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**New insight into device therapy for chronic heart failure**  
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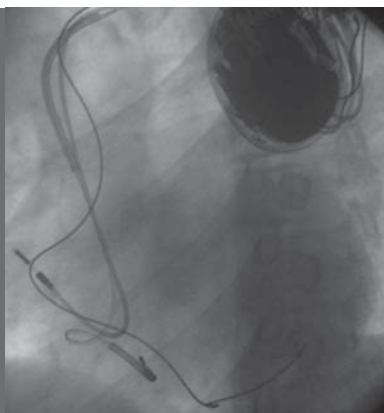
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# Chapter 16



Intrathoracic impedance  
monitoring to predict  
decompensated heart failure

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## ABSTRACT

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Intrathoracic impedance measurement has been introduced in the Insync Sentry biventricular implantable cardioverter-defibrillator (ICD; Medtronic Inc.), and may permit early identification of pulmonary fluid accumulation secondary to left-sided heart failure. An audible alarm (OptiVol alert) can be triggered when the impedance index rises above a predefined level of 60  $\Omega$ -day. The aim of this study was to evaluate the clinical value of OptiVol alert and its prediction for decompensated heart failure. We included 115 consecutive patients (New York Heart Association [NYHA] class 2.8 $\pm$ 0.5 and LV ejection fraction 26 $\pm$ 8%) who received an Insync Sentry biventricular ICD. When presenting with OptiVol alert, current hemodynamic status was evaluated. During follow-up (9 $\pm$ 5 months), there were 45 presentations with OptiVol alert in 30 patients. Only in 15 cases (33%) clinical signs and symptoms of heart failure were present, whereas in the remaining patients clinical signs of heart failure were absent ( $P<0.05$ ). ROC curve analysis showed that increasing the threshold for OptiVol alarm provided a substantial increase in specificity for detection of heart failure, with the optimal cut-off value identified at 120  $\Omega$ -day, yielding a sensitivity of 60% with a specificity of 73%. In conclusion, intrathoracic impedance measurement as present in the Insync Sentry biventricular ICD may be a useful tool for monitoring pulmonary fluid status. The proposed threshold for OptiVol alert of 60  $\Omega$ -day is very sensitive but not specific for assessment of heart failure; adjustment of threshold settings may yield a superior balance between sensitivity and specificity.

## INTRODUCTION

The number of patients with heart failure is increasing exponentially. Much of the medical costs in these patients is related to (re-)hospitalization for decompensated heart failure (1). Therefore, monitoring pulmonary fluid status may be valuable to detect early decompensation, and adjustment of medical therapy may prevent hospitalization. The new generation cardiac resynchronization therapy (CRT) devices (Insync Sentry biventricular ICD, Medtronic Inc, Minneapolis, Minnesota, USA) permit intrathoracic impedance measurements to detect changes in pulmonary fluid status. The feasibility of this device was recently reported by Yu et al. demonstrating an inverse correlation between intrathoracic impedance and pulmonary capillary wedge pressure and fluid balance (2); moreover a decrease in impedance was noted before the onset of patient symptoms and hospital admission for pulmonary fluid overload. Furthermore, an audible alarm (OptiVol alert) can be triggered when a decrease in intrathoracic impedance indicates pulmonary fluid accumulation secondary to left-sided heart failure. Accordingly, these new devices may detect heart failure in the preclinical phase, which may potentially allow adjustment of therapy to prevent heart failure hospitalization. However, the clinical value of this monitoring function has not been shown yet. Therefore, the aim of the study was to evaluate the clinical value of this alarm and its prediction for decompensated heart failure.

## METHODS

### Patients

One-hundred and fifteen consecutive patients with severe heart failure received an Insync Sentry biventricular ICD. Patients were selected according to the traditional criteria for CRT: advanced heart failure (New York Heart Association [NYHA] class III or IV), depressed left ventricular ejection fraction (LVEF, <35%) and prolonged QRS duration (>120 ms). Patients with atrial fibrillation or previously implanted pacemakers were included.

The study protocol was as follows: before implantation clinical status was assessed and echocardiography was performed to measure LVEF. During follow-up standard out-patient clinic visits and biventricular ICD printouts were scheduled every 3 months. Patients were instructed to visit the hospital in case of OptiVol alert.

### Device implantation

A coronary sinus venogram was obtained using a balloon catheter, followed by the insertion of the LV pacing lead. An 8F guiding catheter was used to position the LV lead (Attain-SD 4189, Medtronic Inc., Minneapolis, Minnesota, USA) in the coronary sinus. The preferred position was a lateral or postero-lateral vein (3). The right atrial and ventricular leads were positioned conventionally. All leads were connected to a dual chamber biventricular ICD (Insync Sentry, Medtronic Inc.).

## Intrathoracic impedance monitoring

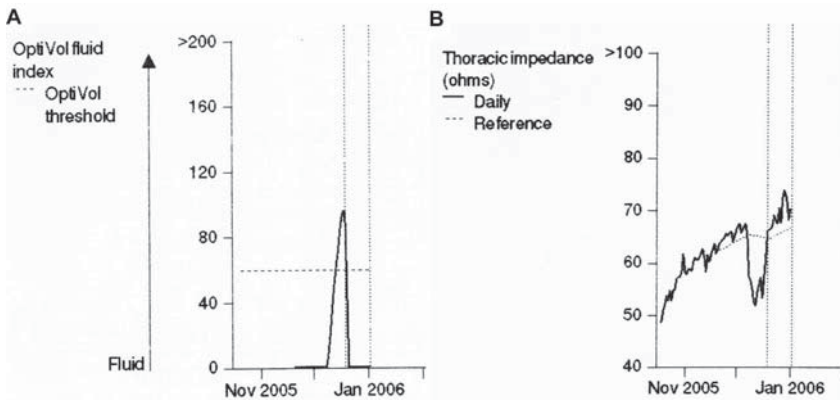
OptiVol fluid status monitoring works by measuring intrathoracic impedance every 20 minutes between 12 a.m. and 5 p.m., using an electrical impulse vector that travels between a lead in the right ventricle of the heart and the pulse generator. As a result the electrical impulse passes through lung tissue. By comparing the daily average impedance values with a reference impedance line, a trend-line can be assessed in the OptiVol fluid index chart (example see Figure 1). Since the device is part of the impedance measurement vector, fluid accumulation in the pacemaker pocket can influence readings; therefore, OptiVol fluid status monitoring is initialized 30 days after device implantation to allow for wound healing.

As fluid accumulates in the patient's lungs, the OptiVol fluid index increases. If the condition is not resolved, and the OptiVol Index crosses a predefined threshold, an observation will be triggered. If enabled, an OptiVol alert will also be audible from the implanted device at a programmed time. When the fluid buildup has been resolved, and the daily impedance value is trending at or above the reference impedance values, the OptiVol fluid index will return to zero.

The OptiVol threshold can be programmed at device implant or at follow-up device checks. In our analysis, the threshold was programmed at the default value of 60  $\Omega$ -day, based on clinical data for optimal sensitivity and low false positive rates (4).

**Figure 1.** Example of OptiVol fluid index

Crossing the OptiVol threshold of 60  $\Omega$ -day triggers the alert (A). The OptiVol fluid index is calculated by comparing the daily average impedance values with a reference impedance line (B). The impedance decreases prior to the alert and increases after increasing diuretics. If the daily impedance moves above the reference trend, the OptiVol fluid index will reset.



## Clinical and biventricular ICD monitoring

During follow-up clinical status and biventricular ICD check up were performed every 3 months in the out-patient clinic. From the biventricular ICD print-outs, OptiVol index trend and thoracic impedance could be determined. Additional visits were planned in case of OptiVol alert. When presenting with OptiVol alert, current hemodynamic status was evaluated by history, drug use, physical examination, laboratory tests and chest X-ray. An alert was assigned as true positive in case of significant heart failure needing medical adjustment and follow-up visits were planned.

**Table 1.** Patient characteristics (n=115)

Age (years)	65±11
Gender (M/F)	95/20
NYHA functional class	2.8±0.5
Ischemic etiology (%)	79 (69%)
QRS duration (ms)	151±35
Rhythm (SR/AF/Paced)	97/11/7
LVEF (%)	26±8
LVEDV (ml)	212±77
LVESV (ml)	160±75
Serum-creatinine (μmol/L)	123±47
Medication	
Diuretics	108 (94%)
ACE-inhibitors	105 (91%)
Beta-blockers	81 (70%)
Spironolactone	42 (37%)
Digoxin	26 (23%)

ACE: angiotensin-converting enzyme; AF: atrial fibrillation; EDV: end-diastolic volume; EF: ejection fraction; ESV: end-systolic volume; LV: left ventricular; NYHA: New York Heart Association; SR: sinus rhythm.

## Statistical analysis

Continuous data are presented as mean ± SD; dichotomous data are presented as numbers and percentages. Comparison of data was performed using the unpaired Students *t* test for continuous variables and Fisher's exact test for proportions. The optimal threshold needed to predict decompensated heart failure was determined by receiver operator characteristic (ROC) curve analysis. For all tests, a P-value <0.05 was considered statistically significant.

## RESULTS

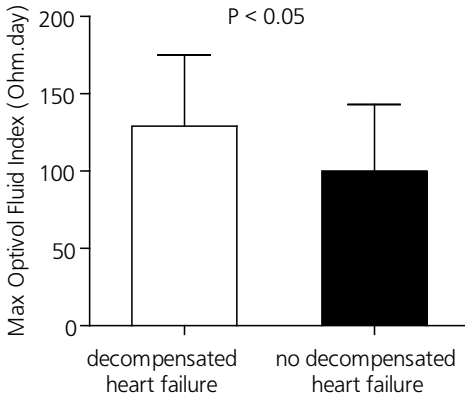
### Patient characteristics

One-hundred and fifteen patients were included in this study (95 men, age 65±11 years). Baseline patient characteristics are summarized in Table 1. Device and lead implantation were successful in all patients without major complications. All OptiVol thresholds were set at 60 Ω·day and an audible alarm was enabled in all patients.

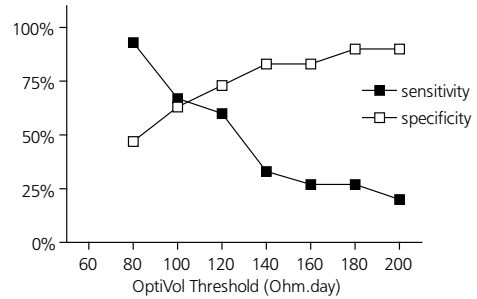
### Optivol alert

During follow-up (9±5 months, range 2 to 19 months), there were 49 presentations with OptiVol alert in 33 patients. Two patients had an alert shortly after LV lead repositioning; one patient had a very high index during a pocket infection and one patient presented with an alert 43 days after implant due to slow wound healing. The remaining 45 OptiVol alerts in 30 patients were analyzed. Baseline characteristics between patients with and without (n=85)

**Figure 2.** Maximum OptiVol Fluid Index ( $\Omega$ -day) in patients with OptiVol alert with and without signs of decompensated heart failure



**Figure 3.** Receiver-operating characteristics curve analysis on the threshold for OptiVol alert ( $\Omega$ -day) in predicting decompensated heart failure



alert were comparable. The time between implant and OptiVol alert was  $238 \pm 105$  days (range 63 to 512 days). In 5 patients the audible alarm was accidentally disabled, resulting in delay in time between alert and presentation of  $6 \pm 10$  days. Mean maximal OptiVol fluid index was  $109 \pm 46 \Omega$ -day.

### True positive vs. false positive alerts

In only 15 alerts clinical signs and symptoms of heart failure requiring medication adjustment were present, whereas in the remaining 30 alerts these clinical signs and symptoms were absent ( $P < 0.05$ ). Only 2 patients with a true positive alert had to be admitted for intravenous therapy. Importantly, no patients were admitted after OptiVol alert for acute decompensation. Of note, the maximum OptiVol index was significantly higher in patients with symptoms of heart failure as compared to patients without symptoms of heart failure ( $129 \pm 46$  vs.  $100 \pm 43 \Omega$ -day,  $P < 0.05$ , Figure 2). Time between implant and alert, and between alert and presentation respectively, were comparable.

In evaluating the biventricular ICD print-outs no causes for inappropriate elevation of the OptiVol fluid index could be determined.

### Prediction of decompensated heart failure

The proposed cut-off value of 60  $\Omega$ -day was very sensitive to detect heart failure, but at the cost of a very low specificity. ROC curve analysis (Figure 3) showed that increasing the threshold for OptiVol alert provided a better balance between sensitivity and specificity, with the optimal cut-off value identified at 120  $\Omega$ -day, yielding a sensitivity of 60% with a specificity of 73%.

## DISCUSSION

The current findings demonstrate that OptiVol intrathoracic impedance measurement may be a useful tool to prevent worsening heart failure symptoms. The proposed threshold for OptiVol fluid alert of 60  $\Omega$ -day is very sensitive but at the cost of a low specificity, since more than half of the alerts were false positive. The maximum OptiVol index was significantly higher in patients with symptoms of heart failure as compared to patients without symptoms of heart failure, and consequently, increasing the threshold for OptiVol alert provided a better balance between sensitivity and specificity to predict decompensated heart failure.

Decompensated heart failure is associated with high morbidity, mortality and treatment costs (1). In addition, a considerable delay between onset of symptoms and initiation of therapy exists; for example Evangelista et al reported a mean delay from the onset of worsening symptoms to hospital admission of 3 days, and almost 30% of the patients had a delay exceeding 5 days (5).

Furthermore, decompensated heart failure is often not recognized clinically. Physicians rely on the subjective assessment of clinical examination, exercise tolerance and changes in body weight; however, patients with chronic heart failure may not have marked clinical signs or symptoms at all. Stevenson et al reported a sensitivity of only 58% for the combination of rales, edema and elevated jugular venous pressure to detect a pulmonary capillary wedge pressure  $\geq 22$  mmHg in patients with moderate-to-severe heart failure (6).

The ability to monitor pulmonary fluid status may permit early identification of decompensated HF; this may potentially reduce hospitalization rate and improve quality of life. Thoracic fluid status monitoring was first tested in the Medtronic Impedance Diagnostics in Heart Failure Trial (MID-HeFT) (2). The study enrolled 33 patients with NYHA class III or IV, scheduled for implantation of an ICD. Nine patients had 24 hospitalizations for heart failure during a mean follow-up of 20 months. Analysis revealed that the impedance was on average  $18 \pm 10$  days (range 3 to 42 days) below the reference value before admission with decompensated HF occurred. A threshold of 60  $\Omega$ -day for impedance was proposed to identify patients who have a high likelihood to develop decompensated heart failure with the need for hospitalization, yielding a sensitivity of 77% (2).

Furthermore, preliminary results in 5 patients demonstrated a good relation between the reduction in pulmonary capillary wedge pressure after treatment for acute decompensated heart failure on the one hand, and the rise in intrathoracic impedance on the other hand ( $r = -0.61$ ,  $P < 0.001$ ).

We evaluated the clinical value of the OptiVol fluid monitoring feature in a prospective setting, and with the use of the proposed threshold of 60  $\Omega$ -day, we detected 45 alerts during follow-up. However, most alerts occurred in absence of heart failure symptoms. As can be observed from Figure 3, a low detection threshold was very sensitive for prediction, but at the cost of a low specificity. Conversely, when using a higher threshold, a substantial increase in specificity is noted, but with a drop in sensitivity. In conclusion, with the proposed cut-off value for the OptiVol threshold of 120  $\Omega$ -day, a reasonable balance between sensitivity and specificity is obtained, although this cut-off value needs further testing in prospective, larger studies. Still, the initial results are promising and are relevant to an increasing number of heart failure patients who are being considered for device therapy.

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