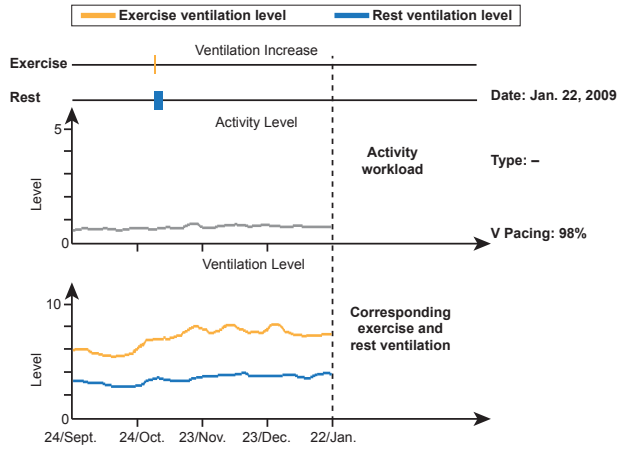
Physiological Diagnostic Algorithm Tracks Ventilation and Workload in Patients With Heart Failure

Written by Larry Hand

A physiological diagnostic (PhD) algorithm in a cardiac resynchronization device called Paradym (Paradym CRT+PhD) has a low sensitivity of 34% and a false-positive rate of 2.4 per patient year. Francisco Leyva, MD, University of Birmingham, Birmingham, United Kingdom, reported on the results the trial Evaluation of a Diagnostic Feature in a Cardiac Resynchronization Therapy (CRT) Device [CLEPSYDRA; NCT00957541]. A subanalysis of the study provided the basis for development of an alternative device-derived risk stratifier of heart failure (HF) events, identifying patients likely to develop HF decompensation in the following month with a Hazard Ratio of 4.4 [Gold M et al. EuroPace 2013 (abstr P1511)].

The HF patient journey has a difficult trajectory with frequent hospital admissions [Cleland JG et al. *J Am Coll Cardiol* 2006], and nothing has been made available to use to predict whether patients would succumb to their disease or return to a more stable path, said Prof. Leyva. But now thoracic impedance can be measured in minute-ventilation (MV=amplitude/period) through a sensor incorporated in the CRT device. From device readings, daily and weekly averages of activity workload and ventilation can be calculated (Figure 1).

Figure 1. Paradym CRT+PhD: Mode of Operation



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In this trial researchers sought to determine the sensitivity of the Paradym CRT+PhD algorithm in detecting potential HF deaths or HF hospitalizations. Since daily activity workloads can change dramatically from day to day, the researchers compared weekly average workloads. Comparing the weekly average on 1 day with the weekly average for the same day a week later can reveal if a condition is worsening or improving.

Eligible patients included those with an HF-related event within 6 months proceeding September 2009, when enrollment began. Eligible patient characteristics were NYHA category III/IV, QRS ≥120 ms, and left ventricular ejection fraction (LVEF) ≤35%. A total of 521 patients were enrolled by April 2011 at centers worldwide: 40 in Europe, 20 in the United States, and 3 in Canada. Baseline characteristics included mean age of 67.4 years, 82% male, QRS 155.3±26.6 ms, and LVEF 25.7%±7.6%. Comorbidities included hypertension and diabetes, 87.1% were taking angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers, and 87.3% were taking β-blockers.

Sixty-six all-cause deaths occurred during the study (15 HF); 127 patients either died (for all cause) or were hospitalized for HF; and 98 patients experienced either HF death or HF hospitalization (Table 1). The Paradym CRT PhD algorithm had 37 true-positives, 1065 false-positives, and 72 false-negatives, for a false-positive rate of 2.4 per patient-year and a sensitivity of 34%. The most lead-related adverse events observed were 41 (7.9%) diaphragmatic stimulations and 38 (7.5%) LV lead dislodgements. The most procedure-related adverse events included 17 (3.3%) pocket infections and 12 (2.4%) pocket hematomas.

Table 1. Clinical Outcomes of CLEPSYDRA

	n (%)
All-cause mortality	66 (13.0%)
All-cause mortality or HF hospitalization	127 (25.0%)
HF death or HF hospitalization	98 (19.3%)
Reasons for death	**n=66**
HF death	15 (2.9%)
Cardiovascular death	33 (6.3%)
Cancer	1 (0.2%)
Infection	3 (0.6%)
Pulmonary edema	1 (0.2%)
Organ failure	3 (0.6%)
Other	10 (1.9%)

HF=heart failure.

Stroke Stratification Scores in the Leipzig Heart Center AF Ablation Registry

Written by Larry Hand

All three stroke stratification scores are associated with risk of thromboembolic events (TE) in anticoagulated patients after radiofrequency catheter ablation of atrial fibrillation (AF). Jelena Kornej,

MD, Heart Center Leipzig, Germany, presented the information from the Incidence and Risk Factors for Thromboembolic Events After Catheter Ablation of Atrial Fibrillation: The Leipzig Heart Center AF Ablation Registry.

The objective of the analysis was to report TE incidence in a large, contemporary AF ablation cohort in patients taking oral anticoagulation (OAC) therapy, and to investigate the value of renal dysfunction and of stroke risk stratification scores in predicting TE after ablation. The scores are $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2. For the latter, renal dysfunction was defined as estimated glomerular filtration rate <60 mL/min.

The study population of the registry included 2069 patients between 2007 and 2011. Mean age was 60 years, 66% were males, 63% had paroxysmal AF, 71% had hypertension, but only 15% had diabetes and 14% had coronary artery disease. Mean scores were $CHADS_2$ at 1.2, R_2CHADS_2 at 1.3, and CHA_2DS_2-VASc at 2.1.

After catheter ablation (CA) patients had outpatient visits at 3, 6, and 12 months. They also had serial 7-day Holter electrocardiogram recordings and were to present immediately if AF symptoms occurred. According to guidelines, recommended OAC treatment was based on $CHADS_2$ scores.

A total of 15 TEs occurred during follow-up, including 5 strokes, 9 transitory ischemic attacks, and 1 system embolism. TE occurred after an average of 11 months (range, 5 to 17 months) following CA, and the international normalized ratio at time of events was 2.51 (Table 1).

In univariate analysis, peripheral artery disease, renal dysfunction, previous thromboembolic events and AF recurrences were associated with TE after catheter ablation. However, in multivariate analysis only three stroke risk stratification scores remained statistical significant predictors for TE during follow up ($CHADS_2$ OR, 2.0; 95% CI, 1.4 to 3.0; p<0.001; R_2CHADS_2 OR, 1.8; 95% CI, 1.3 to 2.5; p<0.001, and CHA_2DS_2-VASc OR, 1.7; 95% CI, 1.2 to 2.3; p=0.001).

Although in the ROC curve analyses 3 stroke risk stratification scores showed modest predictive value (c-index between 0.720 and 0.736), CHA_2DS_2-VASc score differentiated further patients in truly low and high risk strata according to $CHADS_2$ and R_2CHADS_2 of 0 to 1.

An important finding of this study was that AF recurrences conferred a nonsignificant trend for increased TE risk (p=0.056 to 0.077). In this subgroup CHA_2DS_2-VASc had the best predictive value compared with other scores (c-index 0.894, p=0.022 vs $CHADS_2$, p=0.031 vs R_2CHADS_2; Figure 1).

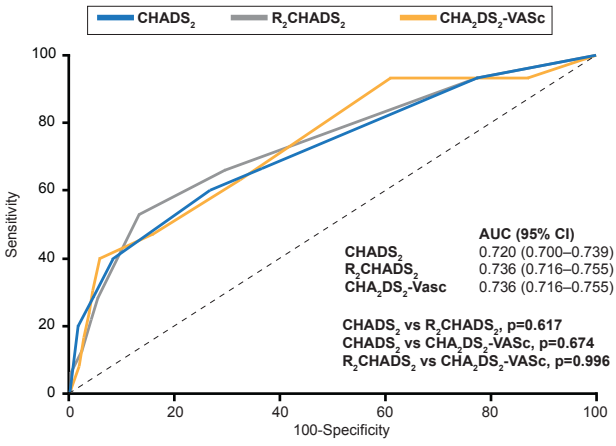
Table 1. Comparison of Patients With and Without Thromboembolic Events During Follow-Up

	No	Yes	p Value
Age, years	60±10	64±11	0.214
Males, %	66	60	0.601
Paroxysmal AF, %	63	53	0.443
Follow-up, months	18 (12–28)	26 (20–35)	0.184
Hypertension, %	71	93	0.055
Diabetes mellitus, %	15	27	0.211
CAD, %	14	27	0.172
Heart failure, %	7	13	0.351
PAD, %	8	20	0.078
Renal dysfunction, %	7	20	0.047
Previous TE, %	9	33	0.001
$CHADS_2$	1.2±0.9	2.1±1.3	<0.001
R_2CHADS_2	1.3±1.1	2.5±1.6	<0.001
CHA_2DS_2-VASc	2.1±1.4	3.5±1.7	<0.001
LVEF, %	59±10	53±16	0.233
LVEDD, mm	49±6	51±12	0.479
LAD, mm	43±6	45±9	0.392
AF recurrence*, %	25.6	53.3	0.014

*1557 (75%) patients with complete rhythm follow-up.

AF=atrial fibrillation; CAD=coronary artery disease; PAD=peripheral artery disease; LAD=left anterior descending; LVEDD=left ventricular end diastolic diameter; LVEF=left ventricular ejection fraction; TE=thromboembolism.

Figure 1. Comparison of Scores as Predictors for Thromboembolism in Patients With AF recurrences



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A low event rate of 0.7%, and the retrospective nature of the study and registry design were considered the most important limitations. Additionally, complete rhythm follow-up was available in 75% of the patients, whereas time of therapeutic range for patients on anticoagulation with vitamin K antagonists was not available at all.

Prof. Kornej concluded that even in anticoagulated patients all three stroke risk stratification scores are useful in predicting thromboembolic events after catheter ablation and stressed the importance to control the AF recurrences during follow up because of their association with thromboembolic complications.

Low Inappropriate Shock Rate With ICD SmartShock Algorithms

Written by Toni Rizzo

Shocks delivered by implantable cardioverter defibrillators (ICDs) can cause anxiety [Sears SF Jr et al. *Clin Cardiol* 1999], decreased quality of life [Schron EB et al. *Circulation* 2002], and mortality [Daubert JP et al. *J Am Coll Cardiol* 2008]. Although ICDs are intended to deliver a shock when needed, inappropriate shocks comprise 2% to 10% of ICD shocks [Schloss EJ et al. *Heart Rhythm* 2013; Moss AJ et al. *N Engl J Med* 2012; Gasparini M et al. *JAMA* 2013].

Painfree SmartShock Technology (SST) is designed to reduce the number of inappropriate shocks with dual- (DR), triple- (CRT), and single- (VR) chamber ICDs. According to Edward J. Schloss, MD, The Christ Hospital, Cincinnati, Ohio, USA, the Study to Evaluate System Safety and Clinical Performance of the Protecta Implantable Cardioverter Defibrillator (ICD) Plus Cardiac Resynchronization Therapy Defibrillator [Painfree SST; NCT00982397] is the first study to evaluate the SmartShock discrimination algorithms for reducing inappropriate shocks by VR-ICDs.

The SST programming for the study used out-of-the box nominal values in current ICDs. The primary endpoint was inappropriate shock-free rate at 1 year post implant. Dr. Schloss previously presented the results for DR- and CRT-ICDs at the Heart Rhythm Society (HRS) 2013 annual meeting [HRS 2013 (abstr 28-04)]. A total of 757 patients were included in the VR-ICD cohort. Follow-up was ≥1 year in 712 patients and <1 year in 45 patients.

At 1-year follow-up, the inappropriate shock-free rate was 97.6% (95% CI, 96.4 to 98.8; Figure 1).

Of the 757 patients, 15 had experienced 19 inappropriate shocks. The causes of the inappropriate shocks were atrial fibrillation or atrial flutter (10 patients, 14 episodes), other supraventricular tachycardia (2 patients, 2 episodes), and over-sensing (3 patients, 3 episodes). The risk of inappropriate shock was not affected by the ventricular tachycardia (VT) therapy zone. Patients with VT shock enabled were 98.1% inappropriate shock-free compared with 97.1% of patients with VT shock not enabled (p=0.38).

The all-cause shock-free rate at 1 year was 91.6% (95% CI, 89.5 to 93.8; Figure 2). There were 252 shock episodes in 53 patients, with 4.8±11.1 episodes per patient. Of these, 175 episodes in 41 patients were appropriate (4.3±6.9 episodes per patient) and 19 episodes in 15 patients were inappropriate (1.3±0.5 episodes per patient). An electrogram was not available for 58 episodes in 5 patients (11.6±17.8 episodes per patient). For the primary objective, patients were censored at the time of a first shock without an electrogram.

Figure 1. Inappropriate Shock-Free Rate at 1 Year

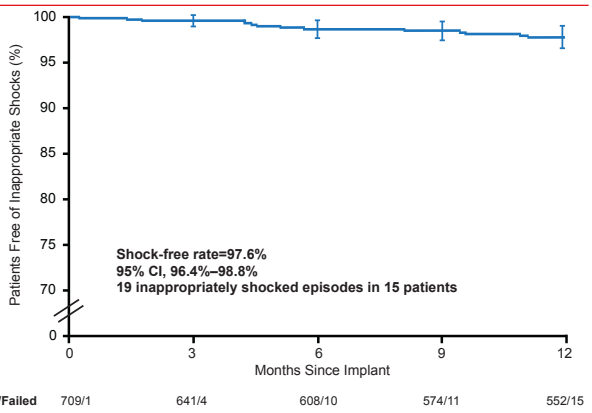

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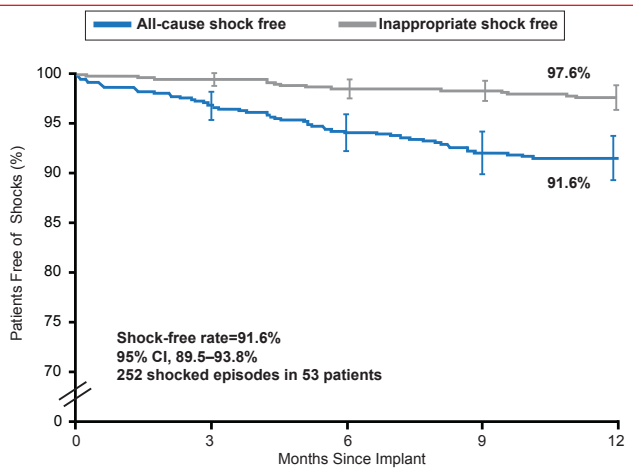
Figure 2. All-Cause Shock-Free Rate at 1 Year



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Sixteen patients died during the 12 months following ICD implantation (mortality rate, 2.4%; 95% CI, 1.5% to 3.6%; Figure 3). There were 3 noncardiac deaths, 5 nonsudden cardiac deaths, and 8 deaths with an unknown cause.