A novel algorithm to assess risk of heart failure exacerbation using ICD diagnostics: Validation from RAFT

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BACKGROUND The integrated diagnostics (ID) algorithm is an implantable device-based tool that collates data pertaining to heart rhythm, heart rate, intrathoracic fluid status, and activity, producing a risk score that correlates with 30-day risk of heart failure (HF) hospitalization.

OBJECTIVE We sought to validate the ID algorithm using the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial.

METHODS Diagnostic measures of the algorithm include OptiVol fluid index, nighttime heart rate, minutes of patient activity, heart rate variability, and combined measure of cardiac rhythm and biventricular pacing. Monthly evaluations of ID parameters were assessed for the development of HF symptoms and hospitalization for HF.

RESULTS A total of 1224 patients were included: 741 (61%) with cardiac resynchronization therapy with defibrillator devices and 483 (39%) with implanted cardioverter-defibrillator only. The mean age was 66 ± 9 years, and 1013 (83%) were men. A total of 37,861 months of follow-up data were available, with 258 HF hospitalizations (event rate 0.68% per month). There were 33 HF hospitalizations during low-risk months (0.21% per month), 123 during medium-risk months (0.66% per month), and 102 during high-risk months (2.61% per month). Compared with low-risk months, and 95% confidence intervals) of HF hospitalizations during medium-risk months was 2.9 (2.0–4.4) and during high-risk months was 10.7 (6.9–16.6). Multivariable analysis demonstrated that each ID variable had independent association with HF hospitalization.

CONCLUSION The risk of HF as determined by the ID algorithm correlated with HF hospitalization and several HF signs and symptoms among patients in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial. This may present a useful adjunct to detect early signs of HF and adjust therapy to reduce morbidity and costs involved with hospital admission.

KEYWORDS Heart failure; ICD; Diagnosis; Algorithm; Hospital admission

ABBREVIATIONS **ACT** = minutes of patient activity; **CI** = confidence interval; **CRT** = cardiac resynchronization therapy; **CRT-D** = cardiac resynchronization therapy with defibrillator; **FI** = fluid index; **HF** = heart failure; **HRV** = heart rate variability; **ICD** = implanted cardioverter-defibrillator; **ID** = integrated diagnostics; **NHR** = nighttime heart rate; **NYHA** = New York Heart Association; **RAFT** = Resynchronization-Defibrillation for Ambulatory Heart Failure Trial

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Introduction

Heart failure (HF) is an issue of significant and increasing burden to population health and health care resources. Approximately 5.1 million Americans suffer from HF with more than 1 million hospitalizations on an annual basis and an average readmission rate of 25% at 1 month.[1] This incurs a $40 billion cost to the health care system annually, with over half of this cost due to hospital admissions. A number of prediction tools have been developed in an attempt to identify patients with HF at high risk of death.[2,3] These tend to require patient evaluation, tests, and laboratory results that must be updated each time a patient's risk is reassessed. The integrated diagnostics (ID) algorithm is an implantable device-based tool that collates data pertaining to heart rhythm, heart rate, intrathoracic fluid status, and activity,

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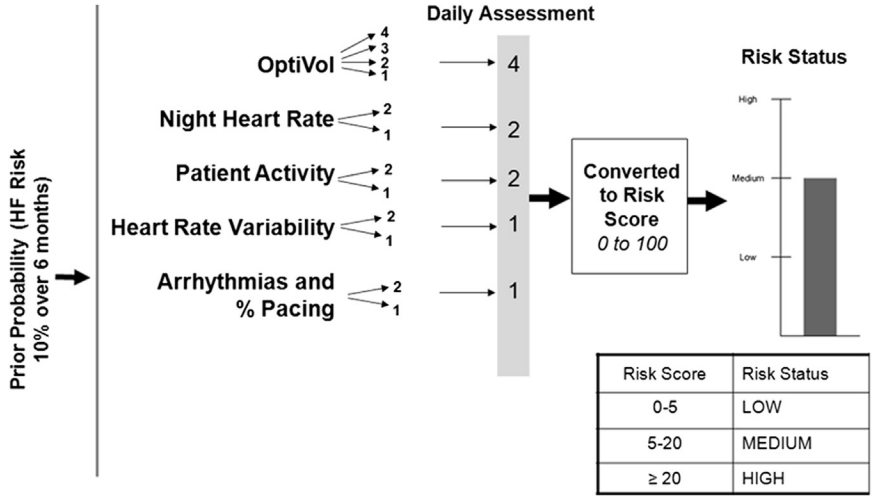

Figure 1 Schematic of the ID algorithm. Participants are assigned a value for each variable on a daily basis. These values are then combined with a risk score that is categorized into low, medium, or high risk. HF = heart failure; ID = integrated diagnostics.

producing a risk score that correlates with a 30-day risk of HF hospitalization.[4] It is a dynamic assessment tool in which variables are continuously updated, and it is widely available in existing implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy (CRT) devices. The cohorts initially used for derivation[5–7] and validation[8–10] of the ID risk score were drawn from prospective nonrandomized studies and included only patients with CRT-D (CRT with defibrillation capability) devices. We sought to further validate the ID algorithm and test its association with HF hospitalization as well as with the incidence of HF symptoms in patients enrolled in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT),[11] a large international clinical trial of patients with congestive HF including both ICD and CRT-D devices.

Methods

RAFT was a multicenter randomized controlled study in patients with New York Heart Association (NYHA) class II or III symptoms, left ventricular systolic dysfunction, and a wide QRS complex. The rationale, design, inclusion/exclusion criteria, and end points have been published previously.[12] Briefly, 1798 patients were enrolled and randomized to ICD or CRT-D. The primary outcome was a composite end point of death from any cause or hospitalization for HF. Hospitalization for HF alone was a prespecified secondary outcome and was defined as admission to hospital for more than 24 hours for treatment of HF. Patients with an implanted device with the capability of monitoring and storing all elements of the ID algorithm were included in this analysis.

Diagnostic measures of the ID algorithm include the following 5 variables with measurement thresholds as determined by previous studies:[8,13,14] (1) Intrathoracic impedance, measured from the right ventricular coil to the pulse generator, was used to compute the OptiVol fluid index (FI), reflecting volume status and lung congestion[15] and stratified to 4 levels of worsening lung congestion: level 1: $0 \leq FI < 30$ ohm-days; level 2: $30 \leq FI < 60$ ohm-days; level 3: $60 \leq FI < 100$ ohm-days; level 4: $FI \geq 100$ ohm-days. (2) Nighttime heart rate (NHR), the average heart rate between midnight and 4 AM, was stratified to 2 levels: level 1: NHR 55–85 beats/min; level 2: NHR ≥ 85 beats/min, ≤ 55 beats/min, or increasing. (3) Number of minutes of patient activity (ACT) per 24-hour period as detected by the device's piezoelectric sensor was stratified to 2 levels: level 1: ACT > 60 min/d; level 2: ACT ≤ 60 min/d or decreasing activity. (4) Heart rate variability (HRV) was measured as the SD of 5-minute medians of intervals over a 24-hour period and stratified to 2 levels: level 1: HRV standard deviation of normal intervals (SDNN) > 60 ms; level 2: HRV SDNN ≤ 60 ms or decreasing HRV. (5) A combined measure of heart rhythm included 4 factors measured over 24 hours: atrial fibrillation burden ≥ 1 h/d, mean ventricular rate during atrial fibrillation ≥ 90 beats/min, a single shock for ventricular tachyarrhythmia whether ventricular tachycardia or ventricular fibrillation or 5 ventricular tachyarrhythmia episodes treated with antitachycardia pacing in 24 hours, and percent pacing in patients with a CRT device $\leq 90\%$ (in whom 100% paced beats is intended), and this combined measure was stratified to 2 levels: level 1: only 1 of 4 criteria met; level 2: 2 or more criteria met. These 5 measures were then entered in a Bayesian belief network[16] to generate a summary HF risk score. The risk score was categorized into low, medium, or high risk for HF. A schematic of the ID algorithm is displayed in Figure 1.

Patients were seen for follow-up 1 month after device implant and every 6 months, consisting of device interrogation, full clinical assessment, and survey of health changes since the last visit. Patients and the treating health team including physicians were blinded to study arm assignment, while a separate health care team including implanting and device management physician was unblinded. All events were adjudicated by an independent, blinded end-point committee. The study was coordinated and database maintained by the Cardiovascular Research Methods Center at the University of Ottawa Heart Institute. The Canadian Institutes of Health