

Worsening Thoracic Impedance as a Ventricular Tachyarrhythmia Risk

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The use of heart failure classification to identify patients with systolic dysfunction who are at risk for ventricular tachyarrhythmias (VAs), sudden cardiac death, and shocks from implantable cardioverter defibrillators (ICDs) is limited by its subjectivity. Measurement of thoracic impedance offers a more objective tool for assessing worsening of heart failure. We sought to look at the correlation between ventricular arrhythmia and heart failure as assessed objectively by thoracic impedance. We reviewed device interrogation data on thoracic impedance from ICD with Medtronic's OptiVol® feature (Medtronic Inc., Minneapolis, MN) at two medical centers. Data from the last two interrogations of the same device separated by at least 2 months were included. An OptiVol fluid index threshold of 60 represented early heart failure prior to appearance of symptoms. VAs included were ventricular fibrillation and/or ventricular tachycardia lasting more than 16 beats. Chi square distribution test was used in statistical data analysis. There were 24 VAs identified among the 322 interrogations reviewed (7.5%). Elevated OptiVol fluid index was seen in 71% (17/24), whereas normal OptiVol index was seen in the remaining 29% (7/24) of these interrogations with VA ($P < .05$). Our review shows that heart failure patients who have VA are approximately 2.5 times as likely to have worsening thoracic impedance as assessed objectively by the OptiVol fluid index. Careful monitoring of the OptiVol fluid index may identify a population at high risk of VA that merits more intense attention.

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KEY WORDS

Ventricular arrhythmias • Heart failure • Thoracic impedance • Implantable cardiac defibrillator

Arrhythmias are common in chronic heart failure and affect outcomes. Left ventricular (LV) dysfunction is a well-established risk factor for sudden cardiac death (SCD); however, the clinical syndrome of congestive heart failure (CHF) is thought to contribute to arrhythmogenesis in patients with ventricular systolic dysfunction.¹ Heart failure is associated with many factors that predispose to ventricular tachyarrhythmia (VA), including increased circulating catecholamines, electrolyte imbalances caused by diuretic use, prolonged repolarization, stretch-induced after depolarizations, and Purkinje system conduction delay.² Monitoring both fluid status and arrhythmias in patients with heart failure may enable better management of arrhythmias in this population. The use of heart failure classification to identify patients with systolic dysfunction who are at risk for VA, SCD, and shocks from implantable cardioverter defibrillators (ICDs) is limited by its subjectivity.³

The diagnostic/monitoring and therapeutic benefits of defibrillators have increased as a result of advancing device technology. Medtronic Corporation (Minneapolis, MN) devised a method to measure, monitor, and transmit changes in thoracic impedance that correlate to the level of pulmonary edema. Although defibrillators with OptiVol® (Medtronic) capability were released in 2004, there are now three devices with this capability: the InSync Sentry, Virtuoso, and Concerto models (Medtronic).

We hypothesized that measurement of thoracic impedance may offer a more objective tool to assess worsening of heart failure and, subsequently, to stratify patients at high risk for VA. Thus, the aim of this study was to evaluate the correlation between ventricular

arrhythmia and heart failure as assessed objectively by thoracic impedance.

Methods

We reviewed data from 161 randomly selected patients with a Medtronic defibrillator device having the OptiVol index measurement feature. A total of 141 patients met our inclusion criteria (120 men and 21 women), and 20 patients were found not to have experienced a true VA. Information was obtained from pools of patients at two medical centers. For study inclusion, each patient chart review had to provide information from two sequential device interrogations from the same device for at least 2 months but not more than 6 months between interrogations. We examined a total of 322 device interrogations. Each patient chart was examined for the following information: (1) elevation of OptiVol fluid index and (2) presence or absence of a VA detected by the device.

Intrathoracic Impedance Monitoring and ICD Data Collection

The intrathoracic impedance monitoring feature of the ICD has been previously described.⁴ In brief,

fluid index threshold of 60 Ω represents a warning of early CHF prior to the onset of symptoms. This level was determined through a research algorithm in an initial impedance monitoring study by Yu and colleagues.⁴ The study algorithm revealed a 77% sensitivity for patients that exceeded the 60 Ω threshold regarding early warning signs of heart failure-related hospitalization.

An interrogation was deemed (+) for elevated thoracic impedance if it exceeded this value. The definition of VA in this study is ventricular fibrillation and/or ventricular tachycardia lasting more than 16 beats (as defined by the device). When identified by the device, the ventricular tachycardia or ventricular fibrillation rhythm strips were confirmed by two separate electrogram reviewers. Those patients who were determined not to have experienced a true VA were left in the study but not included in this subset of (+) VA patients. At this time, no other arrhythmias were included and patients with nonsustained ventricular tachycardia were also excluded from the VA group.

Statistical Analysis

A Chi-square distribution test was used in statistical data analysis. A

The OptiVol fluid index threshold of 60 Ω represents a warning of early CHF prior to the onset of symptoms.

the OptiVol algorithm measures the thoracic impedance between the right ventricular coil and the ICD, and calculates a daily mean. Changes in the daily impedance over time determine a moving average, or reference impedance, which indicates the currently expected daily impedance value. The cumulative difference between the measured daily impedance and the reference impedance is used to calculate a fluid index. The OptiVol

P value < .05 was considered significant for all tests. All statistical analyses were performed with SPSS software (Version 12.0. Chicago, IL: SPSS Inc; 2003).

Results

Of the 322 device interrogations, there were 147 with normal OptiVol fluid index and 175 that exceeded the 60 Ω threshold. The target group of patients with VA totaled 24 (7.5% of the total population of

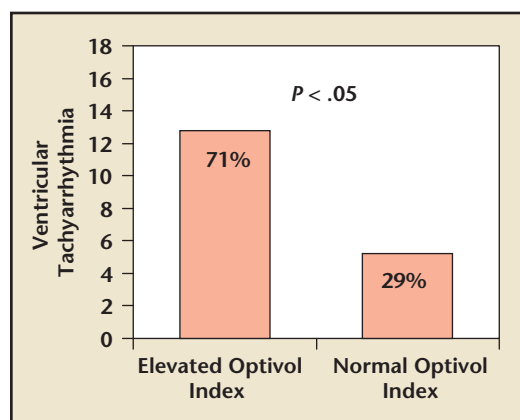


Figure 1. Percentage of ventricular tachyarrhythmias in patients with elevated OptiVol® (Medtronic Inc., Minneapolis, MN) index compared with patients with normal OptiVol index.

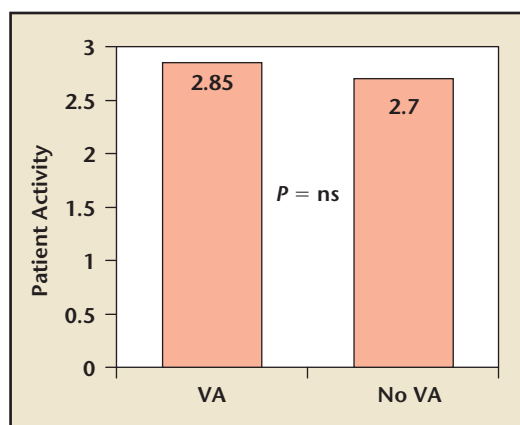


Figure 2. Patient activity level in those with and without ventricular tachyarrhythmia (VA).

studies), and of those identified and confirmed VA, elevated OptiVol fluid index was present in 17 of 24 (71%) interrogations, whereas the remainder of the VA group with normal OptiVol fluid index was 7 out of 24 (29%), following a Chi-square distribution test analysis of these data ($P < .05$) (Figure 1).

Of the 17 documented VA interrogations that correlated with elevated OptiVol fluid index, 13 (76.4%) received an ICD for primary prevention of SCD. Moreover, patients with cardiac resynchronization therapy (CRT) devices with defibrillation capability had three VAs and 100% correlated with high OptiVol fluid index.

Patient activity did not differ between patients who had VA or no VA, with means of 2.85 and 2.7 h/d, respectively (Figure 2). The average age of the population was

68.2 years, and there were 120 men (74.5%) and 41 women (25.5%).

Figure 3 shows device-recorded intrathoracic impedance data from a 58-year-old man with New York Heart Association (NYHA) functional class III CHF and a history of nonischemic cardiomyopathy with an ejection fraction of 20% who had a Virtuoso device implanted for primary prevention of SCD. One year later, the subject had several VA episodes requiring multiple ICD discharges and antitachycardia therapy that correlated with an elevated OptiVol threshold.

Discussion

Electrical devices have emerged as an important new line of therapy for patients with drug-refractory moderate to severe chronic heart failure and major LV dysfunction. Since the introduction of the ICD in humans in 1980, there have been

innumerable technologic advances that revolutionized the way these devices are used. As the focus on prevention of SCD increases, ICDs have been the target of many landmark trials.

Our results show that, in patients with depressed LV function, high OptiVol thresholds are associated with increased risk for VA. We believe our study represents the first investigation of the use of an increased fluid index to predict VA. Our results show that, in patients with LV systolic dysfunction, high OptiVol thresholds may predict VA. This relationship was mostly observed in primary prevention patients, especially in the CRT group, and this fact highlights the usefulness of this technology to predict de novo VA episodes in individuals with heart failure. This relationship was weaker in the secondary prevention group that mostly encompassed patients with non-heart failure indication for ICD implantation. Patients' levels of activity did not correlate with the occurrence of VAs, as both patient groups had approximately the same mean level of activity. This could reflect that NYHA classification did not appear to be predictive of VA in our population. Our data give supporting objective evidence that the clinical syndrome of CHF contributes to arrhythmogenesis.

ICD trials have found that heart failure symptoms are associated with defibrillator therapies. In a recent study that looked at 136 patients with nonischemic cardiomyopathy implanted with an ICD, only acute heart failure hospitalization and nonsustained ventricular tachycardia were found to be independent predictors of appropriate ICD therapy in nonischemic cardiomyopathy with heart rates of 3.5 and 4.2, respectively.⁵ Moreover, the Triggers of Ventricular Arrhythmias (TOVA) study

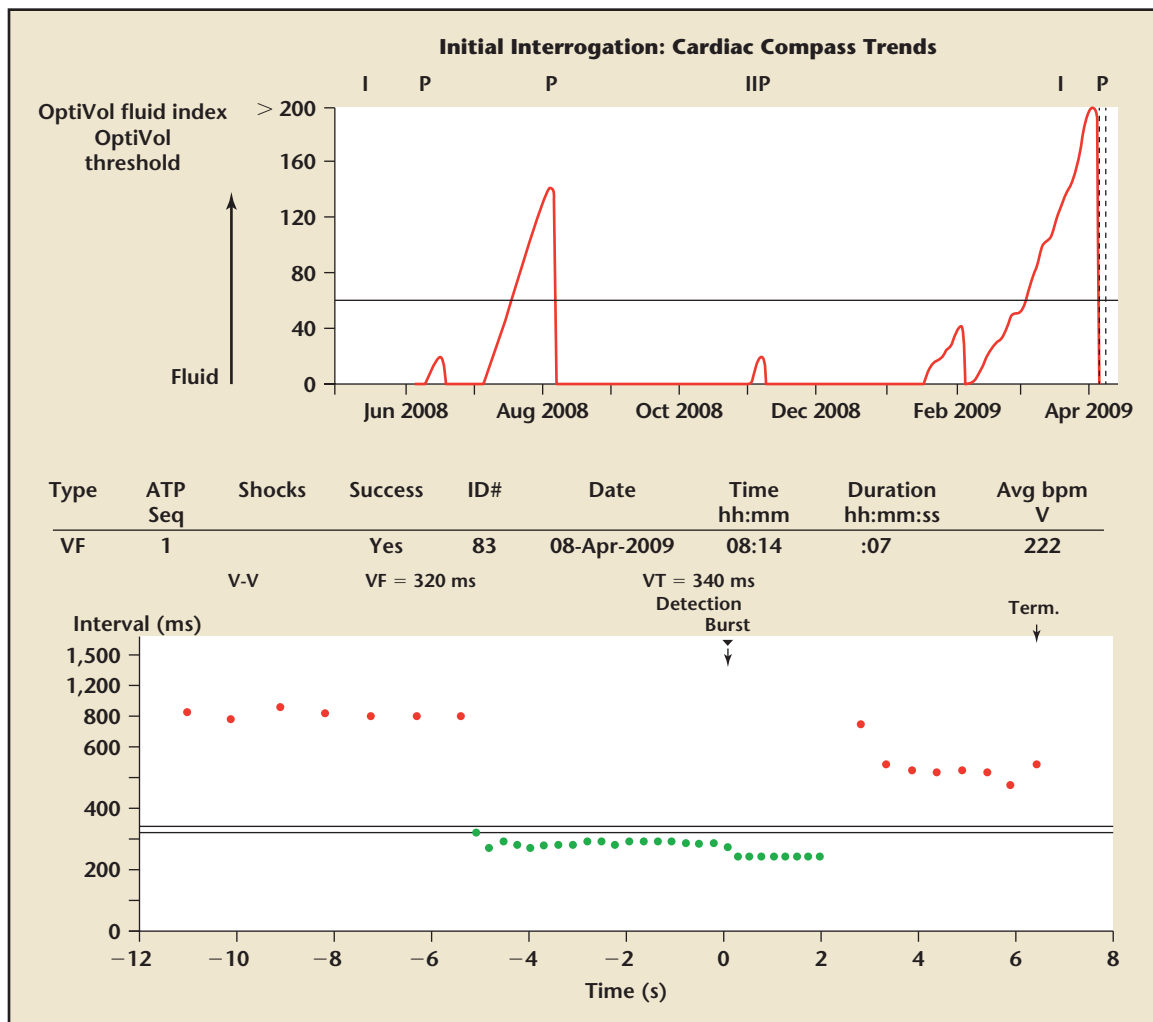


Figure 3. Sample case showing an elevated OptiVol® (Medtronic Inc., Minneapolis, MN) fluid index preceding an episode of ventricular tachycardia.

identified NYHA functional class III as the strongest independent predictor of appropriate ICD therapy.³ The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) found a mortality benefit from ICD therapy for primary prevention among patients with CHF and either an ischemic or nonischemic dilated cardiomyopathy. Subgroup analysis showed that patients with class III heart failure did not appear to benefit compared with patients with class II heart failure.⁶ On the other hand, Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE), which enrolled only patients with a nonischemic cardiomyopathy, found a greater benefit of ICD therapy among patients with class III

heart failure than among patients with class II heart failure.⁷ In the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II), which enrolled only post-myocardial infarction patients, there were no significant differences in the beneficial effect of ICD therapy on survival in subgroup analyses stratified according to NYHA class.⁸ The use of heart failure classification to identify patients with systolic dysfunction who are at risk for SCD is limited by its subjectivity. One study found that NYHA estimates made by two physicians had a reproducibility of only 56% and that only 51% of the estimates agreed with treadmill exercise performance.⁹ A non-invasive objective assessment of the clinical syndrome of heart failure

could potentially improve the accuracy of the diagnosis.

Catanzariti and colleagues¹⁰ demonstrated that an ICD endowed with intrathoracic impedance monitoring could reliably predict heart failure deterioration and hospitalization. Moreover, by allowing timely detection and prompt therapeutic intervention, the alert capability reduced the number of clinical events and heart failure hospitalizations.

The diagnosis and management of heart failure represents an ongoing challenge for health care providers. The natural history of heart failure may be altered by repeated episodes of decompensation requiring hospitalization.¹¹ The rehospitalization rates are elevated

TABLE 1**Demographics of Patients Who Met the Inclusion Criteria**

Number of patients	141
Age	68.2 y
Male (%)	120 (74.5)
Primary prevention (%)	82 (58)
Cardiac resynchronization therapy (%)	70 (49.5)

TABLE 2**Details of Patient Interrogations**

Total number of interrogations	322
Interrogations with high OptiVol® ^a fluid index	175
Interrogations with VA	24
Activity of patient with no VA	2.85 h/d
Activity of patient with VA	2.7 h/d
Interrogations with VA and high OptiVol (%)	17 (71)

^aManufactured by Medtronic Inc., Minneapolis, MN.
VA, ventricular arrhythmia.

in patients with both preserved and decreased LV systolic function and are considered an independent predictor of 1-year mortality, especially in elderly patients.¹² Several trials investigated the potential benefits of continuous monitoring of intrathoracic impedance. Remote monitoring programs have been shown to be effective in reducing morbidity and mortality in heart failure patients.¹³

The Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure (COMPASS-HF) study investigated whether continuous intracardiac pressure monitoring could decrease heart failure morbidity. In that study, when a patient's hemodynamic data deviated from an optimal pressure range, therapy was adjusted in order to restore

pressure to the optimal range. Patients in the remote monitoring group underwent more adjustments to their diuretic therapy and showed a 36% reduction in the relative risk of a first heart failure hospitalization over a 6-month follow-up.¹⁴

Would Treating High OptiVol Readings Decrease the Risk for VAs and Subsequently Lessen the Risk of ICD Discharge?

More advanced ICDs are now collecting information that can be easily extrapolated for use in the clinical setting. For example, the above-listed devices track not only rhythm information and fluid status, but track patient activity, evolving trends in treatment goals, and adherence to treatment plans.

Many offices, particularly heart failure and electrophysiology clinics, employ nurses to track and monitor the growing numbers of patients with heart failure or those who have received device therapy. Nurses in these clinics can use the information provided by these devices to tailor patient-specific therapy goals, titrate medications for optimal effects, and help to control symptoms and decrease hospitalizations. This can also be accomplished with remote monitoring, which does not require potentially frequent office visits to maximize therapies.¹⁵

One of the limitations of our study is that two separate follow-up interrogations not more than 6 months apart were required for study inclusion. Is it possible that patients experiencing VA requiring device intervention, especially a shock, are more likely to adhere to close follow-up and thus the studied population may be biased to include a higher proportion of patients having events?

Another important limitation of this study is the lack of any outcome investigation toward demonstrating a positive effect of preventing ventricular arrhythmias on hospitalization rate, morbidity, or mortality. An established impact of intrathoracic impedance monitoring on survival may be easily extrapolated from other comorbid manifestations of heart failure decompensation, including ventricular arrhythmias. However, this will require a larger-scale clinical trial to demonstrate this expected effect. The sensitivity and positive predictive value of decreased intrathoracic impedance may improve in the long term after device implantation. This positive trend was demonstrated by a study done on CRT devices.¹⁶

The Diagnostic Outcome Trial in Heart Failure (DOT-HF) study was

expected to be reported in 2012, examining 2400 patients with a fluid index alert algorithm used to give early warning of decreasing intrathoracic impedance. The primary endpoint was the composite of all-cause mortality or heart failure hospitalization.¹⁷ This study was stopped prematurely because of slow enrollment, but of the 335 patients enrolled, the investigators were unable to show that the use of intrathoracic impedance with an audible patient alert improves outcome. It actually resulted in increased heart failure hospitalizations and outpatient visits.¹⁸

Conclusions

Changes in thoracic impedance provide an objective measurement of worsening heart failure. Our study shows that heart failure patients who have VA are approximately 2.5 times as likely to have worsening thoracic impedance as assessed objectively by the OptiVol fluid index. Careful monitoring of the OptiVol fluid index may identify a

population at high risk of VA that merits more intense attention. ■

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MAIN POINTS

- Arrhythmias are common in chronic heart failure. Left ventricular (LV) dysfunction is a well-established risk factor for sudden cardiac death (SCD), and congestive heart failure is thought to contribute to arrhythmogenesis in patients with ventricular systolic dysfunction.
- The diagnostic/monitoring and therapeutic benefits of implantable cardioverter defibrillators (ICDs) have increased as a result of advancing device technology; however, the use of heart failure classification to identify patients with systolic dysfunction who are at risk for ventricular tachyarrhythmia (VA), SCD, and shocks from ICDs is limited by its subjectivity.
- Measurement of thoracic impedance offers a more objective tool to assess worsening of heart failure and, subsequently, to stratify patients at high risk for VA.