Feasibility of Frailty Assessment Integrated with Cardiac Implantable Electronic Device Clinic Follow-up: A Pilot Investigation

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Abstract

Background: The concept of frailty was originally created to explain why individuals of the same age have differing risk of disease, and it has since been found to be negatively associated with outcomes for a wide range of medical conditions, including cardiovascular disease and cardiac procedures. Although numerous risk scores and assessment tools have been proposed, opportunities for practical assessment of frailty remain limited. In this pilot study, we examine the feasibility of using routine follow-up of patients with cardiac implantable electronic devices (CIEDs) for assessment of frailty. Methods: From September 2017 through March 2018, 49 consecutive patients seen in CIED clinic were enrolled. Among the frailty assessments performed at the clinic visit included a 4-meter walk time, FRAIL scale calculation, Rockwood Frailty score assessment by another treating provider, mini-cog assessment, and analysis of daily activity measures on the CIED. Results: Among the three device manufacturers of patients’ CIEDs, only Boston Scientific released analyzable activity time series data. On nine patients in whom daily activity data could be analyzed, there was no difference in mean daily activity (148.3 ± 31.9 vs. 100.1 ± 25.1 min/day, p = .27) between patients with and without an abnormal frailty or cognitive assessment, although interestingly, those with an abnormal assessment had a higher standard deviation of activity per day (52.6 ± 5.9 vs. 31.4 ± 4.7 min/day, p = .03). Conclusion: It is possible that a higher variation in daily activity over the course of a year could be a better indicator of frailty or cognitive impairment than average daily activity.

Keywords
cardiovascular diseases and risk, technology, active life/physical activity, assistive devices

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examine within the setting of a cardiac device clinic visit.

Overall, implantation of cardiovascular implantable electrical devices (CIEDs) has increased dramatically in the past few decades. As the overall functionality of these devices has improved, so has potential for use of data collected by the device in management of patients. In addition to providing treatment through pacemaker and defibrillator functions, CIEDs are capable of collecting a wide range of data parameters on the individuals in whom they are implanted. Among the types of information stored and tracked on CIEDs includes information about heart rate, history of cardiac arrhythmias and device therapies, and activity measures. All modern CIEDs have accelerometers, as well as biometric impedance monitors, and adjustable algorithms for monitoring minute-to-minute activity, which can be stored for customizable durations within the device, as well as uploaded to remote monitoring systems. Most modern CIEDs are radiofrequency-capable, meaning that patients seldom have to manually transmit device parameters over the wired telephone or using a modem as in the past. As such, use of CIED data creates an opportunity for monitoring patient data in a manner previously unavailable, and relevant to this investigation, the opportunity to measure with greater precision the daily activities of patients.

In this pilot investigation, we examined the feasibility of examining frailty and mental status, as well as daily activity recorded by CIEDs, in individuals seen for routine device clinic follow-up in cardiology clinic.

Methods

Population

Between September 2017 and March 2018, we recruited 49 consecutive patients who were seen in the device clinic who were over age 65, and willing and able to provide informed consent, and willing to take part in the walk-time, survey/questionnaire assessment, or mini-Cog assessment. We had planned to examine CIED activity data for patients obtained from their respective CIED manufacturers, although we were only able to obtain data from Boston Scientific (N=9 patients) in an analyzable format.

Clinical Assessment

The outcomes measured in this investigation included daily activity obtained from CIED interrogation, clinical frailty assessment and cognitive status assessment using the 4-meter walk time (Abellan van Kan et al., 2009; Afilalo et al., 2014; Cesari et al., 2005; Studenski et al., 2011), FRAIL scale questionnaire (Malmstrom et al., 2014) (see appended), the Rockwood Clinical Frailty Scale (Newman et al., 2001; Rockwood et al., 2000) (https://www.dal.ca/sites/gmr/our-tools/c clinical-frailty-scale.html) (see appendix), and the mini-Cog cognitive status assessment (Agarwal et al., 2016; Fage et al., 2015; Heng et al., 2016; Tsoi et al., 2015). Additional information was collected at the visit, including demographic data; past medical history, focused on cardiac history; falls and fall history; medications; and relevant social history.

a. 4-meter walk: We measured a 4-meter flat surface in close proximity to the device clinic that was free from obstacles, and patients were allowed to walk along this distance at their usual pace, with the investigator timing the speed on a standard stopwatch. If they use assistive mobility devices (i.e., walkers) or supplemental oxygen at home, then were assessed while using these measures. Any time less than 5 seconds was considered normal, and longer a marker of frailty. Stopwatch timer began with the subjects first step forward and stopped upon crossing the front plane of the end line.

b. Mini-Cog assessment: The mini-Cog assessment has two components, and was conducted by a member of the research team. The subject was given, and asked to repeat, three items (apple, penny, and table). He/she was then be given a sheet of paper and pen, and asked to draw a clock face displaying the time “10 past 11 o’clock,”, along with clock numbers. He/she was then be asked to recall the three items. A pass was adjudicated as either one recall of all three items, or recall of one or two items with a correct clock drawn. The clocks will be scanned and stored with the data collection form.

c. FRAIL Scale questionnaire: Questions were asked by a member of the research team at the time of device interrogation.

d. Rockwood Clinical Frailty Scale: The Rockwood (Canadian Study of Health and Aging, CSA) Clinical Frailty Scale is a 9-point categorization scheme in which individuals are categorized by their treating provider into one of nine categories (see appended) of frailty. At the time of enrollment, patients were asked to give the name of a treating provider who knows the patient (physician or nurse) to categorize each subject.

CIED Activity Analysis

Activity time series containing daily activity measured in minutes per day was obtained for all subjects with Boston Scientific devices (N=9). For each subject, the mean, standard deviation, kurtosis, skew, minimum and maximum minutes of activity per day was calculated. A linear model was fit to identify the long-term trend, and the slope and intercept were also stored. To capture autocorrelation structure, the autocorrelation function (ACF)
and partial autocorrelation function (PACF) were collected for lags of 1, 2, 3, 7, and 14 days. To predict future activity measures at 7, 14, 30, 60, and 90 days, a seasonal autoregressive integrated moving average (ARIMA) (1, 0, 1) (1, 0, 1) 7 model was fit to each time series. The coefficients for each subjects’ model (Seasonal AR1, seasonal MA1, AR1, MA1) were also stored for analysis.

Statistical Analysis
Categorical variables were compared using a chi-square test, and continuous variables were compared using a Student’s T-test. Analysis of CIED activity data was performed using RStudio (version 1.2.5019), and other analysis was performed using Stata IC (version 16, Stata, Inc., College Station, TX).

Results
Over a period of approximately 6 months, we found that 25 of 49 patients (51.0%) over age 65 failed at least one of the frailty or cognitive assessments (Table 1). Both clinical assessments (FRAIL score and Rockwood assessment) had complete overlap with the 4-meter walk test, and no patients who were deemed frail by the FRAIL score or Rockwood assessment, or both, had a normal 4-meter walk time. There was some overlap between an abnormal mini-Cog assessment and the three measures of frailty, although six of nine patients

| Table 1. Population Demographics, by Frailty Measure. |
|-----------------------------------------------|
|                                          | *Not frail (N = 24) | *Frail (N = 25) | p value |
|-----------------------------------------------|
| Demographics | | | |
| Mean age (years) | 71.3 ± 5.5 | 79.6 ± 8.4 | .0002 |
| Female sex (%) | 7 (29.2%) | 11 (44.0%) | .282 |
| BMI | 28.0 ± 4.2 | 29.5 ± 5.7 | .3097 |
| Medical History | | | |
| Atrial fibrillation | 13 (54.2%) | 19 (76.0%) | .108 |
| Ventricular tachycardia/fibrillation | 11 (45.8%) | 3 (12.0%) | .009 |
| Heart failure | 6 (25.0%) | 12 (48.0%) | .095 |
| Hypertension | 15 (62.5%) | 22 (88.0%) | .038 |
| Coronary artery disease | 10 (41.7%) | 14 (56.0%) | .316 |
| Stroke/TIA | 3 (12.5%) | 3 (12.0%) | .957 |
| Peripheral vascular disease | 0 (0%) | 4 (16.0%) | .041 |
| Hyperlipidemia | 16 (66.7%) | 18 (72.0%) | .686 |
| Diabetes Mellitus, type 2 | 4 (16.7%) | 11 (44.0%) | .038 |
| Cancer, any type | 4 (16.7%) | 9 (36.0%) | .125 |
| Obstructive sleep apnea | 5 (20.8%) | 11 (44.0%) | .084 |
| Hypothyroidism | 6 (25.0%) | 10 (40.0%) | .263 |
| COPD | 5 (20.8%) | 5 (20.0%) | .942 |
| Chronic kidney disease | 4 (16.7%) | 9 (36.0%) | .125 |
| Falls | | | |
| Arthritis, any location | 10 (41.7%) | 13 (52.0%) | .469 |
| History of falls | 4 (17.4%) | 9 (36.0%) | .147 |
| Number of falls, past year | 1.3 ± 1.0 | 2.3 ± 1.7 | .2547 |
| Echocardiography | | | |
| LVEF | 54.3 ± 14.1 | 58.6 ± 10.4 | .2368 |
| Living situation | | | |
| Lives alone | 3 (13.0%) | 5 (20.0%) | .518 |
| > 10 medications/day | 12 (50.0%) | 19 (76.0%) | .059 |
| Device type | | | |
| Single-chamber PPM | 2 (8.3%) | 1 (4.0%) | |
| Dual-chamber PPM | 8 (33.3%) | 16 (64.0%) | |
| Single-chamber ICD | 2 (8.3%) | 1 (4.0%) | |
| Dual-chamber ICD | 10 (41.7%) | 2 (8.0%) | |
| CRT-D | 2 (8.3%) | 2 (8.0%) | |
| CRT-P | 0 (0%) | 3 (12.0%) | |
| Any ICD | 14 (58.3%) | 5 (20%) | .006 |

Note. *Frailty based on having at least one abnormal study from frailty and minicog assessment. T test used to compare continuous measures and Chi-Squared used for categorical.
Table 2. Frailty Measures.

| Metric                        | Passed | Failed |
|-------------------------------|--------|--------|
| FRAIL score                   |        |        |
| Fatigue                       | 33 (67.4%) | 16 (32.7%) |
| Resistance                    | 32 (65.3%) | 17 (34.7%) |
| Ambulation                    | 30 (61.2%) | 19 (38.8%) |
| Weight loss (>5%)             | 42 (85.7%) | 7 (14.3%) |
| Chronic illness (≥5)          | 43 (87.8%) | 6 (12.2%) |
| Total (≥2)                    | 40 (81.6%) | 9 (18.4%) |

4-meter walk time*             |        |        |
| Average (sec)                 | 3.6 ± 0.7 | 6.3 ± 1.2 |
| >5 seconds                    | 33 (67.4%) | 16 (32.6%) |

Rockwood frailty assessment** | **N = 17 |
| Average                       | 2.9 ± 1.0 | 5 ± 0 |
| >5                           | 11 (64.7%) | 6 (35.3%) |

Mini-Cog assessment            |        |        |
| Recall at least two items     | 40 (81.6%) | 9 (18.4%) |
| Clock draw                    | 42 (85.7%) | 7 (14.3%) |
| Total                         | 38 (77.6%) | 11 (22.5%) |
| Total                         | 24 (49.0%) | 25 (51.0%) |

Note. *Average 4-meter walk time among all individuals was 4.2 ± 1.4 seconds. **Average Rockwood score among all individuals was 3.6 ± 1.3.

(66.7%) had only an abnormal mini-Cog, with no frailty detected using other measures.

Patients with at least one abnormal frailty or mini-Cog assessment tended to be older (79.6 ± 8.4 vs. 71.3 ± 5.5 years), with more medical conditions and were more likely to be on over 10 medications, although fewer had a history of ventricular arrhythmias (12.0% vs. 45.8%) or an ICD implanted (20% vs. 58.3%) (Table 1). As shown in Table 2, the range of patients failing each assessment was between 18.4%, for the FRAIL score, and 35.3%, for the Rockwood Frailty assessment, with most assessments passing roughly 2/3 to 4/5 of the tests.

All but one subject in whom activity data was available via the device’s internal accelerometer had at least 1 year of data, with one subject having only 12 days of data available for analysis (Table 3). Among the various summary measures compiled, we found that patients having failed at least one assessment were more active on average (148.3 ± 63.8 vs. 100.1 ± 56.2 minutes of activity/day) and had a higher single day of activity (Activity max: 356.0 ± 69.7 vs. 194.0 ± 90.5 minutes/day) than those who passed all assessments, but also had more variability in activity across days than those who failed at least one test (Standard deviation of activity: 52.6 ± 11.9 vs. 31.4 ± 10.4 minutes/day). Time series modeling applied to the activity data did not indicate any evidence of a negative trend, or future forecasted activity at 30 or 90 days that was lower among the patients with at least one abnormal assessment, indicating that the activity in subjects determined to have increased frailty or cognitive impairment was not a reliable determinant.

Discussion

In this single-center, feasibility pilot study of subjects over age 65 seen in routine follow-up in a cardiology CIED/device clinic, who were consecutively evaluated for frailty and cognitive assessment, we found that the overall rate of frailty or cognitive dysfunction was relatively high (over 50%). A number of studies have shown feasibility for assessment of frailty using technological devices, and a number of monitors and measures are being developed to test for frailty (Hollewand et al., 2016). Hewson and colleagues used a smartphone app that processed information from a grip ball, triaxial accelerometer, and scale to develop a model for predicting frailty (Hewson et al., 2013). Dunn et al. used an accelerometer to measure activity compared with clinical assessment in liver transplant candidates and found that self-assessments and provider assessments of physical activity do not reliably indicate actual performance (Dunn et al., 2016). One study looked at the DynaPort accelerometer for measuring activity in the home, but the authors did not find acceptable sensitivity or specificity for detection of activity in frail elderly individuals (Groningen Frailty Indicator (GFI) score ≥4, ≥75 years) (Hollewand et al., 2016). In an older population with diabetes and peripheral neuropathy (age, 77 ± 7 years old), a wearable triaxial accelerometer device was predictive of activity and falls (Najafi et al., 2013).

Activity monitors have been used in CIEDs to moderate pacing to activity level (so-called “rate-responsive pacing”) for over 20 years, and have been validated against clinical measurements and external monitors by each of the major manufacturers (Garrigue et al., 2002; McAlister et al., 1989; Padeletti et al., 2006; Roberts et al., 1995), although there is less evidence for comparing these monitors against frailty or hard endpoints. Kramer and colleagues examined CIED activity measures in a remote monitoring database and found that decreased device-measured activity was inversely correlated with mortality for individuals with both ICDs (Kramer et al., 2015) and Cardiac Resynchronization Therapy (CRT) devices (Kramer et al., 2017). These initial studies provide important feasibility that activity data obtained from a CIED might provide a high-quality assessment of frailty.

Despite the limited scale of this pilot investigation, our results suggest several findings that could be useful in planning larger studies of frailty or cognitive assessment within the community of older adults with CIEDs implanted. First, although we did not do a formal reliability assessment, we found the 4-meter walk time to have the most agreement with other measures of frailty designation. It is possible that additional assessments, through use of the FRAIL scale or through contacting other treating providers for information, could potentially be avoided if this simple assessment could be performed. In our study, the 4-meter walk time was incorporated into bringing patients back to the room, and thus caused minimal interruption of the visit.
Second, type 2 diabetes mellitus and hypertension were more likely to be found among patients with markers of frailty, which is to be expected. Past studies have shown that those with hypertension is more likely to be found among frail individuals (Aprahamian et al., 2018) and that the insulin resistance found in type 2 diabetics likely confounds markers of frailty with its contributions to compromised vascular function and impaired skeletal muscle function (Assar et al., 2019). Further analysis is needed to examine the overall contributing role that each comorbidity has on frailty.

Third, we found that patients with an abnormal cognitive or frailty assessment were less likely to have an ICD implanted, despite a greater number of comorbidities and medical problems. This finding is reassuring and suggests that, at least in this population, providers are being thoughtful about weighing the impact of life-prolonging therapies in these patients. Finally, we found that use of activity information from a small number of individuals in whom the device company was willing and able to share analyzable data was not predictive of the frailty assessment results, which raises the question of whether it is worth the challenges of obtaining this data at the level in which it can be analyzed for patterns in activity over time. Interestingly, patients who were deemed frail or with cognitive deficiency had more daily activity on average than those who were not, and although the variability was higher, this result is unexpected given that daily activity is generally viewed as a marker of greater health.

It is interesting to note that there was no difference in the mean daily activity of patients with a normal or abnormal cognitive assessment (148.3 ± 31.9 vs. 100.1 ± 56.2, p = .27). While underpowered due to only nine patients being available to analyze from the Boston Scientific dataset, the patients with an abnormal frailty assessment had a standard deviation of daily activity (52.6 ± 5.9 vs. 31.4 ± 4.7 min/day, p = .03). These findings suggest that in those patients with abnormal assessments of frailty, the daily activity may fluctuate more drastically and be a greater prognostic indicator than the mean daily activity. Those who had results suggestive of frailty were more active on average and, unexpectedly, had more variability in the activity across days. This may suggest that those who are frail have an inconsistent level of activity on a day to day basis. Previous studies by Kramer et al suggested that a decrease in device measured activity was inversely correlated with mortality (Kramer, Tsai, et al., 2017). A larger, more recent study of frail patients in various settings also found that activity and frailty to be inversely related, however cardiac device data was not used to ascertain this (da Silva et al., 2019). This finding will need to be examined further with a larger dataset and with different devices.

While we hope to have demonstrated the feasibility of integrating frailty data indicators with information from ICDs, it is important to note that further studies will be necessary with larger patient cohorts to confirm the links found in this study and in others.

### Conclusion

In conclusion, in this pilot investigation we found that frailty assessment was feasible and practical within the context of a device clinic follow-up visit, and that the relatively simple measure of gait speed captured the majority of patients determined to be frail using other measures. We found that while analysis of activity time series data from CIEDs had some potential for identifying frail subjects, the specific measure identified in this study lacks any clear clinical correlation, and that practical barriers existed to obtaining this information from device companies for analysis. Further work is needed to examine the role of CIED-derived activity analysis for frailty assessment.

### Limitations

Our pilot study is limited by the sample size, as only nine patient had CIED data available for our analysis. In addition, only Boston Scientific provided the data on their devices, which limits our analysis and applicability of our data to other types of CIED. Future studies on this topic would benefit from a larger sample size across various different CIED companies.

### Table 3. Activity Summary Measures Versus Frailty.

| Measure                  | Frail | Failed mini-Cog | Failed either | None | p value |
|--------------------------|-------|-----------------|---------------|------|---------|
| Number                   | 3     | 3               | 4             | 5    |         |
| Mean activity (min/day)  | 155.1 ± 76.4 | 164.9 ± 66.7 | 148.3 ± 63.8 | 100.1 ± 56.2 | .2672   |
| SD (min/day)             | 52.6 ± 14.6 | 56.3 ± 11.2 | 52.6 ± 11.9 | 31.4 ± 10.4 | .0245   |
| Kurtosis                 | 2.9 ± 4.7 | 0.8 ± 1.0 | 2.6 ± 3.8 | 0.03 ± 1.0 | .1818   |
| Slope                    | 0.9 ± 0.9 | 0.7 ± 0.5 | 1.0 ± 0.7 | 0.3 ± 0.3 | .0977   |
| Max                      | 361.7 ± 84.2 | 361.8 ± 84.2 | 356.0 ± 69.7 | 194.0 ± 90.5 | .0218   |
| Min                      | 30.4 ± 12.9 | 38.5 ± 6.9 | 33.2 ± 11.9 | 31.0 ± 32.8 | .9004   |
| 30-day forecast          | 156.0 ± 78.7 | 165.5 ± 67.5 | 146.5 ± 66.9 | 96.6 ± 56.3 | .2628   |
| 90-day forecast          | 154.2 ± 77.8 | 162.7 ± 69.5 | 146.5 ± 65.4 | 100.9 ± 56.6 | .2975   |

Note. *p* value corresponds to t-test comparing failed any test to failed none.
Appendix 1. Frail Scale.

| Clinical Frailty Scale |
|------------------------|
| **1** | **2** | **3** | **4** | **5** |
| **VERY FIT** | **FIT** | **MANAGING WELL** | **LIVING WITH VERY MILD FRAILITY** | **LIVING WITH MILD FRAILITY** |
| People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age. | People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g., seasonally. | People whose medical problems are well controlled, even if occasionally symptomatic, but often are not regularly active beyond routine walking. | Previously “vulnerable,” this category marks early transition from complete independence. While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up” and/or being tired during the day. | People who often have more evident slowing, and need help with high order instrumental activities of daily living (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework. |

**6** **LIVING WITH MODERATE FRAILITY**
People who need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

**7** **LIVING WITH SEVERE FRAILITY**
Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).

**8** **LIVING WITH VERY SEVERE FRAILITY**
Completely dependent for personal care and approaching end of life. Typically, they could not recover even from a minor illness.

**9** **TERMINALLY ILL**
Approaching the end of life. This category applies to people with a life expectancy ~6 months, who are not otherwise living with severe frailty. (Many terminally ill people can still exercise until very close to death.)

**SCORING FRAILTY IN PEOPLE WITH DEMENTIA**
The degree of frailty generally corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal. In moderate dementia, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting. In severe dementia, they cannot do personal care without help. In very severe dementia they are often bedfast. Many are virtually mute.

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Appendix 2. Rockwood Frailty Scale.

Author’s Contribution
All authors contributed in the study.

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Availability of Supporting Data
Upon request.

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The gap between clinically assessed physical performance and actual gait speed in community-dwelling older people is a matter of concern.\(^1\) Recent studies have indicated that self-reported measures of physical activity may provide an inaccurate assessment of true physical performance,\(^2\) highlighting the need for more reliable and valid methods to evaluate physical capacity among older adults.\(^3\) To address this issue, a recent study has employed objective measures of physical performance, such as gait speed, to identify frailty in older adults.\(^4\) The results of this study support the hypothesis that gait speed at usual pace can serve as a predictor of adverse outcomes among community-dwelling older people.\(^5\) Furthermore, these findings underscore the importance of incorporating objective measures of physical function in the assessment of older adults to improve care and reduce the risk of adverse outcomes.\(^6\) It is essential to develop valid and reliable tools for measuring physical activity in frail elderly individuals to facilitate early identification of those at risk for adverse outcomes.\(^7\) The implications of these findings suggest the need for further research to validate the use of objective measures of physical performance in the clinical setting.\(^8\) Overall, these results emphasize the necessity of implementing comprehensive strategies to promote physical activity among older adults, which may help to reduce the risk of adverse outcomes associated with frailty.\(^9\) 

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