assess the efficacy of a unique
The primary findings of this randomized controlled study do not support the concept that adding an intensive home monitoring system to standard care of heart failure reduces the combined end point of cardiovascular death or rehospitalization because of heart failure in a cohort of elderly patients enriched for both women and non-white males.

The special features of the HFHC Trial may indicate that in pharmacologically well-treated and well-informed patients, there is relatively little room left for altering the natural course of the disease. Alternatively, the results of this study might indicate that primary doctors do not respond appropriately to a clinical deterioration as initially detected by the special scale.

The Specialized Primary and Networked Care in Heart Failure trial demonstrated that elderly (mean age 70)

Table 4. Adverse 6-Month Outcomes by Treatment Assignment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standard Care (n = 155)</th>
<th>Alere (n = 160)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality (%)</td>
<td>0.64</td>
<td>0.30</td>
<td>.15</td>
</tr>
<tr>
<td>Cardiac death or heart failure hospitalization (%)</td>
<td>0.72</td>
<td>0.30</td>
<td>.25</td>
</tr>
<tr>
<td>Any hospital admission (%)</td>
<td>0.64</td>
<td>0.30</td>
<td>.15</td>
</tr>
<tr>
<td>Number of hospital admissions (%)</td>
<td>0.64</td>
<td>0.30</td>
<td>.15</td>
</tr>
<tr>
<td>Any ER visit (%)</td>
<td>44.4</td>
<td>45.9</td>
<td>.93</td>
</tr>
<tr>
<td>Number of ER visits (%)*</td>
<td>58.1</td>
<td>54.4</td>
<td>.43</td>
</tr>
<tr>
<td>0</td>
<td>56.1</td>
<td>56.2</td>
<td>.72</td>
</tr>
<tr>
<td>1</td>
<td>27.1</td>
<td>23.8</td>
<td>.16</td>
</tr>
<tr>
<td>2</td>
<td>5.8</td>
<td>10.6</td>
<td>.06</td>
</tr>
<tr>
<td>≥3</td>
<td>11.0</td>
<td>9.4</td>
<td>.09</td>
</tr>
<tr>
<td>Hospital admission reason</td>
<td>42.5</td>
<td>46.8</td>
<td>.44</td>
</tr>
<tr>
<td>Heart failure (%)</td>
<td>23.7</td>
<td>18.8</td>
<td>.31</td>
</tr>
<tr>
<td>Other CAD (%)</td>
<td>12.7</td>
<td>19.0</td>
<td>.16</td>
</tr>
<tr>
<td>Non-CAD (%)</td>
<td>21.1</td>
<td>22.3</td>
<td>.81</td>
</tr>
<tr>
<td>Range (1–5)</td>
<td>5.0</td>
<td>8.0</td>
<td>.22</td>
</tr>
<tr>
<td>Mean hospital readmission (%)</td>
<td>9.3 ± 12.2</td>
<td>10.0 ± 7.3</td>
<td>.22</td>
</tr>
<tr>
<td>Mean heart failure hospitalizations (%)</td>
<td>1.6 ± 0.9</td>
<td>1.8 ± 1.3</td>
<td>.61</td>
</tr>
</tbody>
</table>

ER, emergency room; CAD, coronary artery disease; CVD, cardiovascular disease.
Heart failure hospitalizations and cause of death have been adjudicated.
All other hospitalizations were not adjudicated.

Table 5. Hazard Ratios and 95% Confidence Intervals for the Alere System Versus Standard Care in Patients With Heart Failure

<table>
<thead>
<tr>
<th>6-Month Outcomes</th>
<th>Unadjusted Models</th>
<th>Adjusted Models*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Ratio</td>
<td>95% CI</td>
<td>P Value</td>
</tr>
<tr>
<td>Cardiac death or heart failure hospitalization (%)</td>
<td>0.72</td>
<td>0.46–1.13</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.64</td>
<td>0.30–1.36</td>
</tr>
<tr>
<td>Cardiac mortality</td>
<td>0.54</td>
<td>0.20–1.45</td>
</tr>
<tr>
<td>All-cause hospitalization</td>
<td>1.14</td>
<td>0.82–1.59</td>
</tr>
<tr>
<td>Heart failure hospitalization (%)</td>
<td>0.78</td>
<td>0.48–1.27</td>
</tr>
<tr>
<td>All-cause mortality or all-cause hospitalization (%)</td>
<td>1.07</td>
<td>0.78–1.49</td>
</tr>
</tbody>
</table>

*Adjusted for New York Heart Association at study entry, β-blocker use at baseline, sex, and Na levels.
patients randomized to a community-based disease management program experienced fewer hospitalizations for heart failure and a reduction in hospital days over a 90-day follow-up.\textsuperscript{22} However, in contrast to the design of the HFHC trial, the intervention that was provided in Specialized Primary and Networked Care in Heart Failure was provided in patients’ homes by nurse-managers experienced in heart failure management, despite the fact that patients received their routine care in a community-based internal medicine practice. Thus a key component of successful disease management programs may well be the opportunity for a home visit—even if it occurs only once in the management program.

There are 2 other large studies, both of which had a completely different design and examined the effect of (additional) telephone intervention.\textsuperscript{23,24} Galbreath et al studied 1069 patients with heart failure in a single center and showed that initial weekly and, later, monthly telephone intervention led to a borderline statistically significant reduction in all-cause mortality during an 18-month study.\textsuperscript{24} In another study from Argentina, 1518 outpatients with heart failure were enrolled, and the investigators found a statistically significant 29% reduction in hospital admissions because of heart failure, but no effect on mortality.\textsuperscript{23} In another study, investigators tested the effectiveness of telephone case management in decreasing hospitalizations and improving health-related quality of life and depression in Hispanics of Mexican origin with heart failure.\textsuperscript{25} Hospitalized Hispanics with chronic heart failure were enrolled and randomized to intervention or usual care. Bilingual/bicultural Mexican-American registered nurses provided 6 months of standardized telephone case management. No significant group differences were found in heart failure hospitalizations, the primary outcome variable at 6 months. No significant group differences were found in heart failure readmission rate, heart failure days in the hospital, heart failure cost of care, all-cause hospitalizations or cost, mortality, health-related quality of life, or depression. These different outcomes indicate that 1 model does not fit all patients or all health care systems.

Recently, a long-term prospective randomized controlled study using repetitive education at 6 month intervals and monitoring for heart failure outpatients, the REMADHE study, and Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) studies assessed the impact of nurse-led education and counseling in disease-management programs in heart failure patients. One found benefit to such a group program among a relatively young patient population in Brazil.\textsuperscript{26} The other reported no benefit to individual counseling of older patients in the Netherlands.\textsuperscript{27} The difference between the REMADHE and COACH studies may indicate patient selection and components of the intervention are very important. Two other studies, which were more similar to COACH and reported the most pronounced favorable effects, were conducted in only 2 or 3 dedicated and experienced hospitals.\textsuperscript{28,29} Favorable effects observed in other studies may be attributed to the other components in the programs, but also to direct involvement of the researchers conducting the study in delivering care. It also cannot be ruled out that studies with positive findings were published more often than studies with negative findings, leading to publication bias.\textsuperscript{27}

The findings of the present study, at first glance, seem to be in contrast to those of earlier similar studies, but we believe that these data will contribute to the discussion of optimal design and implementation of heart failure disease management programs. Our results suggest that an infrastructure of trained heart failure specialists who actually manage care is as important as a home monitoring device that reports to busy primary care clinicians.

**Study Limitations**

Because of the nature of the intervention, both patients and the primary research teams could not be blinded to treatment arm. Although this might have introduced some bias into the trial, we believe that the design maximized consistent heart failure baseline care for every patient independent of randomization, which allowed a determination of the true clinical effect of the HFMS. For instance, all patients received an educational handbook and nurse teaching about heart failure. They were provided with benchmarks that defined when a patient should report changes in either symptoms or weight to his or her physician. To minimize ascertainment bias, all telephone data were collected by research staff blinded to group assignment. Similarly, adjudication of events was carried out by an independent committee not affiliated with the randomization or clinical care of the participants in this trial.

**Conclusion**

Advanced monitoring of heart failure patients with an interactive program had no statistically significant effect on cardiovascular deaths and readmission rates within 6 months after discharge in a group of elderly heart failure patients who are Medicare beneficiaries and either women or non-Caucasian males. The lack of effect may indicate that in pharmacologically well-treated and well-informed
patients, there is relatively little room left for altering the natural course of the disease or, alternatively, that the combination of a thorough educational program about the disease and a strong admonition that patients weigh themselves daily and report any changes in weight or symptoms may be as effective as a high-technology and interactive system in keeping patients free of hospitalizations.

References