Frailty, Physical Activity, and Mobility in Patients With Cardiac Implantable Electrical Devices

Daniel B. Kramer, MD, MPH; Timothy Tsai, MPH; Poorna Natarajan, MBBS; Elise Tewksbury, RN; Susan L. Mitchell, MD, MPH; Thomas G. Travison, PhD

Background—This study aimed to demonstrate the feasibility of measuring frailty in patients with cardiac implantable electrical devices while validating the physiologic significance of device-detected physical activity by evaluating its association with frailty and mobility.

Methods and Results—Outpatients with cardiac implantable electrical devices compatible with physical activity analysis with at least 7 days of data were eligible. Office testing included frailty status (Study of Osteoporotic Fractures instrument), gait speed (m/s), mobility according to the Timed Up and Go (TUG) test (seconds), and daily physical activity (h/d) as measured by cardiac implantable electrical device. Among 219 patients, Study of Osteoporotic Fractures testing found 39.7% to be robust, 47.5% prefrail, and 12.8% frail. The mean gait speed for the cohort was 0.8±0.3 m/s, mean TUG time was 10.9±4.4 seconds, and mean activity was 2.8±1.9 h/d. Frail patients were markedly more likely to have gait speeds <0.8 m/s (OR 6.25, 95% CI 1.79-33.3). In unadjusted analyses each 1-hour increase in mean daily activity was associated with a 46% reduction of frail phenotype (OR 0.54, 95% CI 0.40-0.74) versus robust and with a 27% reduction in the odds of having the prefrail phenotype (OR 0.73, 95% CI 0.62-0.86). After adjustment this association per hour of activity persisted, with an adjusted OR for frailty of 0.71 (95% CI 0.51-0.99) and adjusted OR for prefrailty of 0.81 (95% CI 0.67-0.99).

Conclusions—Frailty and mobility limitation are common among cardiac implantable electrical device patients and are correlated to device-detected physical activity. (J Am Heart Assoc. 2017;6:e004659. DOI: 10.1161/JAHA.116.004659.)

Key Words: aging • defibrillation • pacemaker • physical exercise

Cardiac implantable electrical devices (CIEDs), including pacemakers (PM) and implantable cardioverter-defibrillators (ICDs), are the most effective treatments for serious arrhythmias. Geriatric conditions such as frailty and decreased mobility may provide synergistic information regarding outcomes for older recipients of CIEDs. Clinical frailty, commonly understood as decreased biologic reserve or resiliency, is strongly associated with adverse outcomes for cardiovascular patients. In a recent analysis frailty assessed by an algorithm derived from medical claims was identified in 10% of patients in a large nationwide ICD cohort, but to date no studies have reported more direct measurements of the frailty phenotype among individuals with CIEDs. Better tools for identifying frail patients may therefore provide opportunities for targeted testing or interventions that may improve outcomes for this challenging patient population.

Patient physical activity information is collected automatically by many CIEDs via an embedded accelerometer used to guide rate-responsive pacing. Device-specific algorithms use these data to generate estimates of time spent in activity, providing an accessible measure that may align with functional status and the burden of accumulated comorbidity. Although prior studies suggest an association between these activity measures and survival, the relationship between device-detected activity and clinical frailty or mobility measures has not been explored.

Accordingly, this study aimed to demonstrate the feasibility and utility of obtaining tractable measures of the frailty phenotype in patients with CIEDs as part of routine ambulatory care. In addition, we sought to validate the physiologic

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An accompanying Table S1 is available at http://jaha.ahajournals.org/content/6/2/e004659/DC1/embed/inline-supplementary-material-1.pdf

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significance of device-detected physical activity by evaluating its association with frailty and mobility.

Methods

Study Design and Setting
This is a cross-sectional study of patients with CIEDs followed in the ambulatory device clinic at Beth Israel Deaconess Medical Center (BIDMC), an academic tertiary care hospital in Boston, Massachusetts. Eligible subjects were identified from the device clinic appointment schedule and were approached concurrent with their visit. Verbal informed consent was obtained, and participating subjects were provided parking vouchers as reimbursement. The BIDMC and Institute for Aging Research Institutional Review Boards both approved study conduct and procedures.

Study Population
Patients with CIEDs implanted for >2 months were eligible for inclusion. Patients who were unable to provide consent due to language barriers or cognitive dysfunction were excluded. For analysis of device data, only those patients with devices capable of recording physical activity information and those with at least 7 days of device data were eligible.

Clinical Variables
Demographics (age and sex) and medical history were ascertained from electronic health records. Coronary artery disease was defined as prior percutaneous coronary intervention, coronary artery bypass surgery, or myocardial infarction. Congestive heart failure (CHF) was classified according to the New York Heart Association (NYHA) system (I-IV). Presence or absence of chronic lung disease, lower extremity peripheral arterial disease (defined as clinical claudication or prior revascularization intervention), and prior stroke or transient ischemic attack were recorded, as well as device type (pacemaker, ICD, or implantable loop recorder).

Additionally, participants’ self-rated health was obtained by asking participants to classify their overall health status as excellent, very good, good, fair, or poor.

Clinical Frailty Assessment
Clinical frailty was assessed using the Study of Osteoporotic Fractures (SOF) frailty measure, which has been validated in men and women and is predictive of falls, mobility disability, and mortality. In contrast to some other measures of the frailty phenotype commonly used in the research literature, the SOF index is intended to maximize tractability of measurement in a clinical setting, making it ideal for our design. This measure has shown strong agreement with the construct by Fried and colleagues obtained from the Cardiovascular Health Study, widely considered the research standard. We previously showed that the prevalence of prefrailty and frailty by the SOF criteria were equal to those of the more complex Cardiovascular Health Study measure in a large sample of randomly selected, community-dwelling individuals.

Components of the SOF construct include involuntary weight loss (positive response to the query “In the last year, have you lost more than 10 pounds unintentionally, that is, not due to dieting or exercise?”), lethargy (negative response to the query “Do you feel full of energy?”), and inability to perform a repeated chair stands task (moving from a seated to a standing position without use of one’s arms 5 times in succession). Individuals meeting none of these 3 criteria are considered “robust,” those meeting 1 of the 3 are considered “prefrail,” and those meeting 2 or 3 are considered “frail.”

Mobility and Gait Assessments
Mobility was assessed with the Timed Up and Go (TUG) test, which has been shown to be a reliable and valid measure in several studies. After instructed on the test, patients were timed as they rose from a chair, walked 3 m at their usual pace, turned around, walked back, and sat down. Each subject performed the TUG test twice, and the average of these 2 measurements was used in analyses.

Gait speed was measured via the 4-m walk test, which has been previously shown to predict clinical outcomes in select cardiovascular patients. Starting from a standing position, subjects were instructed to walk at their usual speed. The faster of the 2 speeds was selected for analyses as this has been previously considered reflective of usual speed after the subject has become accustomed to the experimental setting. Prevalent “slow gait speed” was defined as a 4-m gait speed less than 0.8 m/s, consistent with other investigations.

Patient Activity
Patient activity in CIEDs is measured through an integrated circuit accelerometer embedded in the pulse generator, which in applicable patients can also be used for rate-responsive pacing. The accelerometer detects both the frequency and amplitude of patient motion and translates this into a proportional electrical signal updated each minute. The specific algorithm for translating these signals into an adjudicated minute of “activity” is proprietary and may vary by manufacturer. For example, in Boston Scientific devices, force of motion of at least 25 milligravities—corresponding to an approximate walking speed of 2 mph—denotes an “active” minute. Device platforms for storing activity information vary,
but they generally track minutes per day of activity according to calendar days. Some specific models that are common in clinical practice (such as the Medtronic Adapta and Sensia pacemaker systems) do not store activity in an analyzable format, so these and similar devices were excluded from our analysis.

All activity information was directly downloaded from the applicable programmer in device clinic at the time of clinical device interrogations. For all manufacturers, the raw data files are encrypted and require translation into an analyzable format using proprietary software specific to each company. These data were then used to calculate activity in hours per day for each patient in the 30 days prior to their in-office interviews. For analyses reported here we restricted attention to participants with at least 7 days’ evaluable data.

Statistical Analysis
Summary statistics were generated for baseline demographics and clinical variables. Characteristics of patients with and without physical activity data available from their devices were compared with Student t tests and Fisher exact tests. For the analytic cohort with device data, multiple linear regression was used to determine associations between gait speed and TUG time on frailty. Logistic regression was used to assess association of slow gait speed with frailty. We then fit a multinomial logistic regression model to estimate the association between clinical frailty and device-detected activity. Age, body mass index, NYHA Class (collapsed into a binary variable comprising Class I versus Classes II through IV), and SF-12 were included in the multivariate model based on the independent strength of association with frailty or activity, theoretical plausibility, and evidence from literature review. Odds ratios (ORs) and 95% confidence intervals (CIs) were generated to quantify associations. Similarly, the association between gait speed, TUG time and device-detected activity was assessed with linear regression, also adjusted for age, body mass index, NYHA class, and SF-12 status.

Prespecified hypothesis testing of the relationships between (1) gait speed, TUG time and frailty, (2) slow gait speed and frailty, and (3) TUG time, gait speed, and frailty and activity were evaluated at the 0.05 level. Analyses were performed in R 3.3.0 using the MASS and nnet packages.21

Results
Derivation of Analytic Sample
Of 448 eligible individuals screened, 418 (93%) consented to enrollment (Figure 1). Of these, device data could be extracted for 219 patients who constituted our analytic sample. Descriptive statistics comparing patients with and without available device data are presented in Table S1. We found no significant difference in distribution of frailty phenotype, gait speed, NYHA Class, or SF-12 status among patients with device activity data compared to those lacking device activity data. There were slight differences in prevalence of coronary artery disease, congestive heart failure, and stroke/transient ischemic attack (TIA) among patients with device activity data. All enrolled patients completed the study protocol, and no adverse events were recorded.

Baseline Characteristics
The table provides summary characteristics for the analytic cohort (N=219) according to frailty status. A total of 87 (39.7%) participants were robust, 104 (47.5%) were prefrail, and 28 (12.8%) were frail. Frail individuals had a greater prevalence of cardiovascular comorbidities including CHF and preexisting stroke or TIA. Frail patients also had a greater likelihood of reporting fair or poor health (45%) than their prefrail (27%) or robust (3%) counterparts. The mean gait speed for the cohort was 0.8±0.3 m/s, and the mean TUG time was 10.9±4.4 seconds. Slow gait speed (<0.8 m/s) was more prevalent among frail patients (89%) than in prefrail (54%) or robust individuals (38%). Physical activity as adjudicated by patients' device averaged 2.8±1.0 hours overall and 3.6±2.0 hours among robust patients, with expected trends toward lower activity in prefrail (2.5±1.8 hours) and frail (1.8±1.2 hours) subjects.

Association Between Mobility and Frailty
Average gait speed in the frail group was significantly lower than that in the robust group (mean difference −0.02 m/s, 95% CI −0.33 to −0.07), but there was no significant difference in gait speed when prefrail and robust groups were compared (mean difference −0.004, 95% CI −0.09 to 0.082). TUG testing for the frail group took over 3 seconds longer on average compared to the robust group (mean difference 3.341, 95% CI 1.53-5.152), but there was no significant difference in TUG time between the prefrail and robust groups (mean difference 0.092 seconds, 95% CI −1.103 to 1.286). There was a strong association between frailty status and mobility. Frail patients were markedly more likely to have gait speeds <0.8 m/s (OR 6.25, 95% CI 1.79-33.3), but this association was not statistically significant for prefrail patients (OR 1.18, 95% CI 0.59-2.38).

Association Between Activity and Frailty
Unadjusted multinomial regression demonstrated a robust association between activity and frailty status (Figure 2), indicating that, on average, a 1-hour increase in mean daily activity was associated with a 6.25 greater likelihood of reporting fair or poor health (95% CI 1.79-33.3), while a 1-hour decrease in mean daily activity was associated with a 0.59 (95% CI 0.30-1.03) likelihood of reporting fair or poor health. This relationship was statistically significant for frail patients (OR 6.25, 95% CI 1.79-33.3) and near significant for prefrail patients (OR 0.59, 95% CI 0.30-1.03).
activity was associated with a 46% reduction of frail phenotype (OR 0.54, 95% CI 0.40-0.74) versus robust, and a 27% reduction in the odds of having the prefrail phenotype (OR 0.73, 95% CI 0.62-0.86). This association persisted after adjustment for covariates: each additional hour of activity was associated with a 29% reduction in the odds of frailty (adjusted OR 0.71, 95% CI 0.51-0.99) and a 19% reduction in the odds of prefrailty phenotype (adjusted OR 0.81, 95% CI 0.67-0.99) versus being robust.

**Association Between Mobility and Activity**

Unadjusted linear regression evaluating mobility endpoints and device-detected activity demonstrated that each hour increase in activity was associated with a decrease in TUG time of 0.83 seconds (95% CI 0.54-1.11, \( P<0.001 \)) and an increase in gait speed of 0.04 m/s (95% CI 0.02-0.06, \( P<0.001 \)). After adjustment for covariates, the relationship with TUG remained statistically significant, with a decrease in TUG time of 0.36 seconds, (95% CI 0.08-0.65, \( P=0.013 \)). The adjusted relationship with gait speed, however, was no longer statistically significant (increase of 0.02 m/s, 95% CI 0-0.04, \( P=0.09 \)).

**Discussion**

This cross-sectional study demonstrates the ease with which clinical frailty and mobility testing can be integrated into ambulatory device assessment, with high rates of enrollment and no adverse events. We found that a relatively high proportion of ambulatory CIED patients are frail, and over half manifest slow gait speed. Our analysis also provides further validation of device-detected activity as a clinically meaningful covariate with clear associations with tractable measures of function and frailty status. Device-detected activity may therefore be clinically useful for identifying patients at risk for frailty or prefrailty.

Formal measurement of geriatric conditions such as frailty, as well as physiologic measures such as gait speed, have been increasingly embedded in the care of cardiovascular patients. These measures are associated with outcomes among patients undergoing cardiac surgery, and transcatheter aortic valve replacement, and in the setting of acute coronary syndromes, and may be superior to traditional covariates included routinely in risk models. However, frailty and mobility testing have not been routinely integrated into studies of electrophysiology patients. Larger observational cohorts such as the National Cardiovascular Data Registry have been used to focus on outcomes of importance to older adults, such as hospice enrollment, but currently do not include frailty or mobility testing. Our study demonstrates the ease and safety with which such measures can be included alongside routine CIED management and provide estimates of the prevalence of frailty and average gait speed and TUG times applicable to future studies.
The results of our analysis of CIED physical activity data and frailty demonstrate that device-detected physical activity is predictive of frailty status and bolsters the potential for the use of activity data as an indicator of risk of frailty and mobility disability. This work thus builds on prior assessments of physical activity among CIED recipients, which have predominantly focused on patients with clinical heart failure and ICDs. For example, Conraads et al evaluated pooled data for 781 heart failure patients from separate clinical trials and found activity shortly after ICD implantation to be predictive of survival (hazard ratio 0.93 per 10 min/day of activity) after adjustment for clinical covariates.4 Baseline and time-varying activity predicted survival in a large nationwide ICD sample,6 and patterns of longitudinal activity have been evaluated as a marker of cardiac resynchronization therapy response. Activity has also been included alongside markers of autonomic function and arrhythmia burden in risk models evaluating heart failure events,28,29 although correlations with 6-minute walk tests have been only modestly successful.5,30 Our study thus broadens the device-detected activity population to include patients without heart failure or ICDs and strengthens the evidence supporting the physiologic importance of these measures.

The ubiquity of well-validated device-detected activity measures provides a tempting target not just for identifying

![Figure 2. Unadjusted association between activity and frailty.](image-url)
Frail patients but to improve clinical outcomes. Identifying patients whose functional trajectories may be trending toward frailty, for example, may trigger additional diagnostic testing or interventions designed to improve or preserve patients’ mobility, quality of life, and/or independence.24 Formal frailty testing of patients found to have new or very depressed activity levels may identify conditions such as incompletely treated heart failure or peripheral arterial disease. Gait speed and TUG testing (or components such as chair stands) contribute to formal assessment of frailty in some measures (such as the Fried criteria and short physical performance battery) while they also independently contribute to a fuller picture of patients’ functional status.2,31–33 Thus, for patients in whom frailty, prefrailty, or mobility limitations are identified, comanagement shared between cardiology and geriatrics may streamline care and rehabilitative efforts focused on preservation of independence.

In addition, remote monitoring, now routine for most CIED patients,34 may support tracking of individual patients’ activity trajectories without the need for in-office assessments. Importantly, frailty itself is not a fixed state but may be dynamic and potentially modifiable, with physical activity itself consistently demonstrated to be the most powerful intervention.3,26,35 The strong and significant independent association between SOF frailty assessment and mobility or mobility limitation we identified appeared to be more consequential and clinically meaningful in magnitude for the complex TUG task than for gait speed itself, which exhibited a statistically significant but modest mean difference of only 0.02 m/s between robust and frail individuals. This finding suggests that frailty status may manifest more noticeably in complex functional activities rather than in gait speed itself. Thus, linking activity measures to both frailty and mobility may not be straightforward at the individual level. However, pairing activity patterns or thresholds aligned with treatment pathways in a prospective way may be an opportunity to leverage the extraordinary amount of data being collected by patients’ devices.

Our study includes potential limitations, including the cross-sectional nature of the data collection, the convenience sampling frame, and restriction of enrollment to individuals at a single ambulatory clinic. Future longitudinal assessments of randomly selected cohorts over a more diverse geographic range will be critical in confirming generalizability of our results to the broader population of men and women with implantable devices. The activity measurements from the devices used in our study have not to our knowledge been validated against other accepted measures of activity such as omnidirectional accelerometry, and the question of whether different manufacturers’ algorithms vary from each other remains proprietary and unknown. Although evaluation of activity in a clinical setting is straightforward, because of data encryption the export of more granular data for statistical analysis requires significant cooperation from manufacturers, which may limit further studies in this area.

In summary, more than half of ambulatory CIED patients are prefrail or frail, and mobility limitations are similarly common. Device-detected physical activity is correlated with these measures and may be clinically useful for identifying patients at high risk for adverse events.

Acknowledgments

Drs Kramer and Travison had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Disclosures

None.

References

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SUPPLEMENTAL MATERIAL
**Table S1.** Characteristics at time of office testing for final cohort of patients with device data available (N = 219) compared with patients who completed the in-office testing but whose cardiac devices did not support analysis of activity data (N = 199). For covariates with categories (such as NYHA Class or device type), test statistics were generated by comparing the largest groups to each other.

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<th>Device Data Available (N=219)</th>
<th>P-value</th>
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<td>N (%)</td>
<td>N (%)</td>
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