HEART FAILURE

RESEARCH ARTICLE

Reach Out and Touch Someone: Telemedicine in the Management of Heart Failure

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ABSTRACT. Heart failure is a diagnosis that confers significant morbidity, mortality, and health-care expenditure. An estimated 5.1 million people carry a diagnosis of heart failure in the United States, and this figure is set to rise. Repeat hospitalizations are a poor prognostic indicator; they also account for a large proportion of the $32 billion dollars spent annually on heart-failure related health-care costs in the United States alone. These observations have led to the search for more effective strategies aimed at early detection and treatment of decompensated disease. Remote monitoring strategies ranging from structured telephone support to implantable hemodynamic monitoring systems have been extensively studied. This paper provides an overview of current remote monitoring strategies and their benefits, limitations, and challenges. Newer technologies that attempt to overcome these challenges will be explored, and, finally, the role of remote monitoring as part of a multidisciplinary, coordinated approach to optimize heart failure management will be discussed.

KEYWORDS. telemedicine, heart failure, remote monitoring.

Introduction

Heart failure (HF) is a complex chronic illness that requires extensive health-care resource utilization. It is the leading cause of hospitalization among elderly people in developed countries.1 The incidence and prevalence are growing and are expected to increase by 25% in 2030.2 An estimated 5.1 million people in the United States3 and at least 10 million people in Europe currently carry the diagnosis despite advances in therapies over the past decade. Moreover, it confers significant morbidity and mortality, with one in nine death certificates citing a diagnosis of HF in the United States. HF was the underlying cause of an estimated 56,000 deaths in 2009.3 The risk of death following hospitalization for an acute exacerbation is significant and rehospitalization during the first month is a poor prognostic indicator.4 The scale of the problem is also highlighted by the fact that over 1 million first-listed hospital discharges in 2010 were attributed to HF and over 3 million physician office visits carried a primary diagnosis of HF.3,5

Traditional episodic or reactive follow-up visits are often inadequate in managing HF patients and frequently fail to predict and prevent rehospitalizations. A multidisciplinary disease management approach that emphasizes patient engagement and close follow-up has enabled health-care providers and patients to better understand and address the complexity of HF. A variety of multidisciplinary care models exist for HF patients. Interventions such as telephone contact and patient education have been shown to reduce all-cause hospitalization.6 Specialized multidisciplinary team-based disease management has been shown to reduce mortality7,8 and is currently a recommended practice in Europe9 and
the United States. However, the resource-intensive nature of this approach limits the number of patients that can be closely followed. Remote patient monitoring systems, or telemonitoring, have been proposed as an effective method to follow-up a large patient population, eliminating the rate-limiting step of face-to-face visits. Initial strategies showed promise, including Internet-based monitoring systems as demonstrated by Kashe et al. which have led to the use of increasingly sophisticated hardware and software.

**Telemedicine**

**The current era**

Telemedicine could be superior to the traditional care model in several ways. Access to specialist care could be made available to a larger number of patients, and it is capable of reaching geographically isolated patients. It may encourage self-care and self-management through an increased awareness of symptoms. The largest potential benefit is the reduction in hospitalizations for HF through early detection of deterioration in a patient’s clinical status. Telemedicine ranges from structured telephone support to direct physiologic data transfer between patient and health-care provider. Several implantable hemodynamic monitoring devices that allow for continuous monitoring of physiologic parameters have been trialed in this evolving field.

**Structured telephone support**

Structured telephone support (STS) is a natural extension to traditional follow-up through the use of telephone calls. Information can be gathered by the health-care team through a series of structured questions to ascertain if there is any evidence of deterioration in a patient’s condition. If necessary, therapy can be administered, and response to therapy can be assessed. Mixed results have been reported in studies to date (Table 1). A meta-analysis of 16 randomized controlled trials (n=5,613) assessing the benefit of STS compared with usual care revealed a significant reduction in HF-related hospitalizations (RR 0.77; 95% CI 0.68–0.87; p=0.0001) but reduction in all-cause mortality was statistically non-significant (RR 0.88; 95% CI 0.76–1.01; p=0.08). Favorably reported secondary outcomes included quality of life, patient knowledge and self-care, improvement in functional class, and cost reduction. Limitations were observed related to publication bias, poor methodological quality, and significant study heterogeneity. In addition, variability in the population studied, the type of remote monitoring used, and the definition of usual care has limited the conclusions that can be drawn.

Two large negative studies have since called into question the role of remote patient monitoring in HF management. The Tele-HF trial studied recently hospitalized patients across 33 cardiology practices in the United States over 180 days. Patients were randomized to either voice-based interactive structured telephone support or usual care. Those in the intervention arm were advised to call a toll-free telephone system and answer a series of questions regarding their general health, weight, and HF symptoms on a daily basis. A clinician then analyzed the information. The primary outcome, all-cause readmission or death within 180 days after enrollment occurred in 52.3% of the telemonitoring group and 51.5% of the usual care group (p=0.75). However, there was poor adherence despite system generated reminders: 14% of patients in the telemonitoring arm of the study never used the system. By the final week, only 55% of the patients were using the system at least three times a week. The authors conclude that this adherence rate is likely a best-case scenario given the resources allocated towards optimizing patient engagement with the study. These findings may instead point towards methodological limitations, particularly with the type of monitoring used and in the way reported variances were dealt with.

The TIM-HF trial studied stable HF patients randomized to either remote monitoring and telephone support or usual care. Patients were given a personal digital assistant (PDA) with a wireless Bluetooth interface. The system collected electrocardiogram data, blood pressure readings, and body weight; this information was then communicated wirelessly to a central location with physician presence 24 h a day, 7 days a week. The primary outcome of death from any cause was similar in the telemonitoring group (8.43 per 100 patient years) and the usual care group (8.68 per 100 patient years). The TIM-HF trial was underpowered to detect a significant difference in mortality between the two groups. The composite secondary outcomes of hospitalization for HF and death due to a cardiovascular cause (14.7% versus 16.5%) highlight the stable nature of the patients recruited in the study given population- and trial-based observations of readmission rates closer to 50%. This highlights the limited benefit of remote monitoring in patients who are well managed on optimal medical therapy.

Though disappointing, the results of these trials should be used to refine and further our understanding of remote patient monitoring in HF. Desai and Stevenson and Desai emphasize the importance of an effective strategy when implementing remote patient monitoring. The premise of remote patient monitoring is that early detection of abnormal physiological para-
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<th>Study</th>
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<td>Koehler et al. (2013)</td>
<td>TM vs. UC</td>
<td>Patients with NYHA class II/III HF; LVEF &lt;35% with decompensation within the past 2 years OR LVEF &lt;25% without decompensation</td>
<td>710</td>
<td>Minimum 12 months</td>
<td>No effect on all-cause mortality (HR 0.97; 95% CI 0.67–1.41, p = 0.87), cardiovascular cause of death or HF hospitalization (HR 0.89; 95% CI 0.67–1.19; p = 0.44)</td>
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<td>TiM-HF study</td>
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<td>Median 26 months</td>
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<td>Dendale et al. (2012)</td>
<td>TM vs. UC</td>
<td>Patients with mean LVEF 35% ± 15% with recent hospitalization for decompensation</td>
<td>160</td>
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<td>Lower all-cause mortality in TM group (5% vs. 17.5% p = 0.01)</td>
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<td>Lower number of follow up days lost, dialysis or death (13 vs. 30 days p = 0.02) No difference in number of HF-related admissions per patient (0.24 vs. 0.42 p = 0.06)</td>
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<td>Goldberg et al. (2003)</td>
<td>TM vs. UC</td>
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<td>280</td>
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<td>WHARF trial</td>
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<td>Mean age 59 years</td>
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<td>56.2% reduction in mortality in TM group (p = 0.003)</td>
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<td>Kielbock et al. (2007)</td>
<td>TM vs. UC</td>
<td>Patients discharged after hospitalization for HF. Mean age 71.7 years</td>
<td>502</td>
<td>12 months</td>
<td>Decreased duration of hospital stay in TM group by 48% (p = 0.01) Lower mortality rate in TM group (14.7% vs. 27.1% p = 0.001)</td>
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<td>Balk et al. (2008)</td>
<td>TM vs. UC</td>
<td>Patients with NYHA class I–IV HF; mean LVEF 31% Median age 66 years</td>
<td>214</td>
<td>Range - 2 to 537 days</td>
<td>No difference in number of days in hospital</td>
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<td>Soran et al. (2008)</td>
<td>TM vs. UC</td>
<td>Patients with NYHA class II–III HF</td>
<td>315</td>
<td>6 months</td>
<td>No difference in number of days alive and out of hospital No difference in QoL scores No difference in self-care behaviors No difference in composite of cardiovascular death, length of stay or rehospitalization within 6 months between the two groups.</td>
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<td>HFHC trial</td>
<td></td>
<td>Mean age 76.8 years Stable patients with LVEF &lt;40% and at least one hospitalization for acute HF in the previous year Mean age 58 years</td>
<td>460</td>
<td>12 months</td>
<td>Lower risk of readmission in TM group (HR 0.5; 95% CI 0.34–0.73, p = 0.01) Decrease in HF-related readmissions (19% vs. 32% p = 0.0001) No difference in cardiovascular mortality No difference in days lost as a result of death or hospitalization between the three groups. Significant (p = 0.032) increase in mortality in UC group (45%) compared with STS (27%) and TM (29%)</td>
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<td>Giordano et al. (2009)</td>
<td>TM vs. UC</td>
<td>Mean LVEF 25%</td>
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<td>TEN-HMS study</td>
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<td>Mean age 67 years</td>
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<td>Mortara et al. (2009)</td>
<td>TM vs. STS vs. UC</td>
<td>Patients with NYHA class II–IV HF; LVEF &lt;40% or abnormal diastology</td>
<td>461</td>
<td>Mean 11.6 months</td>
<td>No difference in reducing bed-days occupancy for HF, cardiac death and hospitalization or number of re-hospitalizations</td>
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<td>HHH study</td>
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<td>Hospitalization for HF in the preceding 12 months On optimal medical therapy</td>
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<td>Chaudhry et al. (2012)</td>
<td>STS vs. UC</td>
<td>Patients with NYHA I–IV HF</td>
<td>1653</td>
<td>180 days</td>
<td>No difference in mortality (11.1% vs. 11.4%, p = 0.88)</td>
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<tr>
<td>Study</td>
<td>Method of monitoring</td>
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<tr>
<td>Tele-HF study</td>
<td>Recently hospitalized for HF</td>
<td>Median age 61 years Patients with stable HF on optimal therapy</td>
<td>1518</td>
<td>36 months</td>
<td>No difference in the composite outcomes of death and readmission (52.3% vs. 51.5%, p=0.75)</td>
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<tr>
<td>Ferrante et al. (2010)</td>
<td>STS vs. UC</td>
<td>No. of patients</td>
<td>1518</td>
<td>36 months</td>
<td>All-cause mortality and risk of hospitalization significantly lower in STS group (31% vs. 26.3% p=0.026 95% CI 0.3–0.34)</td>
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<td>DIAL trial</td>
<td>Mean age 65 years</td>
<td>Mean age 65 years</td>
<td>462</td>
<td>12 months</td>
<td>STS group had improved QoL based on Minnesota living with HF questionnaire (p=0.001)</td>
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<tr>
<td>DeBusk et al. (2004)</td>
<td>STS vs. UC</td>
<td>Patients with NYHA class I–IV HF</td>
<td>462</td>
<td>12 months</td>
<td>No statistically significant difference in HF hospitalizations (HR 0.85 95% CI 0.46–1.57)</td>
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<tr>
<td>Riegel et al. (2002)</td>
<td>STS vs. UC</td>
<td>HF patients discharged from hospital</td>
<td>358</td>
<td>6 months</td>
<td>Statistically significant reduction in HF hospitalization rate at 3 months (45.7%; p=0.03), and 6 months (47.8%; p=0.01)</td>
</tr>
<tr>
<td>Smith et al.</td>
<td>STS vs. UC</td>
<td>Patients with systolic and diastolic HF</td>
<td>1,069</td>
<td>18 months</td>
<td>Statistically significant difference in number of days survived among all patients (509.5 vs. 526.9 days; p=0.04), patients with NYHA III–IV HF (464.2 vs. 511.9 days; p=0.02) and patients with systolic HF (502.1 vs. 526.3 days; p=0.01)</td>
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<td>Tsuyuki et al. (2004)</td>
<td>STS vs. UC</td>
<td>HF patients discharged from hospital</td>
<td>276</td>
<td>6 months</td>
<td>No difference in all-cause physician visits, ER visits or readmissions</td>
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<tr>
<td>Laramée et al. (2003)</td>
<td>STS vs. UC</td>
<td>Hospitalized HF patients with LVEF &lt;40% or radiological evidence of pulmonary edema</td>
<td>287</td>
<td>3 months</td>
<td>Improvements in adherence to self-care activities*</td>
</tr>
<tr>
<td>Hebert et al. (2002)</td>
<td>STS vs. UC</td>
<td>Stable outpatients with HF</td>
<td>406</td>
<td>12 months</td>
<td>Improvements in patient satisfaction (p&lt;0.01)</td>
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<td>Krum et al. (2009)</td>
<td>STS vs. UC</td>
<td>Patients with a recent HF-related hospital discharge, NYHA class II–IV and LVEF &lt;40% or diastolic dysfunction.</td>
<td>405</td>
<td>12 months</td>
<td>Statistically significant difference in all-cause death (HR 1.36 (0.63–2.93); p=0.44) or all-cause hospitalization (HR 0.67 (0.50–0.89; p=0.006)</td>
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</tbody>
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Financial impact of telemedicine

The economic impact of HF is significant, especially among the Medicare (over 65 years) population, where expenditure for treatment of HF is higher than any other diagnosis.16 Medicare beneficiaries with HF have the highest rehospitalization rates among all other conditions, and over a quarter of patients with HF are rehospitalized within 30 days of discharge.17 The total health-care cost attributable to HF in 2013 is $32 billion and is projected to reach $70 billion in 2030.2 Hospitalizations account for 60–70% of these generated costs.18,19 Initial positive outcomes11,21 have led to theories of cost-effectiveness based on a reduction in the number of hospitalizations.11,20

Very little data exist on the actual cost-effectiveness of a remote monitoring strategy for HF. Cost-effectiveness models derived from meta-analyses and disease-related group (DRG) tariffs in Europe and North America20 have shown savings (between €300 and €1000 per patient) primarily related to reductions in hospitalization. Individual studies have shown conflicting results.22-24 The Heart Failure Home Care Trial24 showed in a post hoc Medicare claims analysis that costs were significantly higher in patients randomized to the remote monitoring arm ($17,837 versus $13,886). In a dedicated study of cost-effectiveness, Smith et al.23 used incremental cost-effectiveness ratios to demonstrate significant costs per QALY gained in all patients ($101,120) involved in STS based remote monitoring.

Recent large clinical trials12,13 have shown that remote monitoring is a highly involved process with large volumes of data analysis and subsequent intervention. The human cost of telemonitoring is therefore largely unaccounted for in cost-benefit analyses to date. Effective large-scale utilization of telemonitoring will need additional health-care providers specifically trained in HF disease management.14 The National Home Telehealth Program by the Veterans Health Administration who enrolled over 17,000 patients in a care co-ordination/home Telehealth (CCHT) program highlighted this, with over 5,000 trained staff needed to provide the necessary health informatics, remote monitoring, and disease management.25 The inconsistent results to date reflect the uncertainties surrounding the ideal remote monitoring strategy and patient population. As further progress is made, competition in the product market as well as economies of scale may provide significant cost reductions in future.

Future directions (newer technologies and systems of remote monitoring)

A significant limitation to remote monitoring through either STS or telemonitoring is that the physiological parameters transmitted are limited to vital signs and weight; changes in the latter likely trigger adjustment of diuretic therapy.15 Even traditional patient education and self-management centers upon weight gain. Despite this, less than 50% of patients weigh themselves daily.26 Using weight gain as the sole indicator to predict worsening HF has good specificity but poor sensitivity27 and may not be a useful measure in detecting clinical decompensation when compared with intracardiac pressure monitoring.28 These findings have given rise to the search for a more sensitive, remotely monitored, indicator of fluid status.

PPM and ICDs

Implantable devices such as permanent pacemakers (PPMs), implantable cardioverter-defibrillators (ICDs), or cardiac resynchronization therapy (CRT) devices placed for their primary indication or specifically designed implantable devices can provide continuous hemodynamic monitoring that may allow for timely detection of worsening HF. With over 3 per 1,000 cardiac device implantations being PPMs among Medicare beneficiaries,29 there is potential for these devices to be expanded to include hemodynamic monitoring.

Commonly measured parameters include heart rate, tachyarrhythmias, heart rate variability—a measure of sympathetic tone, use of an accelerometer to detect
patient activity level and shock therapy (appropriate versus inappropriate) have been all shown to predict worsening HF.\textsuperscript{30,31} Intrathoracic impedance, defined as the change in resistance measured between the right ventricular lead tip and the generator can be used as a surrogate for pulmonary vascular congestion.\textsuperscript{32} This has been shown to be a more accurate measure of worsening HF when compared with weight change alone.\textsuperscript{33} Combining measurable variables has added further information, revealing a fivefold increase in the 30-day risk of hospitalization. The prospective study of intrathoracic impedance in the Diagnostic Outcome Trial in Heart Failure (DOT-HF)\textsuperscript{34} disappointingly revealed no improvement in all-cause mortality or HF hospitalizations. There was a notably significant increase in HF hospitalizations and outpatient visits in the access arm. Further prospective studies investigating outcomes in this area are currently ongoing.\textsuperscript{35}

**Implantable hemodynamic monitors**

Worsening HF correlates with increases in end-diastolic pressures,\textsuperscript{36} and the product of increases in pressure over time is closely associated with transition to acute decompensation.\textsuperscript{37} Importantly, these increases in pressures occur several days prior to the development of symptoms.\textsuperscript{36,38} Implantable hemodynamic monitoring could provide the most correlative data and therefore is an area of significant investigation with several device systems that measure pressures in the pulmonary artery, the atria, and the right ventricle.

The first randomized, prospective trial involving implantable hemodynamic monitoring, the COMPASS-HF trial,\textsuperscript{39} utilized a RV pressure sensor with the ability to monitor temperature, heart rate, systolic, diastolic pressures and RV dP/dT, a surrogate for left-sided filling pressures. Two hundred and seventy-four patients with New York Heart Association (NYHA) functional class III and IV were included in the study with 134 patients randomized to the device arm. Follow up at 6 months revealed that 91.5% of patients were complication-free. Likely underpowered, there was no significant difference in hospitalizations, urgent care needs or need for intravenous therapy between the two groups. Further analysis did indicate that patients with persistently high filling pressures were at risk for hospitalization,\textsuperscript{35} adding to the growing body of evidence for further study of hemodynamic monitoring.

The HeartPOD device, a left atrial pressure sensor has been evaluated in patients with NYHA functional class III or IV HF in the HOMEOSTASIS study.\textsuperscript{40} Device functions included measurements of LA pressure, core temperature, intracardiac electrocardiogram tracings, and contained a display with LA pressure readings that advised patients of the readings. In this observational study the intervention was physician guided but patient self-managed. At 25 months of follow-up, there was a significant improvement in NYHA class and optimal medication titration resulting in improvement in LA pressures. Prospective study of LA pressure monitoring is currently ongoing (LAPTOP-HF)\textsuperscript{46} (clinicaltrials.gov).

Pulmonary artery pressure monitoring by a sensor implanted through right heart catheterization (CardioMEMS Heart Sensor) has also been developed. The device does not contain an internal power source; instead, it is powered by an external antenna, forgoing the need for battery replacement. It is comparable to both echocardiography and Swan–Ganz catheterization.\textsuperscript{41} The CHAMPION trial,\textsuperscript{42} a prospective multicenter single blind study conducted to evaluate device safety, revealed a 98.6% freedom from device-related complications. Five hundred and fifty patients with NYHA functional class III HF were enrolled, and at 6 months follow-up there was a 30% reduction in HF-related hospitalizations in the study group (CI 0.6–0.84, p<0.0001). Outcomes were similar in patients with preserved ejection fraction. Significant secondary outcomes included reduction in HF-related hospitalization, reduction in mean pulmonary artery pressure, improved quality of life during the 6-month period, and more days alive outside the hospital. There was no significant difference in survival rates. Further investigation and newer monitoring systems are currently in development.\textsuperscript{43}

The initial studies in implantable hemodynamic monitoring have been promising. Direct measurement of intracardiac pressures and the ability to trigger an alert or advisor system could promote patient self-management as well as self-regulation and administration of therapy in a similar manner to patients with diabetes.

**Computing and software**

Mobile device-based remote monitoring systems are another possibility in the current era. Most cellular phones and tablet computers have the necessary hardware to run a remote monitoring system. These devices have the advantage of being inexpensive and familiar to the patient, and benefit from being easily portable with excellent connectivity options. The study of mobile phone based monitoring is currently in its infancy,\textsuperscript{44} and further investigation is needed. Intelligent software design is another area of active investigation. Guidi et al,\textsuperscript{45} demonstrated the potential of various computer-based intelligence techniques in providing a diagnosis and an algorithm prognosis to assist non-specialist personnel with remote monitoring. The diagnosis and prognosis functions were followed up and used to refine the initial diagnosis in an evolutionary fashion. The combination of sophisticated software with a simple interface on an easily accessible device could promote self-management and improve uptake of the monitoring system.

**Conclusions**

HF management continues to be extremely challenging despite significant advances in medical therapy over several decades. The growing costs, morbidity, and mortality associated with HF have driven this current body of research in remote patient monitoring, a potential solution to the large burden facing health-care in most countries today.
References


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46. Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy (LAPTOP-HF) http://clinicaltrials.gov/show/NCT0112110.

