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Discrepancy between wrist actigraph and polysomnographic measures of sleep in patients with stable heart failure and a novel approach to evaluating discrepancy

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Summary

Wrist-actigraphy is often used to measure sleep characteristics in a variety of populations, but discrepancies between actigraphic and polysomnographic measures have been noted in populations experiencing poor sleep quality. The purpose of this study is to examine the discrepancy between these measures and risk factors for discrepancy in people with heart failure (HF) using a novel index. We used sleep measures simultaneously recorded by actigraphy and polysomnography and clinical data from a cross-sectional study of 155 HF patients [age = 60.5(16.1) years; 65.2% male] recruited from evidence-based HF disease management programs. The discrepancy and consistency between the two measures were evaluated with Bland-Altman plots, intra-class correlations, and a newly developed index that represents activity counts in wake episodes. Overall, participants had short total sleep time [327.7(95.9) mins] and poor sleep efficiency [71.3(16.0) %] on polysomnography. The discrepancies between sleep measures were small in patients less than 60 years old, and there was excellent consistency (intra-class correlation = 0.81), compared to older patients who had poorer consistency (intra-class correlation = 0.53) on total sleep time. Higher daytime motor activity, poor sleep quality, and more severe insomnia were associated with smaller discrepancies in older, but not younger patients, and associations were more sensitively detected by the new index. These findings suggest the importance of aging, disability, and comorbidity that may influence motor activity from which sleep estimates are scored with actigraphy. The new index may be useful in identifying factors associated with the correspondence between actigraphy and polysomnography.

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Keywords

actigraphy; polysomnography; sleep; insomnia; heart failure; discrepancy

Introduction

People with chronic conditions often have disturbed sleep that may contribute to worsening disease, sleep-related symptoms, and decrements in function and quality of life. There is a need for interventions focused on improving sleep that are based on detailed understanding of multiple characteristics of sleep (e.g., timing, duration, sleep quality) during everyday life using accurate measures. While polysomnography (PSG) conducted in laboratory settings is the gold-standard for sleep measurement, it is expensive, intrusive, and difficult to conduct in ambulatory settings. Wrist-actigraphy (ACT) is more feasible in naturalistic environments and frequently used in patients with cancer, heart disease and other prevalent chronic conditions who often have very fragmented sleep secondary to primary sleep disorders, symptoms, disease treatment-related, and advancing age. However, ACT is generally less accurate among people with very fragmented sleep. For example, ACT yielded good to high Pearson correlations (r) with PSG for total sleep time (TST) ($r = 0.79 - 0.92$) among people with good quality sleep, but ACT generally over-estimates sleep time and under-estimates wake time, leading to lower levels of agreement for sleep outcomes that are more strongly dependent upon correct identification of wake, such as sleep onset latency ($r = 0.64 - 0.82$), sleep efficiency ($r = 0.39 - 0.87$) and wake after sleep onset ($r = 0.36 - 0.37$) (Van de Water et al., 2011). Recent data from the MrOs study indicate, as in several other studies, that ACT may over-estimate TST in people with insomnia and under-estimate it in people with sleep disordered breathing (Blackwell et al., 2011).

Given the differences between ACT and PSG in methods of sleep detection (PSG: electrophysiological changes, vs. ACT: motor activity), individuals' patterns of motor activity may influence ACT recordings and detection of wake, when scored using standard sleep algorithms. These variations may be associated with restlessness during sleep associated with nocturnal symptoms or sleep disorders such as periodic limb movements during sleep, sleep disordered breathing (Laakso et al., 2004, Wang et al., 2008) or lower motor activity during wake that is presumed to occur in people with insomnia (Lichstein et al., 2006, Taibi et al., 2013, Blackwell et al., 2011). However, comorbidity, functional disability, aging, or depressed mood, characteristics common to patients with chronic medical disorders, may also contribute to motor activity, the metric used to derive ACT sleep measures, but to our knowledge, the influence of these factors has not been systematically examined in people with serious chronic conditions.

People who have chronic HF have poorer sleep than healthy controls (Redeker and Stein, 2006) and often have sleep fragmentation associated with sleep disordered breathing, (Redeker et al., 2010b) insomnia (Redeker et al., 2010a), nocturnal symptoms, such as nocturia (Redeker et al., 2012), the disease process, comorbidity, and medical treatment. Although measurement of sleep in naturalistic environments is critical to understanding sleep in people with chronic conditions, including people with HF, and a number of studies

have employed ACT to measure sleep in these patients in naturalistic environments, few have addressed the concordance or discrepancy with PSG or the factors that that may contribute to it in HF patients or other groups with serious chronic medical conditions accompanied by comorbidity.

The purposes of this study were to: 1) evaluate the concordance or discrepancy between ACT and PSG in a group of adult patients with stable HF, a group selected because of overall poor sleep quality and the multi-factorial nature of sleep fragmentation and general levels of functional compromise; 2) examine the factors that contribute to concordance or discrepancy; and 3) propose a novel approach to evaluate the discrepancy between these measures and its correlations with the risk factors.

Methods

Study design and Sample

This study was performed with the data extracted from a cross-sectional study conducted to assess the contributions of sleep disorders to daytime symptoms and functional performance in patients with stable HF who were recruited from evidence-based HF disease management programs. In this sample, approximately half of the total sample (N = 173) had significant sleep disordered breathing (Redeker et al., 2010b) and half had insomnia symptoms that were not explained by sleep disordered breathing (Redeker et al., 2010a). We previously reported the associations between sleep disordered breathing, insomnia, daytime symptoms and function (Redeker et al., 2010b, Redeker et al., 2010a, Jeon and Redeker, 2016) and the associations between nocturia and sleep (Redeker et al., 2012). This study was approved by the IRB, and all participants provided written informed consent.

A total of 173 participants who were 18 years of age or older and had stable chronic New York Heart Class I-IV HF (NYHA Classification) with either reduced or preserved ejection fraction were recruited from five HF disease management programs in the Northeastern United States between the years 2003 and 2007. To assure broad variability in sleep characteristics, patients were selected regardless of whether they had complaints about sleep, and no participants had previously completed a focused sleep evaluation. Detailed inclusion and exclusion criteria were previously reported (Redeker et al., 2010a).

Variables and Measures

Sleep—We obtained objective measures of sleep with wrist ACT and unattended PSG collected for one night in participants' homes. PSG data were collected with the Safiro (Compumedics, Inc., Charlotte, NC), miniaturized sleep recorder. A trained registered polysomnographic sleep technologist visited patient's homes and applied the sensors, programmed and turned on the device, and returned in the morning to remove the sensors and retrieve the equipment. Sleep/Wake status and sleep stages were scored manually with Rechtschaffen and Kales criteria using 30-second epochs, and the apnea hypopnea and respiratory disturbance indices were also computed with standard methods. Inter- and intra-rater reliability of the PSG scoring was acceptable (Redeker et al., 2010b).

The Actiwatch-64 (Respironics Mini Mitter, Inc., Bend, OR) wrist-actigraph was used to collect 24-hour activity (activity counts/minute) over 3 days and the night on which the PSG was conducted, but only the ACT data on the night of the PSG were used in the current analysis. We computed standard sleep variables [nocturnal total sleep time (TST), sleep efficiency (SE), sleep latency (SL), and wake after sleep onset (WASO)] with the Actiware Sleep V5 program (Respironics Mini Mitter, Inc., Bend, OR), using standard methods. We used the medium sensitivity setting and the default scoring algorithm to evaluate the data that were collected in one minute epochs. We used event marker recordings and sleep diary entries to indicate lights out times, bed times, and rising times in preparing the data for analysis. We computed the average motor activity count/minute during the time from lights out to rising time in the morning and over the course of the day as defined by the interval that did not include the primary sleep interval. We also computed activity counts per minute during nighttime wake episodes by dividing the total activity counts during the time in bed by the polysomnographic WASO.

We administered the Pittsburgh Sleep Quality Index (PSQI), a reliable and valid self-report instrument (Buysse et al., 1989) to measure habitual global sleep quality and the component scores, as well as the raw sleep duration and sleep latency items in the analyses. We elicited symptoms of insomnia using questions from the Sleep Habits Questionnaire (SHQ) (Baldwin et al., 2001). Insomnia symptoms were measured by a total score, calculated from the items on difficulty initiating sleep, maintaining sleep, and awakening too early in the morning (DIMS).

Daytime Symptoms and Function—Because of our interest in the extent to which mood (i.e., depression), sleepiness, and functional status might influence the correspondence between ACT and PSG, we included the Center for Epidemiological Studies Depression Scale (CESD) (Radloff, 1977) which has good reliability (Cronbach's $\alpha = 0.89$) in the current sample (Redeker et al., 2010a). A score higher than 16 indicates the likelihood of clinically significant depressive symptoms (Lewinsohn et al., 1997). We also used the Epworth Sleepiness Scale (ESS), a self-report measure of sleepiness (Johns, 1991), that had a Cronbach's α of 0.78 in our study (Redeker et al., 2010a).

The Six-minute walk test (SMW), a measure of distance walked in 6 minutes in the clinical setting (Guyatt et al., 1985) was used as an objective measure of functional performance. Description data obtained from this measure was previously reported (Redeker et al., 2010a).

Clinical and Demographic Characteristics—We obtained clinical and demographic data by self-report and medical record review. We used the New York Heart Association Functional Classification and left ventricular ejection fraction, and computed the Charlson Comorbidity Index. (Charlson et al., 1994).

Wake After Sleep Onset (WASO) and nighttime activity counts—Awakenings with lack of movement that are not detected by ACT may be responsible for the discrepancy between ACT and PSG measures, given that ACT metrics are computed from motor activity counts. The graph in Figure 1-A shows the curvature correlation (solid line) between actigraphic WASO ($WASO_{ACT}$; circle A' and B') and the log-transformed nighttime activity

count. Polysomnographic WASO ($WASO_{PSG}$; circle A and B) would be far from the curve as more wake episodes have low activity counts. The discrepancy between $WASO_{ACT}$ and $WASO_{PSG}$ (A and B) would be equivalent with the C_N , which is the distance between observed nighttime activity counts (C_O) and expected nighttime activity counts (C_E) under hypothesizing no discrepancy. We propose the C_N as a new discrepancy metric and more details are described in Appendix A. Correlations between the two discrepancy measures (i.e. $WASO_{ACT} - WASO_{PSG}$ and C_N) and WASO can be mathematically calculated (Appendix B).

Data Analysis—Descriptive analysis was performed on the demographic, clinical, and self-reported data and the PSG and ACT sleep characteristics. The discrepancy and concordance between ACT and PSG measures of total sleep time (TST in minutes), sleep latency (SL in minutes), sleep efficiency (SE in %), and wake after sleep onset (WASO in minutes) were evaluated for all participants and separately for the dichotomized age groups (< 60 vs. ≥ 60 years of age). Bland Altman plots (Bland and Altman, 1986) were used to describe the discrepancies between ACT and PSG measured sleep variables. The discrepancy was examined using paired t-tests, and the consistency was evaluated with intra-class correlation coefficients (ICCs).

We calculated C_N , the discrepancy measure, by subtracting the observed nighttime activity count (C_O) from the expected nighttime activity counts (C_E) from the general linear model (GLM) of the log-transformed nighttime activity count regressed on $WASO_{ACT}$. To assess factors that might contribute to the discrepancies, we calculated correlations between the discrepancy and C_N and demographic and clinical characteristics including age, comorbidity (Charlson Comorbid Index; CCI), sleep quality, insomnia symptoms, depressive symptoms, sleep disordered breathing (respiratory disturbance index), Six-minute walk (SMW), daytime sleepiness (ESS), and daytime activity counts. We did not include SL or SE in the calculation of the discrepancy measure because generally SL has poor validity as an actigraphic measure, and SE is somewhat redundant with WASO and SL.

To understand the associations between motor activity and wakefulness, we also computed correlations between the average activity counts during the nighttime wake intervals and potential clinical and demographic risk factors for the discrepancy. For those variables that were significantly correlated, we also assessed their correlations separately in two age group (< 60 and ≥ 60 years of age). We also used a parsimonious multivariable model to predict C_N using a GLM with stepwise selection.

To compare the correlations between the discrepancy and C_N with $WASO_{PSG}$ and $WASO_{ACT}$, we simulated the correlations in different scenarios using the formulas in the Appendix B. The correlations were calculated based on the sample means ($WASO_{PSG} = 100.1$ and $WASO_{ACT} = 56.7$) and the sample correlation between $WASO_{PSG}$ and $WASO_{ACT}$ ($r = 0.245$) with ranges of standard deviations (SD) for $WASO_{PSG}$ (SD ranged from 40 to 80) and $WASO_{ACT}$ (SD ranged from 20 to 60).

Results

Out of 173 participants in the parent study, we included 155 participants who had simultaneously collected ACT and PSG recordings. Descriptive statistics for the demographic, clinical, polysomnographic and actigraphic sleep variables are presented in Table 1. The sample of 155 includes 101 (65.2%) male and 100 (65.4%) white patients with a mean age of 60.5 (16.1) years and mean BMI of 30.6 (29.5). Forty percent of the participants were classified as having NYHA functional classification class III ($n = 53$ (34.2%)) or IV ($n = 10$ (6.5%)), and the average left ventricular ejection fraction (%) was 32.9 (15.4).

Approximately half of the participants (51.0%) reported insomnia symptoms. The mean CES-D of 17.1 (15.0) and global PSQI of 8.7 (8.0) were greater than the respective clinical cutoffs of 16 and 5, indicating significant depressive symptoms and poor sleep quality. The mean ACT measures of TST (378.6 mins vs. 327.7 mins) and SE (80.0% vs. 71.3%) were higher than those measured with PSG, and the ACT measures of SL (20.9 mins vs. 30.2 mins) and WASO (56.7 mins vs. 100.1 mins) were lower than the corresponding PSG variables.

Older participants (> 60 years) were more likely to be of white race (82.6% vs. 43.3%) and had statistically significant higher left ventricular ejection fractions, poorer NYHA functional class, more comorbidity, higher respiratory disturbance indices, and lower BMI, CESD, and SMW compared to younger participants. Older participants had significantly lower sleep efficiency and greater WASO than younger participants, as measured on PSG.

The mean discrepancies between ACT and PSG on TST (50.91 ± 6.92 mins), SE (8.82 ± 1.36 %), SL (-9.44 ± 3.38 mins), and WASO (-43.56 ± 5.72 mins) shown in Table 2 were statistically significant ($p < .0001$ |Mean discrepancy| > 0), and with the exception of SL ($p = .1657$) and SE ($p = .0746$), significant discrepancies were present in both age groups. The mean discrepancies were statistically greater in the older than the younger participants for all sleep measures with the exception of SL ($p = .9099$). There was a high consistency ($ICC = 0.62$) between ACT and PSG measures of TST, and the consistency was much higher in the younger ($ICC = 0.81$) compared to the older participants ($ICC = 0.53$). Moderate or poorer consistency was observed on SL, SE, and WASO overall and in both age groups.

Bland-Altman Plots of the discrepancies in TST, SL, SE, and WASO are shown in Figure 2. The plots illustrate the greater over-estimates of TST and SE and under-estimates of SL and WASO that lead to greater mean discrepancies and the wider confidence limits for the discrepancies in individual subjects. Most of the total variances in the discrepancies were explained by polysomnographic SE ($r^2 = 0.47$), SL ($r^2 = 0.59$), and WASO ($r^2 = 0.61$), but less of the variance was explained by polysomnographic TST ($r^2 = 0.15$).

Figure 1-B shows the relationships between the log-transformed nighttime activity counts (C_O) with $WASO_{ACT}$ (dark circles) and $WASO_{PSG}$ (white circles). The expected nighttime activity counts (solid line; $C_E = 0.9431 \times \log(WASO_{PSG}) - 1.0107$) were calculated with the estimates of parameters from the GLM. The discrepancy between these two activity counts,

C_N was approximated by the discrepancy between the log-transformed WASOs (See Appendix A).

Table 3 shows the correlations between the demographic and clinical characteristics, depression, daytime sleepiness, functional performance, the discrepancy measures, and average activity counts per minute during the nighttime wake episodes. Positive correlations indicate overestimation of TST by ACT vs. PSG and negative correlations indicate underestimates of WASO by ACT vs. PSG. Older age was associated with over-estimation by ACT and greater discrepancy on TST ($r = 0.35$), greater discrepancy with under-estimation by ACT of WASO ($r = -0.32$), and with C_N ($r = 0.28$). Older age was also associated with less motor activity during nighttime wake episodes ($r = -0.22$), and greater comorbidity was associated only with discrepancy and under-estimation by ACT of WASO ($r = -0.19$).

Poor sleep quality and insomnia were associated with lower C_N (PSQI: $r = -0.16$; DIMS: $r = -0.17$) and greater motor activity during nighttime wake episodes. The highest correlations were observed between C_N and daytime motor activity. Lower daytime motor activity was associated with over-estimation of TST ($r = -0.43$) and under-estimation of WASO ($r = 0.46$) by ACT and C_N ($r = -0.55$). Patients with greater daytime motor activity had greater activity counts during nighttime wake episodes ($r = 0.54$). Daytime motor activity was positively associated with SMW distance ($r = 0.29$) and negatively associated with age ($r = -0.32$), comorbidity ($r = -0.17$), RDI ($r = -0.25$), and NYHA functional classification ($r = -0.15$). We found a parsimonious model for greater C_N (reflecting under-estimates of $WASO_{ACT}$), explained by greater age ($p = .0431$), lower levels of insomnia ($p = .0129$), and less daytime motor activity ($p < .0001$).

The correlations between global sleep quality and its components (PSQI), DIMS, and daytime motor activity and the discrepancy in WASO and C_N were evaluated separately for younger and older patients (Table 4). Less daytime motor activity was significantly associated with under-estimation by $WASO_{ACT}$, greater C_N , and less motor activity during nighttime wake episodes in both age groups. Daytime motor activity was also associated with both $WASO_{ACT}$ and $WASO_{PSG}$, but the correlation was positive for $WASO_{ACT}$ and negative for $WASO_{PSG}$. In patients aged 60 or older, poor sleep quality, longer self-reported sleep latency, more sleep disturbance, and more self-reported use of hypnotic medications were associated with greater $WASO_{ACT}$, but not with $WASO_{PSG}$. Higher levels of those variables and DIMS were significantly associated with less C_N and greater activity counts during nighttime wake episodes. Use of hypnotic medications was significantly associated with less discrepancy in the WASO measures ($r = 0.24$).

Table 5 shows the means and 95% confidence intervals for total sleep time, WASO, C_N , and activity counts during nighttime wake episodes between participants with and without insomnia by age. PSG total sleep time was lower in older adults with insomnia compared to younger participants, and ACT total sleep time was similar due to the greater over-estimation by ACT. There was a significant difference in $WASO_{PSG}$ by age, but not by insomnia. However, a relatively greater under-estimation of WASO ($WASO_{ACT} = 48.4$, 95% CI = [35.0, 62.7] vs. $WASO_{PSG} = 123.4$, 95% CI = [104.7, 142.2]) was observed in older

patients without insomnia who had a greater C_N (1.11, 95% CI= [0.83, 1.39]) and fewer activity counts during nighttime wake episodes (61.5, 95% CI= [23.5, 99.6]) than others.

We calculated the expected correlations between the discrepancy measures (i.e. $WASO_{ACT} - WASO_{PSG}$ and C_N) and WASO based on sample standard deviations in Table 1 and formulas in Appendix B. The C_N has a relatively greater association with $WASO_{ACT}$ ($r = -0.63$) than $WASO_{PSG}$ ($r = 0.47$), while the discrepancy in WASO has a stronger association with $WASO_{PSG}$ ($r = -0.78$) than $WASO_{ACT}$ ($r = 0.38$). Figure 3 shows the expected correlations of the discrepancy with the two WASO measures and the negative correlations of C_N with ACT and PSG WASOs (Appendix B) across different standard deviations of $WASO_{PSG}$ and $WASO_{ACT}$. In the correlations with $WASO_{PSG}$ (Figure 3-A & B), the discrepancy of WASO is expected to have relatively greater correlations compared to C_N across the given range of standard deviations of WASOs. On the other hand, Figure 3-C & D show that relatively greater correlations between C_N and $WASO_{ACT}$ are expected.

Discussion

To our knowledge, our study was the first to evaluate the correspondence and discrepancy between actigraphic and polysomnographic sleep characteristics (TST, SL, WASO) and their associations with demographic and clinical patient characteristics, symptoms and functional characteristics among people with HF. Total sleep time was reliably measured by actigraphy, especially in younger adults, but other actigraphic sleep measures had poor consistency with PSG measures. The validity of sleep time is generally consistent with recent studies in other populations. For example, Marino and colleagues (Marino et al., 2013) evaluated the concordance between these measures in healthy people and people with insomnia, and others examined the correspondence in people with schizophrenia (Baandrup and Jennum, 2015). Our study extended these and other previous studies by including people with poor self-reported and objectively measured sleep quality due to insomnia, sleep disordered breathing, and possibly HF itself, as well as overall low levels of daily motor activity and function (measured by the SMW), and high levels of comorbidity.

Our study extended previous research with the discovery that the consistency between ACT and PSG measures was weaker in patients aged 60 or older than younger adults. Lower PSG-measured sleep time compared to ACT, led to over-estimation of total sleep time with actigraphy in older adults and a lack of ability to differentiate sleep efficiency between the two age groups with ACT. Thus, both total sleep time and sleep efficiency, as measured with ACT, may not be accurate measures, especially in older adults. Similar discrepancy patterns were previously observed in a study designed to validate actigraphy with 889 males aged 65 and older (Blackwell et al., 2011), and similar over-estimates and underestimates of total sleep time and WASO, respectively, were obtained by detecting wakefulness with the proportional integration mode (PIM) and time above threshold (TAT) used on another brand of actigraph (Blackwell et al., 2011).

Our finding that ACT measures of sleep are less accurate in older adults, despite better self-reported sleep quality and less insomnia than younger people, contrasts with previous studies in which discrepancies between ACT and PSG were attributed to insomnia and lying

awake at night without moving (Sivertsen et al., 2006, Natale et al., 2009, Sadeh, 2011). In these studies, ACT over-estimated sleep time in people with insomnia. On the other hand, in our study, motor activity counts during nighttime wake episodes among younger patients were consistently independent from overall sleep quality and insomnia. However, older participants had higher motor activity during nighttime wake episodes when they reported poor sleep quality and insomnia symptoms that might be attributed to restlessness. Lower activity counts during nighttime wake episodes were observed in older participants without insomnia symptoms, but not in younger participants. It is possible that some of the older participants who reported no insomnia symptoms stayed in bed without recognition of wakefulness as classified by PSG and did not recognize insomnia.

Sleep disordered breathing may increase the discrepancy between ACT and PSG measures of sleep (Ancoli-Israel et al., 2003, Morgenthaler et al., 2007, Wang et al., 2008, Pallin et al., 2014) through its contribution to restless sleep or frequent awakenings. However, we found that the respiratory disturbance index (RDI) had small correlations with the discrepancy in TST and WASO, but no correlation with the C_N and nocturnal activity during wakefulness. Our finding may be explained by a previous study that examined the validation of ACT for obstructive sleep apnea (OSA) patients in which the investigators found similar epoch-by-epoch sleep/wake agreement between ACT and PSG between OSA and non-OSA patients (Wang et al., 2008). On the other hand, Blackwell (Blackwell et al., 2005) found that sleep disordered breathing (SDB) is associated with under-estimation of TST by ACT and argued that this association was due to falsely identified wake episodes from the detection of SDB-related movement with ACT while the patient was actually asleep. Further research is needed to reconcile these disparate findings.

Older adults had lower daytime motor activity and lower activity counts during nocturnal wake episodes, and these levels may be responsible for the greater discrepancy between ACT and PSG. The associations between Six Minute Walk Test performance, comorbidity, and motor activity with discrepancies in total sleep time and WASO suggest that aging or immobility associated with HF, comorbidity, or fatigue may influence sleep scoring with actigraphy through their effects on motor activity. When occurring during sleep, motor activity may reflect restlessness that may lead to false detection of wake episodes on ACT, reducing the discrepancy between ACT and PSG. Alternatively, some of the nocturnal activity counts may be associated with arising at night to urinate or other intentional activities. Further studies are needed to evaluate the nature and purposeful or non-purposeful reasons for the detected activity and our findings should be confirmed and extended in a prospective study with multivariate analyses.

The apparent influence of motor activity, as recorded by ACT, on concordance and discrepancy of ACT with PSG measures of sleep suggests the critical importance of the physics of the actigraph sensor and the software thresholds used for detecting sleep/wake. We used the medium threshold on the commercial Actiware software because of evidence that it is the least subject to bias in patients with bipolar disorder (Kaplan et al., 2012) and athletes (Fuller et al., 2017), but this level may need to be adjusted to accommodate differences in motor activity associated with aging, restless sleep, disability, comorbidity, and fatigue in people with chronic conditions, such as HF.

Depressive symptoms are associated with adverse sleep outcomes and may be associated either with depressed or agitated motor activity. However, our findings of correlations of depression only with self-reported sleep quality (PSQI) and insomnia (DIMS), but not with any of the ACT or PSG sleep measures or the discrepancies between them suggests that depressive symptoms do not contribute to discrepancy or concordance of ACT and PSG measures. This finding contrasts with a previous study that suggested that depression increases the discrepancy in ACT and PSG measures in young adults with depression, regardless of the sensitivity settings used for actigraphy (Jean-Louis et al., 2000).

This study demonstrated two approaches to measuring the discrepancy between $WASO_{ACT}$ from $WASO_{PSG}$ and a novel measure, the C_N . The associations between WASO and demographic and clinical characteristics likely explain the discrepancy and C_N metrics. For instance, age had a substantively greater correlation with $WASO_{PSG}$ compared to $WASO_{ACT}$, and it was reflected in a greater correlation between age and the discrepancy of WASO, which has a relatively great correlation with $WASO_{PSG}$ compared to the C_N . In the simulation study, we demonstrated different associations between the discrepancy of WASO and C_N and $WASO_{ACT}$ and $WASO_{PSG}$, and those differences produced inconsistent correlations with clinical characteristics when using C_N vs. the discrepancy in WASO. Because of its strong correlations with $WASO_{PSG}$, the discrepancy of WASO was not associated with self-reported insomnia and sleep quality, while the C_N had significant correlations which could be explained by average movements during nighttime wake episodes.

The new index, C_N , which represents motor activity and detects nighttime wakefulness with lower daytime motor activity in patients with chronic HF, may also be increased in individuals with other kinds of disabling chronic conditions (e.g., chronic pain conditions, chronic obstructive pulmonary disease). Although daytime behavior and nighttime sleep have usually been considered separate phenomena, the C_N may provide a useful metric in evaluating the success of disease management in a unitary way that address both daytime and nighttime motor activity as reflected in this measure. Future research is needed to evaluate the extent to which changes in the C_N correspond to clinically relevant changes in disease management and patient status in HF as well as other chronic conditions. Nighttime restlessness and wake bouts, as well as decreased motor activity are common in many chronic conditions, and improvements in these phenomena are likely important consequences of improved disease management. Although the computation of C_N requires a PSG study that is associated with some expense and burden, use of this metric may assist in adjusting for the discrepancy between ACT and PSG for specific patients and may be useful in adjusting for ACT measures over time in order to approximate PSG measures. However, we recognize that this may be limited by night-night variability in these measures and future research is needed to assess the usefulness of this measure as well as its ability to predict important outcomes.

Strengths and Limitations

Strengths of this study included the use of standardized sleep measures and the inclusion of participants with a common and disabling health condition (HF) for whom sleep is an

important determinant of health and quality of life. Our sample, drawn from evidence-based HF disease programs broadly represents HF patients in the U.S. population who have both HF with preserved and reduced ejection fraction and was diverse in terms of age, gender, and racial representation. We used a commercially-available actigraph that is often used in research and used the default threshold scoring, which is consistent with the majority of publications using this specific device, to maximize the generalizability of our findings to studies using this technology. Use of the commercial software facilitates replication in other studies, and past research suggests that the medium threshold has the smallest bias for TST, SE, WASO, and SL (Kaplan et al., 2012, Fuller et al., 2017). Given the wide array of available ambulatory sleep monitoring devices available to researchers and consumers, standardization of methods seems to be an important goal. On the other hand, development of a specialized algorithm to adjust for motor activity accounts specific to people with chronic conditions and at various ages may increase the sensitivity and specificity to sleep and wake. Future studies should be conducted to compare the use of different activity thresholds and different actigraph devices, as well as specialized algorithms that may be tailored to specific populations, given differences in their physical and mathematical properties. Studies are also needed to examine how those findings and relationships with C_N may with varying software thresholds for the device and if they would be consistent regardless of night-night variability. It is also important to understand how the relationship between the C_N and daytime motor activity may be associated with circadian rhythms of actigraphy over consecutive nights and to determine the relative contributions of these factors to clinical outcomes in HF patients.

Limitations of this study included its retrospective nature and the imbalance in gender, comorbidity and the frequency of sleep disordered breathing between the older and younger HF participants. Given that sleep patterns, as well as levels of motor activity have significant night-night variability, use of data from a single night likely does not represent daily variability in these phenomena, and the discrepancy and concordance between ACT and PSG may vary accordingly. Likewise, the intrusive nature of PSG, although recorded in home environments, may have influenced the ACT data. Our measurements of insomnia, depression, and sleep-reflect habitual/chronic phenomena, and the associations between these variables and the ACT and PSG may have nightly variability. Future studies are needed to prospectively address these concerns.

In conclusion, age and low levels of daytime motor activity may explain the discrepancy between ACT and PSG among patients with fragmented sleep, low levels of function, and high levels of comorbidity, while insomnia and poor sleep quality were associated with substantive nocturnal motor activity that was responsible for reducing the discrepancy between these two measures. Our new index C_N successfully captured those relationships.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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A) Expected log-transformed nighttime activity (C_E) across WASO

B) Observed log-transformed nighttime activity (C_O) across WASO

Figure 1.
Relationship between log-transformed nighttime activity counts and WASOACT.

Figure 2.
Bland-Altman plots of total sleep time, sleep latency, sleep efficiency, and WASO.

Figure 3.

Expected correlation between two discrepancy metrics and WASO from simulation.

Note. Corr(PSG) and Corr(ACT) are correlation coefficients of discrepancy (or CN) with WASOPSG and WASOACT, respectively. SD(PSG) and SD(ACT) are standard deviation of WASOPSG and WASOACT, respectively.

Table 1

Comparison of younger and older adults on clinical, demographic, and sleep variables (N=155)

	All N=155 Mean (SD) / N (%)	Age < 60 years N=69 Mean (SD) / N (%)	Age 60 years N=86 Mean (SD) / N (%)	Difference p-value
Demographic Variables				
Age	60.5 (16.1)	45.8 (9.4)	73.1 (8.0)	
Male	101 (65.2%)	40 (56.0%)	61 (70.9%)	.0924
White	100 (65.4%)	29 (43.3%)	71 (82.6%)	<.0001
Clinical Variables				
Left ventricular ejection fraction (%)	32.9 (15.4)	28.6 (13.9)	36.3 (15.8)	.0022
Charlson Comorbidity Index	2.4 (1.5)	2.0 (1.2)	2.7 (1.6)	.0020
NYHA Classification				
I	3 (1.9%)	2 (2.9%)	1 (1.2%)	.0407
II	89 (57.4%)	44 (63.8%)	45 (52.3%)	
III	53 (34.2%)	21 (30.4%)	32 (37.2%)	
IV	10 (6.5%)	2 (2.9%)	8 (9.3%)	
Body Mass Index	30.6 (8.2)	33.5 (9.6)	28.2 (5.9)	.0001
Clinical Depression (CES-D)	17.1 (11.0)	20.0 (11.2)	14.6 (10.3)	.0022
Self-Reported Sleep Quality (PSQI)	8.7 (4.1)	8.6 (4.2)	8.7 (4.1)	.8810
Insomnia (DIMS)	79 (51.0%)	38 (55.1%)	41 (47.7%)	.3598
Respiratory Disturbance Index (RDI)	24.1 (18.8)	19.4 (15.3)	27.9 (20.4)	.0047
Six Minute Walk (SMW)	987.8 (429.1)	1122.8 (411.1)	870.7 (412.1)	.0004
Daytime Sleepiness (Epworth Scale)	8.3 (4.4)	8.0 (4.7)	8.4 (4.1)	.6230
Polysomnographic Sleep Characteristics				
Total Sleep Time (min)	327.7 (95.5)	342.8 (96.7)	315.5 (93.2)	.0767
Sleep Latency (min)	30.2 (35.4)	31.0 (43.2)	29.6 (27.7)	.7974
Sleep Efficiency (%)	71.3 (16.0)	76.9 (13.1)	66.7 (16.6)	<.0001
WASO (min)	100.1 (67.6)	73.1 (59.1)	121.8 (66.5)	<.0001
Actigraphic Sleep Characteristics				
Total Sleep Time (min)	378.6 (101.3)	359.3 (106.5)	394.1 (94.7)	.0329
Sleep Latency (min)	20.9 (27.1)	22.2 (28.8)	19.8 (25.7)	.5889
Sleep Efficiency (%)	80.0 (13.1)	80.1 (11.7)	80.0 (14.2)	.9496
WASO (min)	56.7 (45.9)	49.4 (36.9)	62.8 (51.5)	.0637
Activity Counts Per Minute – Daytime	218.1 (116.9)	249.5 (120.8)	193.4 (108.2)	*.0016
Activity Counts Per Minute – Nighttime	18.3 (17.9)	17.4 (17.2)	19.1 (18.4)	*.1979
Activity Counts Per Minute During Nocturnal Wake Episodes	116.5 (130.2)	136.2 (133.9)	100.3 (125.6)	*.0090

Note.

* P-values for Activity Counts Per Minute Variables were obtained from Log-transformed scores.

Mean discrepancy and intra-class correlation coefficient (ICC) between actigraphic and PSG sleep measures (N=155)

Table 2

	Discrepancy (ACT – PSG) Mean ± Standard Error			Consistency ICC		
	All	Younger than 60	60 or older	All	Younger than 60	60 or older
Total Sleep Time (min)	50.91 ± 6.92	16.43 ± 7.72	78.6 ± 9.90	0.62	0.81	0.53
Sleep Latency (min)	-9.44 ± 3.38	-8.81 ± 6.28	-9.96 ± 3.40	0.13	0.01	0.33
Sleep Efficiency (%)	8.82 ± 1.36	3.14 ± 1.74	13.44 ± 1.88	0.34	0.35	0.38
WASO (min)	-43.56 ± 5.72	-23.76 ± 7.64	-59.82 ± 7.93	0.28	0.22	0.27

Table 3

Associations between clinical and demographic characteristics, daytime symptoms, Six Minute Walk and discrepancy metrics (n=155)

Variables	Discrepancy of TST ($TST_{ACT} - TST_{PSG}$) Pearson's r (p-value)	Discrepancy of WASO ($WASO_{ACT} - WASO_{PSG}$) Pearson's r (p-value)	C_N Pearson's r (p-value)	Activity Counts Per Minute in Nocturnal Wake Episodes Pearson's r (p-value)
Age	0.35 (<.0001)	-0.32 (<.0001)	0.28 (.0004)	-0.26 (.0010)
Comorbidity	0.13 (.1085)	-0.19 (.0188)	0.11 (.1798)	-0.11 (.1705)
Total Sleep Quality (PSQI)	0.05 (.5084)	0.09 (.2841)	-0.16 (.0421)	0.19 (.0205)
Insomnia (DIMS)	0.07 (.3801)	0.07 (.3938)	-0.17 (.0309)	0.19 (.0207)
Depression (CESD)	-0.01 (.9234)	0.02 (.7704)	-0.06 (.4294)	0.09 (.2929)
Respiratory Disturbance (RDI)	0.13 (.0986)	-0.14 (.0846)	-0.01 (.8984)	-0.02 (.8531)
Six Minute Walk (SMW)	-0.17 (.0400)	0.14 (.0979)	-0.10 (.2563)	0.08 (.3237)
Sleepiness (ESS)	-0.08 (.3051)	-0.10 (.2118)	0.00 (.9459)	-0.03 (.7437)
Daytime Activity Counts Per Minute	-0.43 (<.0001)	0.46 (<.0001)	-0.55 (<.0001)	0.54 (<.0001)

Note. Correlation coefficients of Daytime Activity Counts Per Minute and Nocturnal Wake Episodes were calculated with Log-transformed scores. Positive coefficients with discrepancy of TST and negative coefficients with discrepancy of WASO represent greater discrepancy between ACT and PSG (i.e. overestimates and underestimates of TST and WASO, respectively). Positive coefficient with C_N represents greater discrepancy.

Table 4

Associations between Wake after sleep Onset (WASO), discrepancy metrics, PSQI subscales, insomnia, and daytime activity counts in younger (< 60yrs) and older (≥ 60yrs) patients

Variables	Younger than 60 (N=69)					60 or Older (N=86)				
	WASO _{PSG} Pearson's <i>r</i> (p-value)	WASO _{ACT} Pearson's <i>r</i> (p-value)	Discrepancy (WASO _{ACT} - WASO _{PSG}) Pearson's <i>r</i> (p-value)	C _N Pearson's <i>r</i> (p-value)	Activity Counts Per Minute in Nocturnal Wake Episodes Pearson's <i>r</i> (p-value)	WASO _{PSG} Pearson's <i>r</i> (p-value)	WASO _{ACT} Pearson's <i>r</i> (p-value)	Discrepancy (WASO _{ACT} - WASO _{PSG}) Pearson's <i>r</i> (p-value)	C _N Pearson's <i>r</i> (p-value)	Activity Counts Per Minute in Nighttime Wake Episodes Pearson's <i>r</i> (p-value)
Total Sleep Quality (PSQI)*	0.04 (.7266)	0.04 (.7519)	-0.02 (.8874)	-0.00 (.9645)	0.02 (.8859)	0.07 (.5187)	0.33 (.0021)	0.18 (.1005)	-0.29 (.0058)	0.33 (.0020)
Overall Sleep Quality	0.02 (.8919)	0.08 (.5021)	0.03 (.7925)	-0.04 (.7241)	0.03 (.7874)	0.06 (.6009)	0.27 (.0139)	0.14 (.2020)	-0.29 (.0060)	0.30 (.0053)
Sleep Latency	0.20 (.0970)	-0.06 (.6023)	-0.22 (.0637)	0.16 (.1825)	-0.17 (.1627)	0.01 (.9378)	0.20 (.0641)	0.15 (.1684)	-0.25 (.0202)	0.31 (.0036)
Sleep Duration	0.06 (.6041)	0.21 (.0824)	0.06 (.6054)	-0.13 (.2740)	0.12 (.3438)	0.02 (.8724)	0.05 (.6568)	0.03 (.7848)	-0.06 (.5507)	0.04 (.7227)
Habitual Sleep Efficiency	-0.07 (.5600)	0.02 (.8386)	0.08 (.5086)	0.02 (.8497)	-0.01 (.9570)	0.05 (.6321)	0.15 (.1737)	0.07 (.5458)	-0.10 (.3728)	0.13 (.2213)
Sleep Disturbance	0.03 (.7829)	0.07 (.5554)	0.01 (.9315)	-0.00 (.9695)	0.05 (.6536)	0.08 (.4519)	0.25 (.0215)	0.11 (.3295)	-0.26 (.0171)	0.26 (.0176)
Use of Sleep Medication	-0.08 (.5274)	-0.05 (.6654)	0.04 (.7367)	-0.05 (.6599)	0.08 (.5147)	0.01 (.9383)	0.34 (.0017)	0.24 (.0298)	-0.24 (.0288)	0.27 (.0104)
Insomnia (DIMS)	0.12 (.3461)	0.07 (.5847)	-0.07 (.5779)	-0.07 (.5678)	0.06 (.6161)	-0.07 (.5462)	0.15 (.1801)	0.18 (.1074)	-0.26 (.0036)	0.29 (.0069)
Activity Counts Per Minute in Daytime	-0.26 (.0389)	0.26 (.0415)	0.39 (.0016)	-0.55 (<.0001)	0.51 (<.0001)	-0.32 (.0035)	0.21 (.0574)	0.44 (<.0001)	-0.50 (<.0001)	0.53 (<.0001)

Note. Correlation coefficients of Daytime Activity Counts Per Minute and Nocturnal Wake Episodes were calculated with Log-transformed scores.

Table 5Sleep measures, C_N , and activity counts during nighttime wake episodes by age and insomnia symptoms

	Younger Patients		Older Patients	
	Insomnia (N=38) Mean [95% CI]	No insomnia (N=31) Mean [95% CI]	Insomnia (N=41) Mean [95% CI]	No insomnia (N=45) Mean [95% CI]
Total Sleep Time (min)				
PSG	341.3 [311.4, 371.2]	344.7 [311.6, 377.8]	287.6 [258.8, 316.3]	341.0 [313.6, 368.5]
ACT	358.6 [326.5, 390.7]	360.1 [324.6, 395.7]	378.2 [347.3, 409.1]	408.6 [379.1, 438.1]
WASO (min)				
PSG	78.4 [58.0, 98.7]	66.8 [44.2, 89.3]	120.0 [100.3, 139.6]	123.4 [104.7, 142.2]
ACT	53.2 [39.0, 67.5]	44.7 [28.9, 60.4]	77.9 [64.2, 91.6]	48.4 [35.0, 62.7]
C_N	0.25 [-0.05, 0.56]	0.38 [0.05, 0.72]	0.44 [0.15, 0.73]	1.11 [0.83, 1.39]
Activity Counts Per Minute in Nocturnal Wake Episodes	152.1 [111.6, 192.5]	116.8 [72.0, 161.6]	140.9 [101.9, 179.8]	61.5 [23.5, 99.6]