Performance validation of a fluid index derived from intrathoracic impedance in predicting heart failure events in a large real-world population of patients with Cardiovascular Implanted Electronic Devices

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**Introduction**: Implanted cardioverter defibrillators (ICD) and cardiac resynchronization therapy defibrillators (CRTD) measure intrathoracic impedance and derive a surrogate measure for intravascular and interstitial fluid volume. We validated the performance of a fluid index derived from intrathoracic impedance in predicting impending HF events (HFE) in a large real-world cohort of patients.

**Methods**: Patients with cardiovascular diseases were included from the Optum® EHR de-identified database during 2007-2017. In this cohort, we identified patients with Medtronic ICD/CRTD implants with OptiVol2.0 feature. The previously reported OptiVol2.0 fluid index looks for sustained decrease in intrathoracic impedance compared to an expected normal (reference) impedance as a surrogate for increased fluid in intravascular and interstitial space. HFE was defined as an ED or observation unit or inpatient stay with primary diagnosis of HF and IV diuretics administration. Sensitivity was defined as the percentage of HFEs preceded by fluid index exceeding a threshold within the last 30 days. Unexplained detections were fluid index threshold crossing events not followed by an HFE within 30 days. Sensitivity and unexplained detection rate of the fluid index crossing various thresholds is estimated using a generalized estimation equations (GEE) model.

**Result**: A total of 21,069 patients with 1.5±1.2 years of follow-up met inclusion criteria. The average age of patients was 67.8 ±12.6 years, with 72% being males, 70% with history of HF diagnosis, and 51% (49%) had ICD (CRTD) devices implanted. A total of 1812 patients (8.6%) had 2853 HFEs during follow-up. The receiver operating characteristics curve of sensitivity and unexplained detection rate for fluid index based prediction of HFE is shown in figure. In this cohort of patients with all ICD/CRTD devices, at nominal threshold of 60 Ω-days, 57% of the HFEs were predicted in the 30 days prior to event with an unexplained detection rate of 1.1 per patient year of monitoring. The performance results underestimate the sensitivity and overestimate the unexplained detection rate as it was derived from a real-world cohort of patients and the diagnostic data was not blinded from physicians who may have acted based on the data and prevented HFEs.

**Conclusion**: The study validates that the intrathoracic impedance derived fluid index can predict impending HFEs in a large real-world population of patients with ICD/CRTD devices.