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Dynamic factor analysis of seasonal variation in daily physical activity in individuals with heart failure and implanted cardiac devices

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ABSTRACT

Background: The purpose of the present study was to determine the presence and magnitude of seasonal variation in daily physical activity (PA) in those with heart failure (HF).
Methods: Retrospective study and dynamic factor analysis (DFA) of Patient Activity data from Medtronic implanted cardioverter defibrillator and cardiac resynchronization devices (ICD/CRTs).
Results: In a data set of 435 patients, distinct states/trends were identified by DFA including a classic, sinusoidal pattern of seasonal variation and a pattern of decline over the course of 12 months, which were associated with specific clinical characteristics. Overall, model fitting was good.
Conclusions: Those with low comorbidities, better NYHA Class, higher BMI, no hospitalization, and male sex demonstrated greater seasonal variation of at least 40 min per day between winter (lowest PA) and spring/summer (highest PA). Those with female sex and hospitalization demonstrated overall downward trajectories of approximately 40 and 80 min, respectively, over the course of the year.

Introduction

In individuals with heart failure (HF), daily physical activity (PA) is associated with many important clinical endpoints including actual and predicted mortality risk,[1–4] aerobic capacity,[1] health-related quality of life,[5–7] sympathetic nervous system activity,[8,9] hospitalization[10–13] and ability to participate in activities of daily living.[5–7] Additionally, amount of sedentary time is a better predictor of HF-related prognosis and mortality than is exercise testing.[4] Improving daily PA is therefore an important clinical outcome. However, interventions that are consistently demonstrated to be effective in objectively improving daily PA are elusive[14] as daily PA is a health behavior that is resistant to change in individuals with HF.[13,15]

Interventions for increasing PA can be directed at increasing exercise (i.e. structured PA), increasing all other activities of daily living/decreasing sedentary time (i.e. unstructured PA), or increasing total daily energy expenditure[16] (i.e. the sum of unstructured and structured PA, termed "daily PA" in the present manuscript). Similar to that found in individuals with chronic lung disease,[17–20] a potentially significant confounding factor in research studies investigating interventions to improve daily PA in individuals with HF is seasonal variation of daily PA.[21] Seasonal variation of daily PA is an increase in daily PA/total energy expenditure with warmer temperatures and greater daylight hours (spring and summer months) followed by reductions in daily PA with colder weather and less daylight (winter months), and is not limited to interventions that are conducted outside. In patients with HF, Shoemaker et al[21] observed that seasonal variation may have confounded the effect of interventions to improve daily PA due to rolling enrollment throughout the year. To our knowledge, no prior study has successfully accounted for the potentially confounding effect of seasonal variation in daily PA in studies investigating interventions to improve daily PA in individuals with HF.

Regarding the presence and magnitude of seasonal variation in daily PA in individuals with HF, there are conflicting results and different methods used between studies. There were no observed differences in a study comparing pedometer counts between different

Abbreviations: HF, Heart failure; PA, Physical activity; ICD/CRTs, Implanted cardioverter defibrillator and cardiac resynchronization devices; DFA, Dynamic factor analysis; NYHA, New york heart association; BMI, Body mass index

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groups of subjects for each season[1] or in a longitudinal study of daily PA measured using the Short-form International Physical Activity Questionnaire.[13] Two studies[22,23] using longitudinal data single-axis accelerometer data recorded from Medtronic implanted cardioverter defibrillator and cardiac resynchronization devices (ICD/CRTs) demonstrated a seasonal pattern of daily PA of 20–24 min per day. However, when adjusting for overall activity level and number of comorbidities, those who were more active (greater than 2.2 h per day) and had fewer comorbidities (8 or less) had a seasonal difference of 42 min per day vs 6 min per day for those who were inactive and had a greater number of comorbidities.[23] This suggests that there may be a heterogenous effect of season on daily PA.

The effect of season on daily PA may have implications beyond its impact on clinical trial design and interpretation. Seasonal changes in sympathetic nervous system activity (a significant component of the neuroendocrine dysfunction in HF) may increase during the winter months which may in part be responsible for increased hospitalizations during the winter months,[10–13] in addition to increased hypertension, increased rates of respiratory disease and influenza, higher depression, and pollution.[11] This was seen in various regions including more temperate climates like Brazil, but has mostly been studied in regions with colder winters and greater seasonal variations in temperature. Although Levin et al[11] observed a 30% increase in hospital admission secondary to HF during the winter months in Brazil, their study did not observe a statistically significant effect of temperature. Whether interventions to increase or preserve daily PA during the winter months results in reduced hospitalization has not been studied.

Given that seasonal variation in daily PA in patients with HF has the potential to confound clinical trials investigating interventions to improve daily PA, may account for alterations in sympathetic activity-mediated increases in wintertime hospitalizations, and has yet to be definitively established and quantified, the purpose of the present study was to: (1) more definitively estimate the magnitude of daily PA seasonal variation in individuals with HF and ICD/CRT devices, (2) identify the clinical characteristics of those who have the greatest seasonal variation in daily PA, and (3) to triangulate the results of Shoemaker et al.[22,23] using a similar sample in a different year using raw daily PA and advanced time series statistical modeling.

Methods

Study design and measure of daily physical activity

The present study was a retrospective chart review of patients in West Michigan with HF and Medtronic ICD/CRT devices. The objective was to examine the presence and magnitude of seasonal change in daily PA between November 1, 2016-October 31, 2017. The primary measurement/source of data was the Patient Activity measure from Medtronic ICD/CRT devices, which "include a single-axis accelerometer that records daily PA in one-minute increments for every minute a patient is moving at an equivalent of 70–80 steps per minute."[23] The total number of minutes of activity per day is stored in ICD/CRT device for a rolling 14-month period. Although strong correlation with and agreement between the triaxial accelerometer and Patient Activity measures has previously been demonstrated,[24] the ICD/CRT-based measure of daily PA does not account for intensity of activity.

Patient selection

Potentially eligible patients were identified by generating a list of patients with HF managed by the Spectrum Health Cardiac Device Clinic who had one of the five most common devices (Protecta, Evera, Viva, Viva Quad, and Claria MRI series models) and had an in-clinic device interrogation between November 1, 2017 and December 31, 2017. Given the rolling 14-month data storage, use of this date range would identify patients likely to have Patient Activity data for the entire one-year target sampling period. The data for these potentially eligible subjects was securely transmitted by Medtronic following execution of a data sharing agreement.

Patients were included if they: (1) had a diagnosis of HF due to ischemic or non-ischemic cardiomyopathy, (2) were New York Heart Association (NYHA) Class I-IV, (3) were managed by the health system's medical group, and (4) had a Medtronic ICD/CRT device.[23] Exclusion criteria were: (1) incomplete Patient Activity data for the entire sampling frame (November 1, 2016-October 31, 2017), (2) documented conditions that limited ambulation including wheelchair use, severe orthopedic condition, stroke or other neurologic disease, or amputation, (3) history of left ventricular assist device implantation, (4) greater than five hospitalizations for any reason, or (5) major cardiovascular or orthopedic surgical procedure during the sampling frame, including coronary artery bypass grafting, aortic aneurysm repair, joint replacement, amputation, or spinal surgery.[1]

Data collection procedures

Patient Activity data were cleaned to remove any patient who did not have complete Patient Activity data for the entire 1-year sampling frame. The remaining potentially eligible patient records were then imported into a secure web-based data collection repository.[25] The investigators then reviewed electronic medical records to determine the remaining patients who met the inclusion and exclusion criteria. If included, the investigators recorded clinical characteristics [age, sex, etiology of cardiomyopathy, NYHA Class, device type, left ventricular ejection fraction, Charlson Comorbidity Index, number and length of hospitalizations (based on local/in-system electronic health record data), and nearest weather reporting station (based on home address)].[23]

Meteorological data including daily average temperature, average wind speed, relative humidity, precipitation, and snow for the November 1, 2016-October 31, 2017 period were obtained from the Local Climate Dataset[26] and total daylight hours were obtained from the United States Naval Observatory.[27] Given that West Michigan experiences significant variations in average daily temperature (0–85°F), precipitation (0–2.5 inches), snow fall (0 to up to 30 inches), daylight (8–16 h), and wind speed (0–30 mph) over the course of a year, it was important to account for the effect of these meteorological variables in the time series analyses described below. The study protocol was approved by the health system's Institutional Review Board (Protocol #2018–187).

Statistical analysis

The Multivariate Auto-Regressive State Space package available for R Statistical Software was used to implement Dynamic factor analysis (DFA).[28,29] DFA is a type of dynamic linear model following the form presented in Zurr et al.:[30]

$$y_t = Z\alpha_t + c + Dx_t + e_t$$

The model is intended to use linear combinations and factor loadings, with offsets, to identify common underlying trends in multivariate Patient Activity time series data ($Z\alpha_t + c$), while accounting for clinical characteristics as explanatory covariates (Dx_t) error/noise (e_t). In the present analysis, DFA was used to identify common states (patterns) among different combinations of seven dichotomized clinical characteristics/explanatory covariates (therefore a total of 14 time series) along with meteorological data as covariates to help reduce/explain as much noise in the data as possible. The seven clinical characteristics (age, sex, body mass index, NYHA Class, comorbidities, hospitalization, and baseline activity level) and their associated cutoff values used in the modeling were the median values with one exception: Patient Activity was dichotomized using a previously established value of 132 min per day which differentiated between

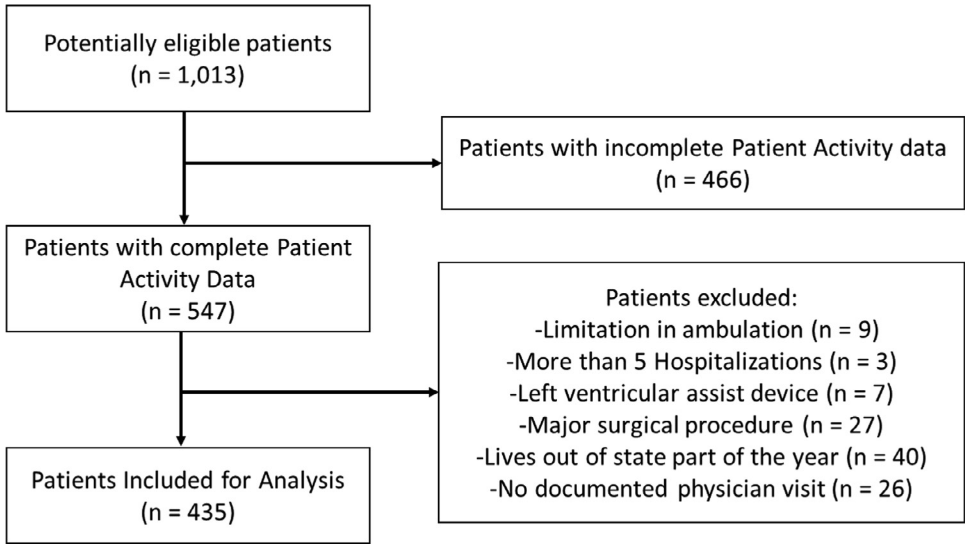

Fig. 1. Patient Inclusion/exclusion flow chart.

those with low and high levels of daily PA and which were associated with prognosis.[3] Each of the 14 time series parameters were standardized to have a mean of zero and standard deviation of one. As noted above, meteorological variables (daylight hours, average temperature, average wind speed, snow, and precipitation) were gathered from four weather reporting stations (MKG, GRR, TVC, AZO). Weather data from the closest station to each subject was used to ensure the most accurate weather data. However, the data were very similar between the four reporting stations and were therefore averaged together for each variable.

DFA models were run for a number of *m* hidden states between 2 and 5, as well as various meteorological variables as covariates. Akaike's Information Criterium was used to select the final model covariates and number of states. Varimax rotation was then applied to the fitted model to maximize the difference in factor loadings between the distinct states.

The fits obtained from the DFA models were then compared against the observed values, and the residual sums of squares were computed for each of the 14 time-series to scrutinize the model fitting. The covariance matrix of the observation error from the final fitted model was transformed into a dissimilarity matrix based upon Euclidian distance (root sum-of-squares), from which multidimensional scaling was applied to evaluate relationships in covariance amongst the 14 time-series. A Generalized Additive Model with a thin-plate spline function was applied to display the observed and fitted lines for each of the 14 time-series from the seven dichotomized clinical variables to assess model fitting and to identify the way in which each factor contributed to the underlying states. Lastly, simple non-parametric correlation coefficients (Kendall's Tau), adjusted for multiplicity using the Bonferroni-Holm method, were calculated to compare which of the hidden states correlated most strongly with the meteorological explanatory variables.

Table 1
Descriptive statistics.

	All Subjects $n = 435$	Subjects without Hospitalization $n = 368$	Subjects with ≥1 Hospitalization $n = 67$
Age	69 (11.6)	68.7 (11.8)	70.8 (10.6)
Sex (% male)	76.6%	76.6%	76.1%
BMI (kg/m^2)	31.1 (7.0)	31.0 (6.8)	31.4 (7.9)
LVEF (%)	37.1 (13.7)	37.3 (13.7)	35.3 (13.5)
Charlson Comorbidity Index (score)	2.23 (1.6)	1.9 (1.4)	3.8 (1.7)*
Charlson Comorbidity Index ≤2 (%)	62.8%	69.3%	26.9%*
Overall Activity Level (mins)	167.4 (109.5)	174.6 (111.5)	127.8 (88.2)*
Etiology (% Ischemic)	59.1%	58.4%	62.7%
Device Type (% Bi-V)	64.4%	34.5%	41.8%
NYHA-FC			
I	45.1%	47.8%	29.9%*
II	36.6%	34.0%	50.7%*
III	17.5%	17.4%	17.9%
IV	0.9%	0.8%	1.5%
Hospitalizations			
1 or more (%)	15.9%	–	–
Hospitalizations (number)	–	–	1.4 (0.78)
Length of Stay (days)	6.5 (5.9)	–	5.3 (0.65)

$P<0.05$ between patients with and without hospitalizations; Abbreviations: BMI, Body Mass Index; LVEF, Left Ventricular Ejection Fraction; NYHA-FC, New York Heart Association-Functional Class; Bi-V, Bi-Ventricular pacemaker (vs implanted cardioverter defibrillator or other pacemaker function only).

Univariate analyses with independent t tests and Chi Square were used to compare patient groups based upon relevant clinical characteristics identified by the DFA.

Results

A total of 1013 records were identified for patients with Protecta, Evera, Viva, Viva Quad, and Claria MRI series models. Of those, 547 had complete Patient Activity data for the entire one-year observation period, with 435 ultimately meeting all inclusion/exclusion criteria (Fig. 1). Descriptive statistics of the sample are provided in Table 1. A summary of the meteorological variables is presented in Fig. 2.

For the overall sample, a sinusoidal pattern was observed with a peak seasonal difference of 35.3 min per day. The lowest activity levels occurred during late December-late January (lowest average was

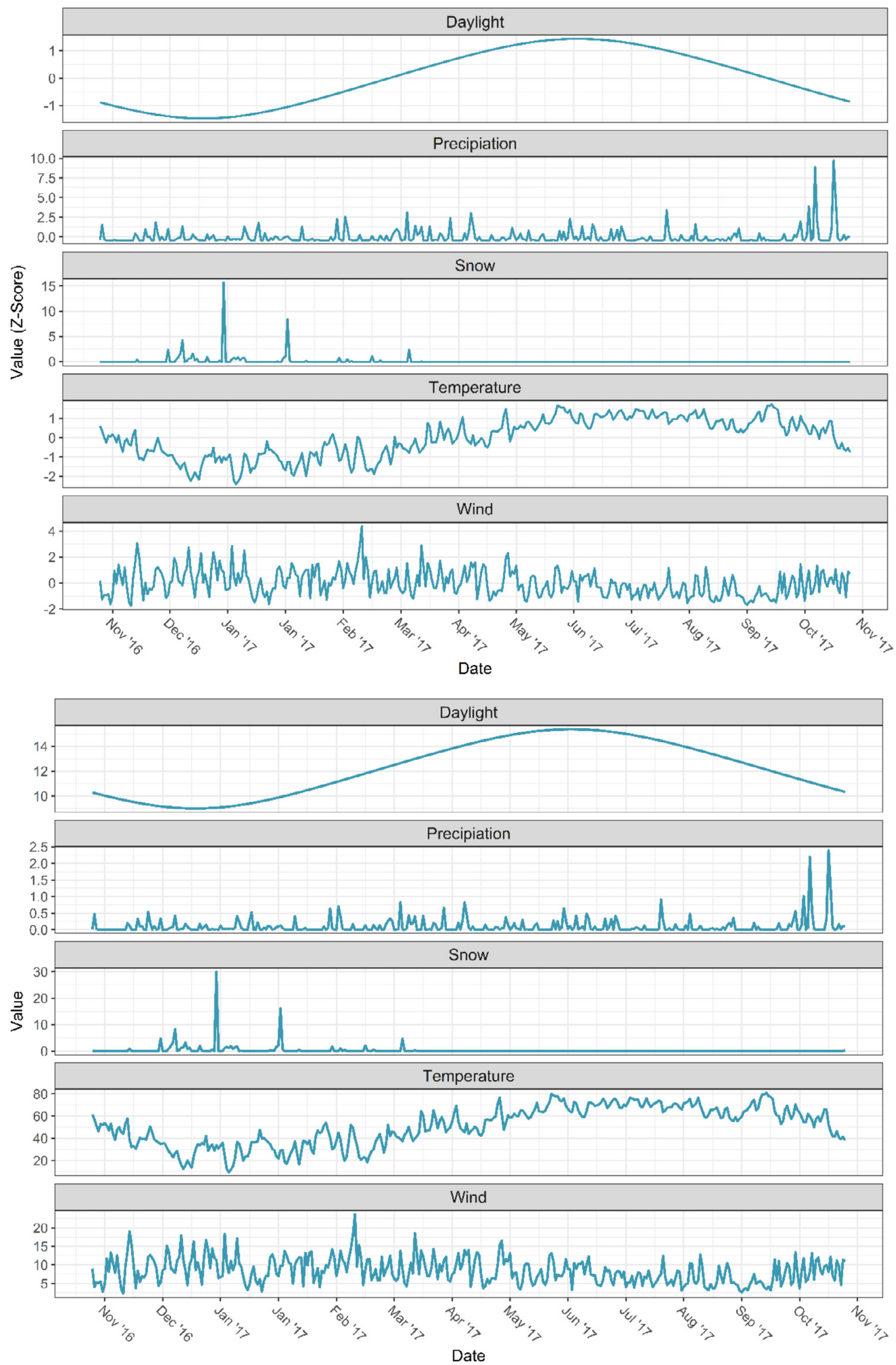

Fig. 2. Meteorological variables.
Y-axis for the upper panel uses standardized z scores; Lower panel *Y*-axis units are: Daylight (hours), Precipitation (inches), Snow (inches), Temperature (degrees Farenheit), Wind (miles per hour).

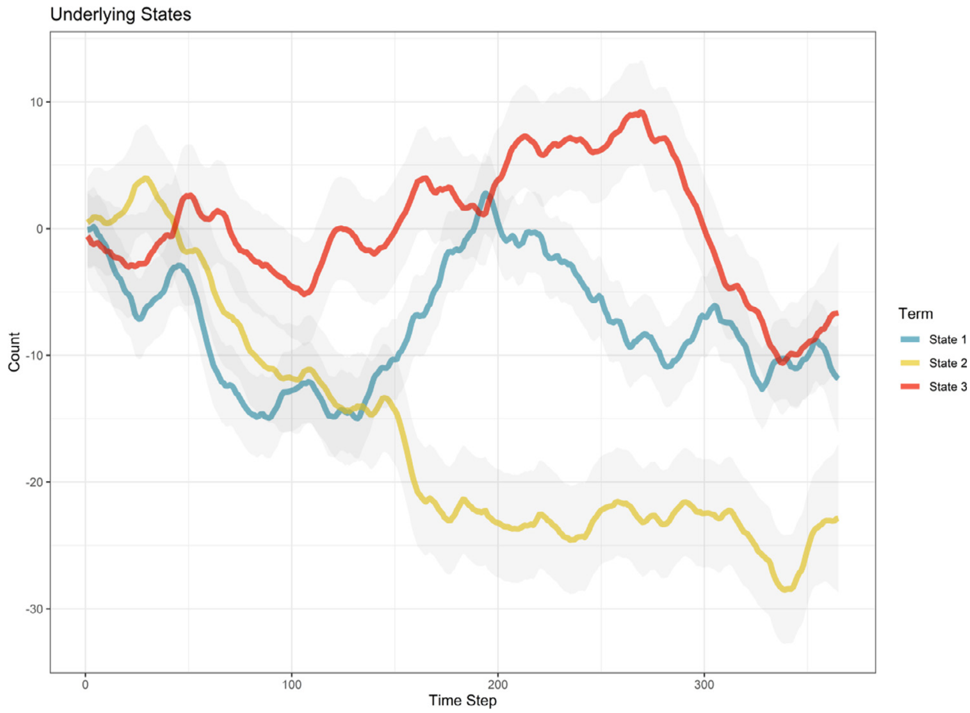

Fig. 3. Dynamic factor analysis-derived underlying states.

151.1 min per day) and the highest activity levels mid-to-late May (highest average 186.4 min/day).

DFA revealed three distinct underlying states/patterns of Patient Activity (Fig. 3). State 1 demonstrated a sinusoidal pattern of Patient Activity with the lowest activity levels in January and February, and the highest activity levels in May. State 2 demonstrated a decline in activity throughout the winter that largely stabilized in April through October but with a transient decrease in October. State 3

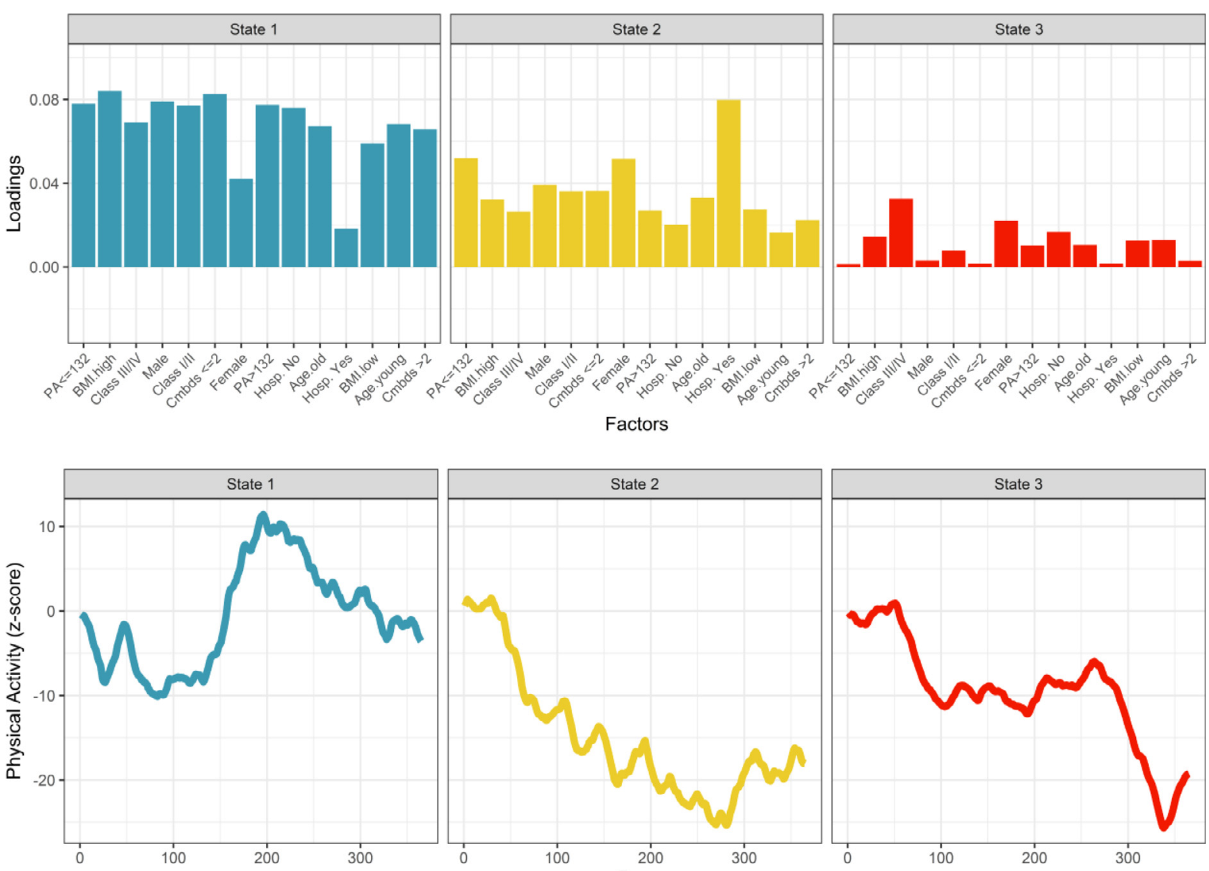

Fig. 4. Dynamic factor analysis factor loadings.

Table 2
Correlation coefficients between latent states and meteorological variables.

	Daylight	Temperature	Snow	Wind	Precipitation
State 1	0.331**	0.2337**	−0.2703**	−0.0258	−0.0454
State 2	−0.5268**	−0.4702**	0.3381**	0.1377*	0.0009
State 3	0.4301**	0.2606**	−0.1197*	−0.0217	0.0148

Kendall's Tau Correlation coefficients.
** $p < 0.01$;.
* $p < 0.05$; p-values adjusted for multiple testing using Bonferroni-Holm adjustment.

demonstrated a sinusoidal pattern similar to State 1 but with less of a decline in the winter and a peak in July.

Factor loadings for the three distinct states that emerged with Varimax rotation are presented in Fig. 4. For State 1, the contributions to the model were fairly similar for all factors/clinical characteristics except female sex and hospitalization. The model for State 2 was predominantly influenced by hospitalizations, female sex, and low overall activity level. The model for State 3 contains no time series with factor loadings greater than 0.4, and it is speculated to be most useful as a linear combination with States 1 and 2.

Given that States 1 and 2 were the most different, especially in regard to hospitalization, univariate analyses were used to compare clinical characteristics of patients with and without hospitalizations (Table 1). Those individuals with hospitalizations had significantly greater comorbidity, lower overall activity level, and disproportionately fewer individuals with NYHA Class I HF.

Assessment of the simple correlation coefficients and evaluation of multidimensional scaling also reveal a unique pattern within the model structure. Regarding the influence of meteorological variables on daily PA models (Table 2), there were strong positive correlations between the daylight and temperature covariates and State 1 and a negative correlation between snowfall and State 1. This pattern appears to be inverted when looking at correlations with State 2, with negative correlations with daylight and temperature, and a positive correlation with snowfall.

Multidimensional scaling (Fig. 5) revealed stark clusters of similar covariance patterns between the 14 different time series of Patient Activity based on dichotomized clinical characteristics. Low comorbidities, low NYHA Class, low BMI, non-hospitalized, young age, and male sex time series illicit a cluster, meaning that the Euclidian distance between these time series is small, and they share similar observation errors within the model. By contrast, the time series representing the PA of individuals who were older, hospitalized, high comorbidities, and low overall physical activity created a looser cluster but still indicate that these time series also share similarities in their observation errors within the model. Lastly, the time series representing the physical activity of females and NYHA Class II/IV show very little similarity of observation errors to other factors/clinical characteristics.

Similarly, the time series for the female and hospitalized factors/clinical characteristics have the highest factor loadings in State 2 and the highest sums of squares error (Fig. 4 and Table 3) indicating that the model fit more poorly relative to the others. The time series representing the median Patient Activity of non-hospitalized, low comorbidity, high physical activity, and male individuals yielded the lowest sums of squares error, indicating, at least superficially, a better model fit when compared to the other time series.

In considering the fit of the DFA modeling for each factor/clinical characteristic (Fig. 6), each factor had considerable variability but overall good fitting of the models. In consideration of the way in which the magnitude of seasonal variation in daily PA may be impacted by each clinical characteristic, low comorbidities, low NYHA Class, higher BMI, non-hospitalized, and male sex each demonstrated greater seasonal variation/sinusoidal wave heights of 40–80 min per day. Fig. 6 also demonstrates, as previously noted, individuals with hospitalization declined in activity over the course of the year.

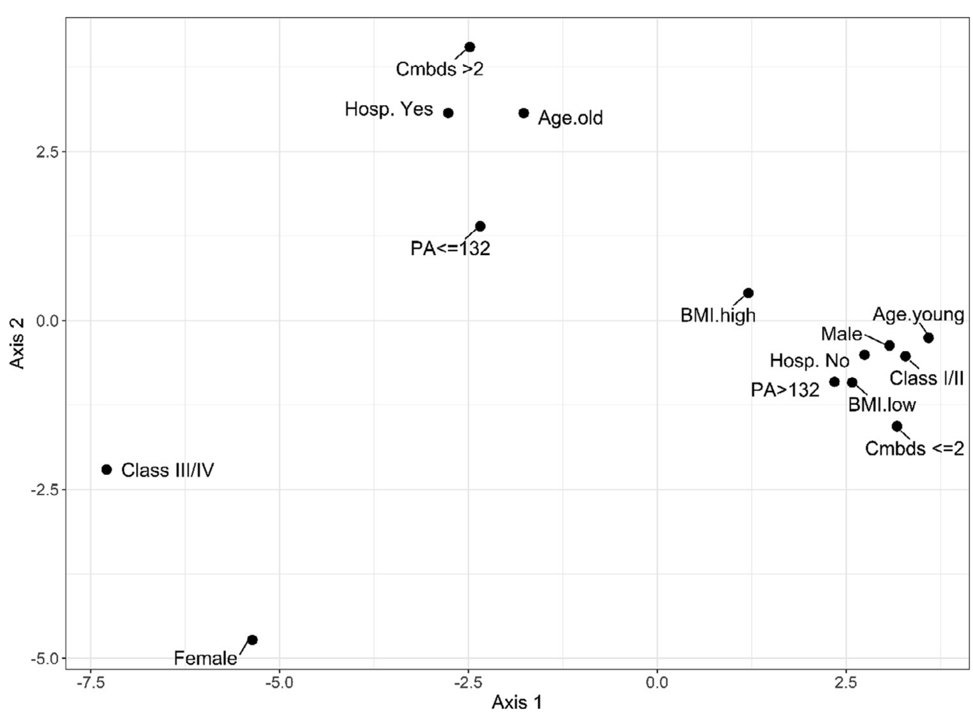

Fig. 5. Multidimensional scaling of covariance matrix.
Converting the covariance matrix to a dissimilarity matrix and applying multidimensional scaling, allows for the visualization of interactions in variability between the clinical characteristics not captured by the states identified in Dynamic Factor Analysis. Points in close proximity indicate high correlation and therefore a large amount of shared information not captured by the states or the associated explanatory variables.
PA, Patient Activity; BMI, body mass index; Hosp, hospitalizations; Cmbds, Comorbidities measured by the Charlson Index.

Table 3
Factor loadings and sum of squares for fitted model.

	Factor Loadings			Sum of Squares		
Time-Series	State 1	State 2	State 3	$\sum_t y_{it}^2$	$\sum_t e_{it}^2$	$1-(\sum_t e_{it}^2/\sum_t y_{it}^2)$
Male	0.078	0.039	0.004	364	138.193	0.620
Female	0.041	0.052	0.024	364	242.761	0.333
Class I/II	0.076	0.036	0.009	364	140.288	0.615
Class III/IV	0.067	0.026	0.033	364	199.738	0.451
Hosp. No	0.075	0.020	0.018	364	136.849	0.624
Hosp. Yes	0.018	0.080	0.002	364	214.930	0.410
Cmbds <=2	0.082	0.036	0.003	364	148.553	0.592
Cmbds >2	0.065	0.022	0.004	364	190.826	0.476
PA<=132	0.077	0.052	0.002	364	161.627	0.556
PA>132	0.077	0.027	0.011	364	143.452	0.606
Age.young	0.067	0.016	0.014	364	177.172	0.513
Age.old	0.066	0.033	0.011	364	174.606	0.520
BMI.low	0.058	0.027	0.013	364	166.192	0.543
BMI.high	0.083	0.032	0.016	364	145.783	0.599

PA, Patient Activity; BMI, body mass index; Hosp, hospitalizations; Cmbds, Comorbidities measured by the Charlson Index.

Discussion

The present study sought to triangulate previous research findings on seasonal variation in daily PA in individuals with HF using DFA, a more advanced, comprehensive statistical analysis approach for time series data. DFA holds a unique place in time series analysis, in that it allows for a thorough examination of autoregressive multivariate data while allowing consideration for explanatory variables. Moreover, it can serve to address and simplify the high dimensionality of multivariate time series. This allows researchers to answer the question "What is going on?" when simultaneously comparing multiple time series.[30] Using this approach, we were able to triangulate the presence and magnitude of seasonal variation of daily PA while providing insight into the clinical characteristics that influence the extent to which season impacts daily PA.

Presence and magnitude of seasonal variation

The present study reveals seasonal variation with an average difference of 35.3 min per day with lowest activity levels during late December to late January and highest activity levels in mid to late May. With regard to the magnitude and timing of seasonal variation, these results for the overall sample are similar to previous studies. In a small pilot study of 18 patients,[22] daily PA was lowest in January/February, highest in July and October, with a difference of 18–22 min per day. In another larger sample of 168 patients,[23] the lowest levels of PA occurred in February, the highest levels occurred during June, with a difference of 24 min per day.

Association between clinical characteristics and seasonal change in daily PA

The present study provides several novel observations about the way in which clinical characteristics and meteorological variables influence seasonal variation of daily PA in individuals with HF. First, those with male sex, low comorbidities, higher baseline daily PA, no hospitalizations, and a lower (better) NYHA Class demonstrated a seasonal, sinusoidal pattern of daily PA. This is based upon the multidimensional scaling, correlations, and factor loadings which identified this population as those who were associated most strongly with State 1. This is similar to findings of a previous study[23] where individuals with higher baseline activity and fewer comorbidities had the greatest seasonal variation. That study, however, used a more basic statistical approach not ideally suited for time series data while accounting for various combinations of clinical characteristics or controlling for meteorological data. The present study used a larger sample size and a more robust statistical approach and thus defines a population expected to be most prone to seasonal variation in studies of daily PA.

A second novel observation made by the present study is that different combinations of clinical characteristics may influence seasonal variation in more complex ways than just simply obtunding the magnitude of seasonal differences. Indeed, States 2 and 3 suggest two

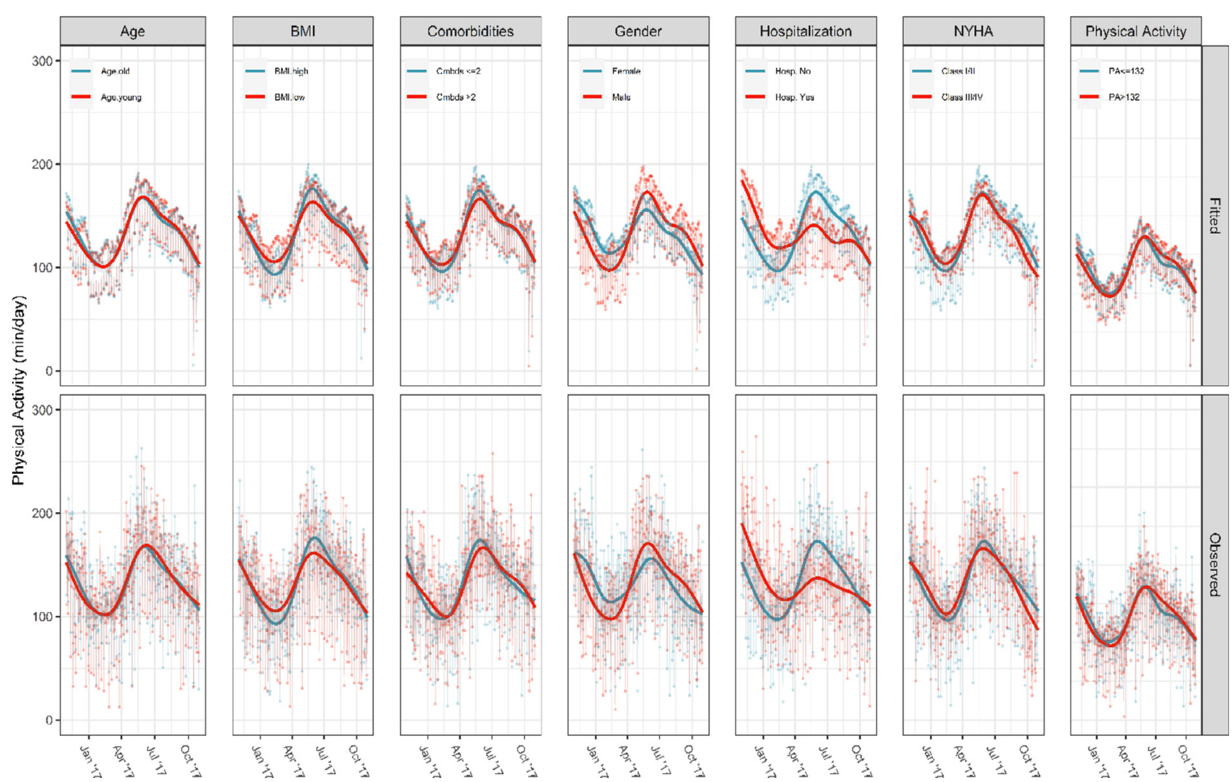

Fig. 6. Dynamic factor analysis for fitted estimates vs observed values for each of the 14 factors.

other patterns of daily PA over the course of a year: One which demonstrates a decline over the course of a year with a slight rebound in the Fall (State 2), and another which demonstrates a stepwise decline (State 3). Regarding State 2 and a pattern of declining daily PA over the course of a year, previous research is conflicting. One previous study failed to find evidence of decline in daily PA using cluster analysis, however, that study did not utilize activity data from a single year for all subjects which precluded the use of season, meteorological data, and varying combinations and clinical characteristics for identifying patterns in the time series data.[3] However, another observed that those individuals with greater comorbidities declined by 20 min per day over the course of the year.[23]

In the present study, DFA modeling for each factor/clinical characteristic (Fig. 6) revealed that those with female sex and hospitalization demonstrated overall downward trajectories of approximately 40 and 80 min, respectively, over the course of the year. Indeed, individuals characterized by State 2 were those with female sex, low baseline daily PA, and those who were hospitalized. Twenty three of the 59 patients who were hospitalized had their first stay during the first four months of the observation period (during the winter), and therefore might account for a failure to recover or continue decline in daily PA, especially those 17 subjects who had multiple hospitalizations. However, it is unclear why the present study failed to replicate the Shoemaker et al.[23] results with regard to comorbidities, although it may be due to the fact that the 2019 study used a simple count of comorbidities and the present study used the Charlson Comorbidity Index. It also is important to note that DFA point-estimates are calculated as linear combinations of all latent states. Therefore, the presence of an obscure state may not necessarily represent any meaningful clinical trend independently, but rather reduce model variation synergistically while in concert with other states.

Regarding State 3, it can be noted that the apparent pattern in Fig. 3 is different than in Fig. 4. The reason for this difference is that Fig. 4 reflects the results of varimax rotation which was performed on the factor loadings to maximize the differences between states. This is common procedure and allows for easier interpretation in discussing differences in factor loadings between states. Characterizing the individuals represented in State 3 is difficult as the factor loadings for clinical characteristics are quite low.

Relationship between meteorological variables and daily PA

A fourth novel observation made by the present study was in regard to the apparent disparate relationship between meteorological variables and daily PA states identified by DFA. The primary purpose of the present study was not to examine this relationship as this has been well-studied in the elderly and reported elsewhere,[31–34] where temperature and daylight appear to drive the seasonal differences in daily PA. Rather, inclusion of meteorological variables was used to help reduce noise in the data by controlling for these variables, and the associations analyzed were between meteorological variables and the time series patterns (i.e. the States), not directly with daily PA. However, some findings regarding the meteorological variables are worth noting and may be hypothesis-generating. For example, the final fitted DFA model minimized AIC with a binary weekend variable, daylight, temperature, and precipitation values as explanatory variables. Yet, precipitation does not correlate with any of the latent states. It may be that precipitation's effect on daily PA is not apparent when considering daily PA over the course of a year, but may be important to control for when measuring daily PA during shorter time frames (1 to 2 weeks).

Implications for future research and clinical practice

Given that clinically meaningful changes in daily PA are approximately 1 h,[2] changes of up to 80 min per day that result from season alone could significantly exaggerate or mask treatment effects depending on the timing of baseline and follow-up measurement of daily PA. This has relevance for both clinicians and researchers for considering and/or controlling for the confounding effect of season (e.g. daylight and temperature). This is especially true for those subjects/patients characterized by State 1 (male sex, low comorbidities, higher baseline daily PA, no hospitalizations, and a lower (better) NYHA).

As noted above, sympathetic activity-mediated increases in wintertime hospitalizations may be associated with wintertime reductions in daily PA. However, given that those who declined over the one-year period were characterized by having one or more hospitalizations, it is unclear whether lower daily PA is a cause or consequence of hospitalizations, or whether there are other significant confounding variables not accounted for in the present paper. Clinically, these individuals comprising State 2 may be the more important individuals to further study and understand as they may also have the overall worse clinical outcomes and may need the most intensified medical management. It is not clear whether these individuals are good candidates for clinical trials investigating interventions to improve daily PA (i.e. whether daily PA be refractory to intervention or whether it would result in improved clinical outcome).

Limitations

The present study overcame several limitations of similar prior studies in that it had a significantly larger sample size, used the raw daily Patient Activity data (vs. weekly averages or visually estimated bi-monthly averages), and used advanced statistical techniques to account for the influence of a variety of variables on time series data modeling. There are, however, several limitations. First, the DFA model was performed by sub-setting the same sample of subjects into dichotomous time series. While the initial sample of subjects was quite large, and the utility of DFA quite flexible, any assumption of independence between these 14 time-series cannot be assured. Additionally, due to the nature of 14 time series data used by DFA, individual variability of daily PA may be ignored as the daily PA over time is averaged in each category of demographic characteristics. However, assessing changes in PA at the individual level was not a focus of this analysis. Rather the intent was to integrate a novel analysis method to better understand the overall temporal trends in an aggregated patient population. Therefore, by examining the median PA levels for each of the 14 time series, we can gain greater insight as to the effects of meteorological variables and temporal evolution of PA in conjunction with one another. Therefore, the results of this analysis do not reflect the change in PA over time for one individual, but a large sample of similar individuals. Future work could focus on tailoring this analytical approached to examine individual variability more closely.

Second, although the meteorological data from each station were similar, averaging the meteorological data from each station may have resulted in missing important associations meteorological variables, daily PA, and clinical characteristics. Further, the results may not be generalizable to individuals living in different climates or individuals with HF without ICD/CRT devices.

Given that hospitalization emerged as a clinical characteristic that appeared to have an influence on seasonal variation in daily PA, a third limitation of the present study is that we were unable to account for hospitalizations that did not occur within the large regional quaternary care health system in which the study was conducted.

A fourth potential limitation was the use of the median to dichotomize BMI and the CCI, rather than slightly different and more clinically relevant cut-offs of < 25 kg/m^2 and score of ≥ 4,[35–39] respectively. The clinically relevant cut-offs would have resulted in a smaller group size that may have been less robust/more prone to outliers. Despite this risk, performing DFA with the more clinically relevant cut-offs resulted in nearly identical results. However, presentation and interpretation of those results is significantly more complex and less intuitive and therefore not presented in the present paper.

Lastly, because the present study was a retrospective study, we could not account for extended periods of travel to regions with a different climate for extended periods of time if there was not evidence in the clinical documentation of such travel.

Conclusions

Seasonal variation in daily PA is present in some individuals with HF and ICD/CRT devices, where those with low comorbidities, low NYHA Class, higher BMI, no hospitalization, and male sex demonstrated greater seasonal variation of at least 40 min per day. However, those with female sex and hospitalization demonstrated overall downward trajectories of approximately 40 and 80 min, respectively, over the course of the year. Accordingly, clinicians and researchers using interventions to improve daily PA should account for seasonal variation and should determine whether those individuals who are at risk for decline should be studied separately and whether they are able to improve in daily PA to prevent hospitalizations and/or decline in daily PA.

Declaration of Competing Interest

None.

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