Thoracic Impedance as an Early Indicator of Decompensation In Patients with Heart Failure

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ABSTRACT

Heart failure is a major public health problem. Patients are generally elderly and severely ill, suffer from multiple comorbidities, and require frequent hospitalizations for acute decompensation. Each episode of decompensation may worsen underlying cardiac function and propel patients closer to complete cardiac failure and death. A new cardiac resynchronization device that utilizes impedance monitoring to track daily intrathoracic fluid status may help clinicians predict episodes of decompensation. The device is extremely sensitive to changes in fluid status, and may help guide therapy and prevent hospitalizations. At Lancaster General Hospital, we have implanted more than 170 of these devices, and found them to contribute important information to outpatient management strategies.

HEART FAILURE: THE SCOPE OF THE PROBLEM

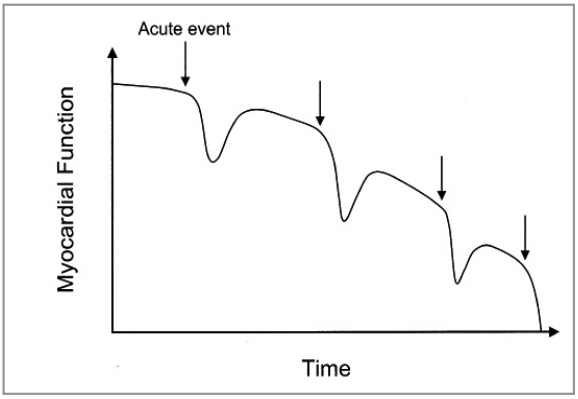
The incidence and prevalence of Heart Failure (HF) have reached epidemic proportions in the United States, and, as the general population ages, it is unlikely to abate. Recent estimates suggest that as many as 5 million individuals (2.3% of the total population) are living with some degree of cardiac dysfunction, and more than 550,000 new cases are diagnosed each year.[1]

Heart failure is associated with significant morbidity and mortality, and massive consumption of healthcare resources. Between 1992 and 2001, the number of emergency department (ED) visits for acutely decompensated HF (ADHF) accounted for almost 3% of all ED visits made during the decade — a total of 10.4 million actual HF-related presentations. Rehospitalization for HF-related causes is common, reaching 20% at 30 days, and 50% within 6 months. Between 1993 and 2003, HF-related mortality increased 20.5%, and in 2003, the overall HF-related death rate was 19.7%.[1] In 2006, almost $30 billion will be spent on HF in the U.S., and it will be the single greatest Medicare expense.[1]

THE PHYSIOLOGY OF THE PROBLEM

Heart failure is a progressive syndrome that begins with structural and/or mechanical deficiency in the heart's pumping action. Mechanical deficiencies induce a cascade of neurohormonal adaptions that increase cardiac contractility, fluid and sodium retention, vasoconstriction, and myocardial remodeling. Such alterations temporarily help maintain hemodynamic stability, but ultimately contribute to the degeneration of cardiac function, and to symptoms caused by fluid dysregulation, respiratory and perfusion problems, and hemodynamic instability.

Figure 1: Contribution of acute events to the progression of heart failure. With each admission for acute heart failure syndromes, there is short-term improvement; however, the patient leaves the hospital with a further decrease in cardiac function.



Source: Gheorghiade M, De Luca L, Fonarow GC, Filippatos G, Metra M, Francis GS. Pathophysiologic targets in the early phase of acute heart failure syndromes. *Am J Cardiol.* 2005;96[suppl]:11G-17G.

Decompensation, or the transition from hemodynamic stability to instability, is a repetitively injurious event. Patients who decompensate are typically elderly, take multiple medications, and suffer from multiple comorbidities, the most common being hypertension (72%), coronary artery disease (57%), diabetes (44%), previous myocardial infarction (31%), and chronic renal insufficiency (30%).[2] Three-quarters have pre-existing HF, and one-third of these patients have a

history of recent hospitalization for HF. Hospitalization for treatment with intravenous diuretics, vasoactive drugs, or inotropic medications is often required to stabilize ADHF patients. Although the in-hospital mortality of 4%, may appear relatively modest, this figure readily escalates in high-risk subgroups such as those requiring admission to the intensive care unit (11%), those with renal dysfunction (9.4%), and — worse yet — those with both renal dysfunction and low systolic blood pressure (20%). Almost three-quarters (72%) of ADHF patients are Medicare recipients.

Decompensation may be catalyzed by acute events such as myocardial infarction or pulmonary embolism, or worsening cardiac function. Cardiac dysfunction may also be exacerbated by preventable causes such as non-compliance with medications/dietary restrictions, or inappropriate medication use. Dyspnea occurs in approximately 90% of patients, peripheral edema in 66%, and pulmonary congestion in 75%.[2] It may well seem counterintuitive, but half of ADHF patients are hypertensive (systolic blood pressure >140 mmHg) when first seen, and 48% are normotensive (SBP 90-140 mmHg). *Only 2% present with low cardiac output (SBP <90 mmHg).* The vast majority of patients (up to 80%) present to the ED, perhaps indicating the acuity with which symptoms become manifest.

Each ADHF episode may result in irreversible myocardial damage, evidenced in some studies by troponin leaks, and increases in inflammatory cytokines that may induce myocyte apoptosis (programmed cell death).[3] Despite restoration of hemodynamic stability, the myocardial damage sustained may further undermine cardiac function, propelling patients towards complete cardiac failure **(Figure 1)**.

THE "EARLY WARNING" HYPOTHESIS

The onset of ADHF symptoms occurs over the course of hours to days, but slow fluid accumulation may begin several days or weeks earlier,[4] damaging the myocardium before it becomes symptomatic. If intrathoracic fluid levels could be routinely monitored, it would be hypothetically possible to detect fluid accumulation before the onset of symptoms. This early warning could be used to adjust medications, and possibly to prevent decompensation and its associated hospitalization, morbidity, and drain on healthcare resources. Unfortunately, current approaches to monitoring fluid status, such as patient-reported daily weight, natriuretic peptide levels, and noninvasive bioimpedance, have proved inaccurate and unreliable.

THE SOLUTION

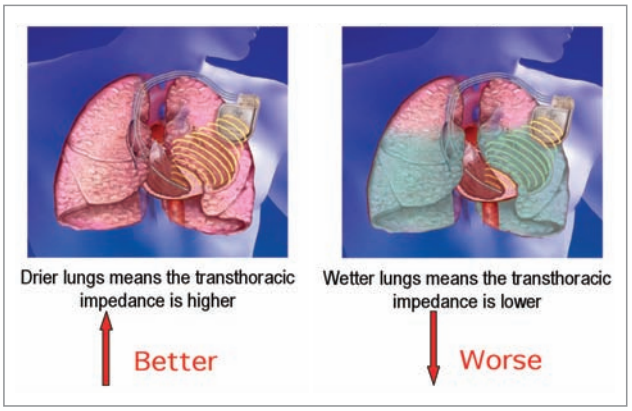
At Lancaster General Hospital (LGH), we recently began utilizing a new implantable cardiac defibrillator/pacemaker/resynchronization device (described in detail below) that provides standard synchronization support and defibrillation, and monitors fluid volume by tracking intrathoracic impedance. Although this approach to outpatient management is still in the preliminary stages, we anticipate that routine monitoring of intrathoracic impedance will serve as an early warning system that allows medications to be adjusted prior to the onset of severe symptoms, thus averting hospitalization. This approach is possible because of the well-coordinated inpatient and outpatient HF practices at LGH.

CARDIAC RESYNCHRONIZATION THERAPY (CRT)

Individuals with advanced HF (e.g., New York Heart Association [NYHA] class III-IV, and left ventricular ejection fraction [LVEF] ≤35%), in addition to impaired contractility, also suffer from conduction delays that disrupt synchronous ventricular beating. The resulting dyssynchrony further undermines patients' hemodynamic stability, worsens prognosis, and increases mortality. Implantable cardiac resynchronization devices that stimulate both right and left ventricular contractions can ameliorate the dyssynchrony, and produce significant improvements in exercise tolerance, quality of life, and NYHA functional status.[5] CRT is indicated for HF patients with NYHA III-IV, QRS duration >120 ms, and LVEF ≤35%.

The newer CRT device in use at LGH is the InSync Sentry™ CRT-D (Medtronic, Minneapolis, MN) with automated intrathoracic fluid status monitoring (OptiVol™ Fluid Status Monitoring). **(Figure 2)** The device, in addition to providing synchronization, tracks intrathoracic impedance by sending an electrical impulse across the chest from the generator's "can" to the right ventricular coil every 20 minutes between noon and 5 p.m. The device then records the impedance — the resistance to the electrical current. As fluid accumulates in the chest, resistance to the current falls, and thus impedance decreases. As fluid recedes, the impedance increases. Impedance measures are combined for a daily average, and daily averages are combined to calculate changes that develop over long periods of time. The impedance data are extracted from the device and analyzed during routine follow-up. There is no uniform reference — patients serve as their own controls.

Figure 2: The concept: OptiVol™ measurements are made across the thorax during noon and 5 p.m. to ensure that the fluid is as diffuse as possible when the measurements are taken. The impedance change is directly and inversely related to the fluid accumulation. A series of impedance measurements trending lower indicate that fluid is building up. Conversely, a series of impedance measurements trending upward indicate that fluid levels are getting better (i.e., the patient is drying out.)



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REPORTS IN THE LITERATURE

Few studies evaluating the clinical utility of impedance monitoring have been conducted. Initial animal studies found that implantable CRT-based impedance monitoring reflected HF status. A handful of subsequent small-scale human studies have demonstrated an inverse correlation between decreasing impedance (i.e., increasing edema), and increasing pulmonary capillary wedge pressure (PCWP) and symptomatic acute HF.[6,7,8] Impedance monitoring is reported to have a 76.9% sensitivity for predicting hospitalization for fluid overload, with a low incidence of false-positive readings.[8] Patients tend to become symptomatic after a 12% or more decrease in impedance, and, in one study, this marker was used as a threshold to commence therapy.[7] Of 18 patients who experienced an average 13.7% decrease in impedance, and received some type of medication adjustment, only 2 progressed to actual decompensation requiring hospitalization. Thus, *16 potential hospitalizations were averted*. Larger, prospective studies evaluating this strategy are clearly needed and warranted.

THE LGH EXPERIENCE

LGH has one of the largest experiences in the country with CRT devices, and, in particular, the newer impedance-monitoring devices. Since November 1998, we have implanted more than 1,100 CRT devices, and are currently following more than 500 HF patients with implants. As of January 2006, more than 170 CRT devices with impedance monitoring had been implanted. The use of these devices in made feasible by LGH's well-integrated inpatient and outpatient HF clinics.

Our inpatient program at LGH utilizes a multi-disciplinary approach to HF management, with a team that includes HF specialists, electrophysiologists, nurse practitioners, pulmonologists, nephrologists, and surgeons. Multidisciplinary care improves patient quality of life, reduces hospitalizations and costs, and may improve prognosis.[9] The program facilitates rapid access to specialized tests, as well as reliable adherence to guidelines, education, and follow-up. Enrollment criteria are shown in **Table 1**. The clinic coordinates patient care with the outpatient clinic (The Heart Group), which ensures continuity of care, and adequate follow-up.

TABLE 1: CRITERIA FOR ADMISSION TO THE LANCASTER GENERAL HOSPITAL HEART FAILURE PROGRAM

- Primary diagnosis of heart failure
- Chronic heart failure or previous hospitalization for heart failure
- New York Heart Association Functional Class III-IV (or high risk of decompensation)
- Acceptance of protocols and guidelines
- No intensive care requirements
- Referred to program by cardiologist

In 2005, 457 patients were admitted to the LGH HF program, and 375 of these patients met the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) HF Hospital Quality Measures (HQM) criteria. Among these patients, there was an average 1.2 annual hospital admissions with an average length of stay of 10.2 days; 15.5% of patients required multiple admissions. 59% were men, and the average age was 70.3 years. In 2005, 7 patients died, and 19 were referred to hospice. HQM goals were more often achieved in patients in the LGH HF program than among patients not in the program. There was greater use of guideline-recommended therapies such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and beta-blockers, and, importantly, patients in the program were more likely to receive discharge instructions.

It is within this framework that we have begun to use impedance monitoring. The feasibility of this strategy, and its role in a coordinated and continuous care environment such as that at LGH, is illustrated by two of our cases.

Case Report #1: On April 7, 2005, a 66-year-old women with nonischemic cardiomyopathy and a LVEF of approximately 35% presented to the HF clinic complaining of shortness of breath. She had a history of hypertension, diabetes, paroxysmal atrial fibrillation, and depression. A previously implanted pacer cardiodefibrillator had reached its end of life. Medications at the time of presentation were quinapril, carvedilol, spironolactone, bumetanide, digoxin, and coumadin. She reported decreased activity; however, impedance monitoring indicated a normal fluid status. B-type natriuretic peptides (BNP) levels were modestly elevated (185 pg/mL). She was treated for bronchitis.

One month later, on May 3, 2005, the patient was seen for follow-up: she was asymptomatic and reported an increasing activity level despite decreasing impedance, an indication of fluid accumulation. Approximately 3 weeks later, on May 23, she was seen in the HF clinic and reported decreasing activity, but no dyspnea. Impedance monitoring indicated the presence of edema, and although her BNP had decreased to 153 pg/mL, we increased her diuretic dosage. On June 13 she reported weight gain despite no obvious fluid retention, and the BNP had fallen to 107 pg/mL. The impedance tracking was reset. In September 2005, she had gained 25 pounds, BNP was 100 pg/mL, chest x-ray was normal, impedance below threshold, and she was asymptomatic.

The case illustrates important limitations of current diagnostic strategy, and the potential role for impedance fluid monitoring. BNP is often used in the diagnosis of HF, but in this case it did not correlate with the onset of congestion. Indeed, BNP remained relatively low, while fluid volume increased. This patient's clinical deterioration may have gone unrecognized until she became severely symptomatic. Impedance monitoring in an environment with routine follow-up helped therapeutic decision-making, and timely adjustment of diuretics may have prevented a more severe clinical scenario.

Case Report #2: An 85-year-old man with ischemic cardiomyopathy and a LVEF of 30% was seen in the HF clinic on April 26, 2005. He was diabetic, hyperlipidemic, had a history of atrial flutter, and was taking lisinopril, metoprolol, bumetanide, amiodarone, and coumadin. CRT pacing was 100%, and his BNP, at 490 pg/mL, was elevated. Because of a serum creatinine of 2.7 mg/dL, his diuretic dosage was decreased.

On May 20, 2005, impedance monitoring indicated fluid accumulation, and an underlying atrial fibrillation. CRT pacing during atrial fibrillation was only 54.3%. Three days later, the patient was again seen in the HF clinic where his diuretic dosage was increased. His creatinine and BNP remained elevated (1.9 mg/dL and 467 pg/mL, respectively). Decompensation was most likely catalyzed by atrial fibrillation that caused inconsistent biventricular pacing; these events preceded the fall in impedance.

In August 2005, the patient was seen in the HF clinic. He had gained weight, BNP was 728 pg/mL, and the impedance was falling, indicating the onset of edema and eventual decompensation. We increased his diuretic dosage, and although his condition was worsening, hospitalization was prevented.

CONCLUSIONS

Intrathoracic impedance monitoring, used as a surrogate for fluid volume in HF patients, may facilitate better outpatient management by enabling early detection of fluid changes. The impedance monitoring device is highly sensitive to changes in fluid volume, and the data garnered on fluid status may help guide routine outpatient care by alerting physicians to changes in disease status that warrant changes in therapy. Impedance monitoring may prove to be particularly valuable when used in conjunction with other monitoring technologies. Clinical trials designed to evaluate the clinical utility of impedance monitoring are needed.

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