Gynecologic Oncology 137 (2015) 448–455

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Circadian actigraphic rest–activity rhythms following surgery for endometrial cancer: A prospective, longitudinal study

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HIGHLIGHTS

- On average, endometrial cancer patients demonstrated significant disturbances in actigraphic rest–activity patterns initially post-surgery with significant improvement 4 months post-surgery.
- However, obese patients and those having more invasive surgery revealed more impaired rest–activity patterns throughout 4 months of surgical recovery.

ARTICLE INFO

Article history:
Received 16 December 2014
Accepted 2 April 2015
Available online 21 April 2015

Keywords:
Endometrial cancer
Actigraphy
Circadian activity rhythm
Laparotomy
Laparoscopic
Obesity

ABSTRACT

Objective. To investigate (1) circadian rest–activity rhythm disturbances among endometrial cancer patients as they recover from surgery in comparison to a historical reference group of women with no cancer history and (2) health- and treatment-related predictors of dysregulated rest–activity rhythms in endometrial cancer patients.

Methods. 60 endometrial cancer patients participated in a prospective, longitudinal study with actigraphic assessment at 1 week, 1 month, and 4 months post-surgery. 60 women without cancer from an epidemiological sample completed one actigraphic assessment, acting as a reference group.

Results. On average, results revealed initial significant rest–activity dysregulation at 1 week and 1 month post-surgery for the endometrial cancer group and then significant recovery in rest–activity patterns at 4 months post-surgery. Similarly, the cancer group had significantly more impaired rhythms than the reference group at 1 week post-surgery, but demonstrated comparable rhythms by 4 months post-surgery. Among the health- and treatment-related variables examined, obesity and receipt of more invasive surgery were found to predict more impaired rhythms at all time points.

Conclusion(s). The current study highlights significant disturbances in rest–activity patterns for endometrial cancer patients initially during surgical recovery followed by improvement in these patterns by 4 months post-surgery; however, obese patients and those having more invasive surgery demonstrated more impaired rest–activity patterns throughout the 4-month recovery period. Further research is warranted to understand how more impaired rest–activity patterns relate to health and quality of life outcomes.

1. Introduction

A host of biological processes occur within living organisms in circadian cycles over an approximately 24-hour period. Circadian rhythms are orchestrated endogenously by the central clock in the suprachiasmatic nucleus (SCN) within the hypothalamus and also are behaviorally based in that they are sensitive to external input such as light–dark exposure, which sends signals directly from the eyes to the SCN [1]. Consistent circadian rhythms (i.e., staying within synchronization of an approximately 24-hour day) through biological and behavioral processes are related to more positive health outcomes, whereas circadian dysregulation has been linked with poorer health outcomes [2]. In the context of cancer, circadian dysregulation, as measured by melatonin suppression, cortisol flattening, and history of shift work, has been related to increased risk of tumor initiation and progression (reviewed in Eismann et al.[3]).

An alternative marker of circadian rhythm dysregulation is the diurnal pattern of rest and activity as measured by wrist-worn actigraphy.

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http://dx.doi.org/10.1016/j.ygyno.2015.04.001
0090-8258/

This objective and non-invasive measure involves a watch-like device that is typically worn on the non-dominant wrist and measures activity level through accelerometry in small intervals (e.g., 1 min) continuously over 24-hour periods. Resulting data are then analyzed to quantify several indices of the rest–activity cycle including mean activity level, differences between highest and lowest activity levels, the regularity of the rest–activity cycle, and the timing of peak activity.

Cross-sectional actigraphic studies in breast, metastatic colorectal, and non-small cell lung cancer populations have demonstrated associations between indices indicating greater dysregulation of circadian rest–activity rhythms (including lower mean activity level, less differentiated highest and lowest activity values, and delayed timing of peak activity) and greater sleep disturbance, fatigue, depressive symptoms, anxiety symptoms, and body mass index (BMI) [4–8]. Less rest–activity consistency has also been associated with flattened cortisol rhythms in breast and metastatic colorectal patients and increased inflammation and tumor-related symptoms in metastatic colorectal patients [9,10]. Longitudinal studies of breast and metastatic colorectal cancer patients demonstrate changes in rest–activity rhythms during the course of treatment and recovery [11–16]. For example, women with breast cancer showed increasingly dysregulated rest–activity rhythms as chemotherapy progressed, with a return to rhythms comparable to a healthy reference group by 1 year post-chemotherapy. Longitudinal studies of women with breast cancer also further support a relationship between impaired rhythms and greater fatigue, depressive symptoms, and BMI. Longitudinal studies of metastatic colorectal patients showed that more irregular rhythms predicted tumor response as evaluated by CT scans, and, ultimately, survival. Thus, rest–activity regulation/dysregulation shows promise as a biobehavioral measure of functioning, recovery, and overall quality of life in cancer patients.

Women with endometrial cancer comprise the largest population of female cancer survivors after breast cancer. The sequelae of surgery and adjuvant therapy, psychological stress, disrupted daily routines, physiological changes (e.g., inflammation and hormonal alterations), and pre-morbid increased risk for obesity that accompany an endometrial cancer diagnosis are likely to be associated with changes in rest–activity patterns. However, no studies have examined rest–activity patterns in endometrial cancer patients specifically, and there is only one previous study of a mixed sample of gynecologic cancer patients [17]. This study found that patients on multiple agent chemotherapy were more likely to have a higher dichotomy index (i.e., the ratio of nighttime activity to daytime activity) than those on single agent chemotherapy. A higher dichotomy index was associated with greater fatigue, less efficient sleep, and more depressive symptoms during post-chemotherapy intervals. Our study sought to investigate circadian rhythm disturbances among endometrial cancer patients. To address the limitations of prior work in this area, we utilized a prospective, longitudinal study that allowed us to examine changes in rest–activity patterns at specific post-surgical milestones, and we compared findings to a reference group of women with no cancer history.

The current study had three objectives. First, we examined changes in rest–activity patterns during the 4 months following surgery for endometrial cancer. Second, we investigated the extent to which rest–activity rhythms of women with endometrial cancer differed from rhythms of a historical reference sample of women with no history of cancer. We hypothesized that women with endometrial cancer would have significantly more dysregulated rest–activity patterns but that rhythms would normalize as surgical recovery progressed. Our final objective was to examine health- and treatment-related predictors (age, body mass index, cancer stage, surgery type, adjuvant chemotherapy, and adjuvant radiation therapy) of dysregulated rhythms. We hypothesized that women undergoing more invasive surgery and more extensive adjuvant therapy and those with obesity would have more dysregulated rest–activity patterns and a slower recovery of rhythms.

2. Methods

2.1. Participants

Participants were 60 women who were enrolled in a larger study of sleep disturbance and quality of life following surgery for endometrial cancer. Women who underwent surgery for an endometrial malignancy of any stage at the University of Wisconsin Carbone Cancer Center were eligible. Women with a prior history of cancer or those with recurrent cancer were excluded. Those included in the present analyses had completed at least one valid actigraphic assessment.

A historical reference sample of 60 women with no history of cancer was drawn from the Biomarker Project sample of the MIDUS (Midlife Development in the United States) study. MIDUS is a national survey of 7108 adults ages 25 to 75 at study start. The Biomarker Project included 1255 participants who completed a broad panel of physiological assessments from 2004 to 2006; of this sample, 440 participants completed actigraphic assessment. The final reference group comprised 60 women who were matched to the cancer sample based on age (±3 years of age) and also on education level and race when possible,

Table 1
Demographic and medical characteristics for the cancer and reference groups.

Variable	Endometrial cancer group ($N = 60$)	Reference group ($N = 60$)
Age in years, *M*(*SD*), median	60.6(9.3), 59.5	60.6(9.5), 59.0
Marital status, *n*(%)		
Married/partnered	31(52)	36(60)
Single	14(23)	3(5)
Divorced/separated	7(12)	15(25)
Widowed	6(10)	6(10)
Missing	2(3)	0(0)
Race, *n*(%)		
African-American	2(3)	7(12)
Caucasian/White	54(90)	50(83)
Native American	1(2)	0(0)
Multi-racial	0(0)	3(5)
Missing	3(5)	0(0)
Education, *n*(%)		
<12 years	1(2)	0(0)
High school graduate	10(16)	11(18)
Some college/trade school/associates	18(30)	21(35)
College graduate	15(25)	16(27)
Post-graduate degree	13(22)	12(20)
Missing	3(5)	0(0)
Annual family income, *n*(%)		
≤25,000	13(21)	15(25)
25,001–55,000	18(30)	20(34)
55,001–85,000	12(20)	11(18)
>85,000	14(24)	14(23)
Missing	3(5)	0(0)
Occupation, *n*(%)		
Work, part- or full-time	33(55)	35(58)
Disabled	4(7)	1(2)
Homemaker	4(7)	2(3)
Retired	16(26)	17(28)
Unemployed	0(0)	1(2)
Other	0(0)	4(7)
Missing	3(5)	0(0)
Body mass index (BMI), *n*(%)		
BMI < 30 (non-obese)	12(20)	35(58)
BMI ≥ 30 (obese)	48(80)	25(42)
Cancer stage, *n*(%)		
Stage 1	46(77)	–
Stage 2	1(2)	–
Stage 3	11(18)	–
Stage 4	2(3)	–
Surgery, *n*(%)		
Laparotomy	23(38)	–
Laparoscopic	37(62)	–
Adjuvant chemotherapy, *n*(%)	19(32)	–
Adjuvant radiation therapy, *n*(%)	20(33)	–

which resulted in a well-matched sample on these variables (see Table 1).

2.2. Procedure

Women with endometrial cancer were enrolled in the study during acute surgical recovery on the inpatient hospital unit. After providing informed consent, participants completed actigraphic assessments at three time points: approximately 1 week, 1 month, and 4 months post-surgery. The reference group also provided informed consent and completed one actigraphic assessment as part of their participation in the MIDUS study. All study procedures were reviewed and approved by the University of Wisconsin Health Sciences Institutional Review Board.

2.3. Actigraphy

Wrist actigraphy (Actiwatch 64, Mini-Mitter, Bend, OR) was used to measure rest–activity patterns for both samples. Participants were instructed to wear the actigraph on their non-dominant wrist. Endometrial cancer patients wore an actigraph for a 3-day period at each assessment point while going about their usual activities and routines. Activity data were collected in 1-minute epochs (intervals). The reference group completed a 7-day actigraphic assessment, collected in 30-second epochs. The reference group's data were converted to 1-minute epochs for rest–activity rhythm analyses (detailed below), and 3 days from the 7-day period were selected to correspond to the matched cancer patient's 3-day actigraphic collection period. Both groups completed concurrent sleep logs to document sleep patterns and off-wrist activity (e.g., to take a shower).

2.4. Actigraphy analyses

For both groups, all actigraphy data were downloaded to Actiware software. Off-wrist activity noted in the sleep log was excluded from analysis. Epoch-by-epoch activity counts (1-minute intervals) were exported to SAS and analyzed using traditional cosinor analysis, simultaneously fitting 24-hour and 12-hour rhythms to the data [18]. This model yields 3 different indices of rest–activity rhythms: mesor, amplitude, and acrophase. Mesor is the mean activity level, or intercept of the model, with lower values indicating less activity. Amplitude is the rhythm height, or the difference between maximum activity and minimum activity, with lower values indicating a weaker rhythm. Acrophase is the time of day the rhythm peaks, with later times indicating a more “night owl” pattern, and earlier times indicating a more “morning lark” pattern.

To ensure that each 3-day period was not missing a large portion of data, we excluded any actigraphic assessment that included less than 80% of the data (the equivalent of at least approximately 2.5 days of data). Endometrial cancer patients had 80% useable data at each time point as follows: 83% ($n = 50$) at 1 week, 85% ($n = 51$) at 1 month, and 75% ($n = 45$) at 4 months. The majority of participants (i.e., 82%) had actigraphy data at 2 or more time points. Reasons for missing data were as follows: having less than 80% useable data ($n = 5$), actigraphy error ($n = 4$), patient death ($n = 2$), and participant not wearing the actigraph ($n = 23$). All individuals in the reference group had at least 80% useable data.

2.5. Demographic, health, and treatment variables

Endometrial cancer patients reported demographic variables at the first study assessment. Body mass index (BMI, kg/m^2) at the time of study entry was abstracted from the medical record from a recent physical exam. Cancer stage (using the American Joint Commission on Cancer Staging Manual, 7th edition [19]), surgery type, adjuvant chemotherapy, and adjuvant radiation therapy were also abstracted from patient medical records under the supervision of a board certified oncologist (SR). Health and treatment variables were categorized as follows: BMI category (non-obese, BMI < 30, or obese, BMI ≥ 30), cancer stage (I and II versus III and IV), surgery type (laparoscopic or laparotomy), adjuvant chemotherapy (yes or no), and adjuvant radiation therapy (yes or no). For the reference sample, demographic variables were collected via phone interview.

2.6. Statistical analyses

Descriptive statistics for demographic and medical characteristics of the cancer and reference groups were computed. To address the first objective regarding changes in rhythms following surgery, each rest–activity index (i.e., mesor, amplitude, and acrophase) was modeled over time using linear mixed models, fitted with restricted maximum likelihood methods. Time was a continuous variable in these models, and both the intercept and slope were specified as random effects to allow for participant differences at study start and to allow for individual differences in slope over time. Whether actigraphy was collected over a weekend versus non-weekend was included as a covariate in all analyses. To address the second objective regarding differences between endometrial cancer patients and the reference group, actigraphic indices from cancer patients at all time points were compared to the reference sample using linear regression while controlling for BMI due to group differences in obesity. To address the final objective regarding health- and treatment-related predictors of actigraphic indices, linear mixed models were used as specified for the first research objective with a separate model for each predictor variable along with time and the interaction of each variable with time. This allowed us to determine whether these variables predicted overall rhythm dysregulation as well as the recovery trajectory. When significant main effects or interactions were present in any of the above analyses, appropriate pairwise comparisons were computed. SAS software (SAS Institute Inc., Cary, NC) was used for all data analyses, and alpha was set to .05.

3. Results

3.1. Participants

Table 1 provides demographic and medical variables for the patient and reference groups. The groups were similar on all demographic variables except BMI. Women with endometrial cancer had a higher BMI ($M = 38.7$; $SD = 10.9$; median = 38.1) than the reference group ($M = 30.3$; $SD = 11.2$; median = 28.4; $t(118) = -4.2$, $p < 0.0001$). Of note, the majority of patients who underwent adjuvant chemotherapy (95%; 18/19) received a standard 6 cycle carboplatin/taxol regimen. The remaining patient was on a clinical trial protocol and received 2 cycles of cisplatin followed by 4 cycles of carboplatin/taxol.

3.2. Rest–activity rhythm trajectories during surgical recovery

Fig. 1a–c presents rest–activity rhythm trajectories of endometrial cancer patients during surgical recovery and rest–activity indices for the reference group. Participants demonstrated patterns of recovery over the course of the study. In particular, mixed models revealed significantly increasing overall activity (mesor; $F(1,48) = 53.9$, $p < .0001$) and increasing rhythm height (amplitude; $F(1,48) = 44.3$, $p < .0001$) over the course of the post-surgical recovery. Pairwise comparisons revealed that both mesor and amplitude remained similar from 1 week to 1 month (both $p = .2$), but significantly increased from 1 to 4 months ($p = .001$ and .002, respectively). The peak of the rest–activity rhythm (acrophase) demonstrated only a trend of activity peaking earlier in the day over the course of recovery ($F(1,48) = 4.0$, $p = 0.05$). For further illustration, Fig. 2a–f presents mean activity level data by the hour for a participant with a more challenging rest–activity recovery

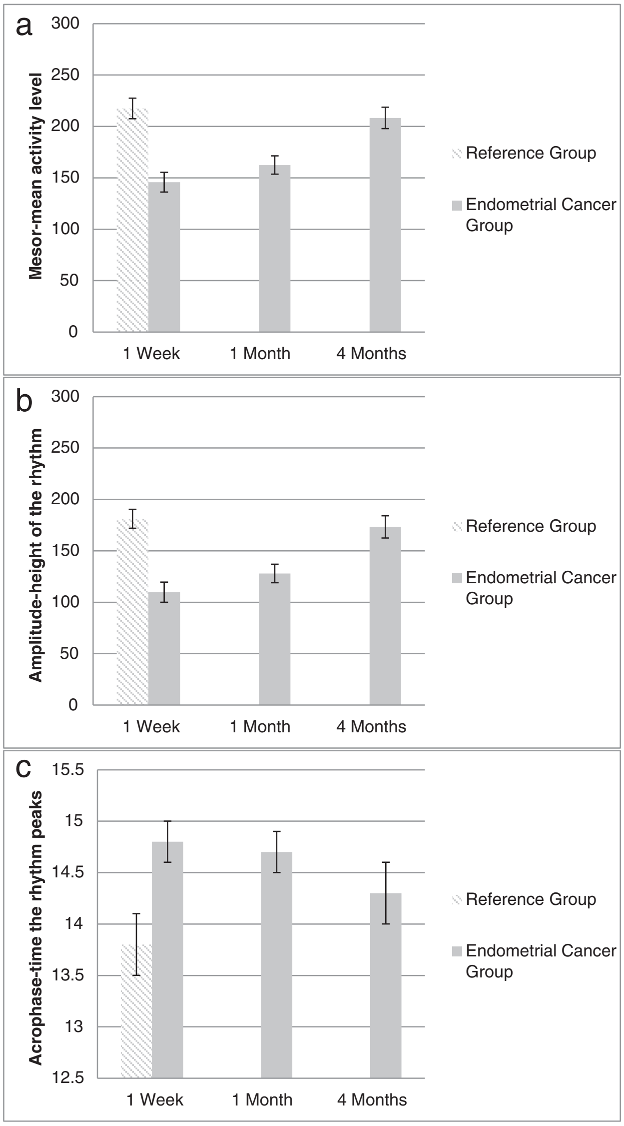

Fig. 1. a–c. Estimates of actigraphic rest–activity pattern variables for endometrial cancer patients from mixed models controlling for weekend or non-weekend collection are illustrated. Reference group values were drawn from simple univariate statistics. For mesor and amplitude, there was a significant increase between 1 and 4 months post-surgery, and cancer patients had significantly lower values than the reference groups at 1 week and 1 month, all $p < .05$. For acrophase, cancer patients differed from the reference group at 1 week post-surgery, $p = 0.003$.

(a–c) and a participant with a more favorable rest–activity recovery (d–f).

All the following analyses controlled for BMI, given significant differences in obesity between the cancer and comparison groups. Compared to the reference group, patients had significantly less activity (mesor) and less rhythm height (amplitude) at 1 week ($t = -6.1$; $t = -6.0$, respectively, both $p < .0001$) and then trended toward less activity and less rhythm height at 1 month post-surgery ($t = -2.0$, $p = .05$; $t = -1.9$, $p = .06$, respectively). By 4 months post-surgery, patients were not significantly different from the reference group on mesor or amplitude ($p = .3$ and .07, respectively). Cancer patients also had a later peak of the rest–activity rhythm (acrophase) at 1 week when contrasted to the reference group ($t = 2.8$, $p = .01$), but there were no differences in acrophase values between groups at 1 and 4 months post-surgery ($p = 0.2$ and 0.1, respectively).

3.3. Predictors of rest–activity rhythm trajectories among endometrial cancer patients

Out of the health- and treatment-related variables examined, results revealed both BMI and more invasive surgery (laparotomy) were consistent significant predictors of lower mesor and amplitude at all time points. Given the relationship between BMI and surgery type, with obese women having a greater likelihood of undergoing more invasive surgery (44% (21/48) of obese patients as contrasted to 17% (2/12) of non-obese patients in the current sample), surgery type and BMI category were used as covariates, respectively, to cautiously investigate the predictive value of BMI category and surgery type. Thus, the remaining text and figures present data considering these covariates.

After controlling for surgery type (which was a significant predictor in all analyses), BMI category was a significant predictor of both mesor and amplitude ($F(1,36) = 4.3$, $p = 0.04$ and $F(1,36) = 6.3$, $p = 0.02$, respectively) during surgical recovery. There was no significant BMI × time interaction, indicating that patients who were obese demonstrated significantly less mean activity and less differentiated rhythms than non-obese patients across all time points (pairwise comparisons all $p < .05$). Fig. 3a–b illustrates these relationships.

After controlling for BMI category (which was a significant predictor in all analyses), there was also a main effect for surgery type in that patients who had laparotomies had significantly lower mesor and amplitude values than patients who had laparoscopic surgeries ($F(1,36) = 5.9$, $p = 0.02$ and $F(1,36) = 5.1$, $p = 0.03$, respectively) throughout surgical recovery. There was no significant surgery × time interaction, indicating relatively consistent group differences over time. That is, those patients having more invasive surgery had more dysregulated rest–activity rhythms at all time points than those with less invasive surgery (pairwise comparisons all $p < .05$). Fig. 4a–b illustrates these relationships.

Age, cancer stage, adjuvant chemotherapy, and adjuvant radiation therapy were not significant predictors of rest–activity variables over the course of recovery.

4. Discussion

Results of the present study highlight significant disturbances in rest–activity rhythms experienced by endometrial cancer patients during the initial months following surgery. Specifically, the endometrial cancer group showed lower mean activity level (mesor) and weaker rhythms (amplitude) at 1 week post-surgery relative to an age-matched reference group. Both mesor and amplitude improved significantly to levels commensurate with the community-based reference group by 4 months post-surgery. Despite the initial significant dysregulation observed, on average, patients appeared to show a good recovery. These findings are similar to a longitudinal study of actigraphic rest–activity patterns in breast cancer patients receiving chemotherapy, which demonstrated a decline in rest–activity rhythms from baseline to cycle 4 of chemotherapy and then a return to rest–activity rhythms similar to a reference group 1 year after the start of chemotherapy [11].

Although there was improvement on average in the current sample of endometrial cancer patients, there also was substantial variability in rest–activity indices. Our analyses of individual differences in health- and treatment-related variables indicated that women who were obese and those undergoing laparotomy had more impaired rest–activity recovery trajectories than non-obese patients and those undergoing laparoscopic surgery across all study assessments. Due to overlap of obesity and surgery type within our sample, we cautiously controlled for each variable when examining the prediction of the other variable, and both predictors remained significant. More specifically, obese patients and those receiving laparotomies had significantly lower mean activity levels and a weaker rhythm at all time points compared to non-obese patients and those receiving laparoscopic surgery. Furthermore, those women who had a laparotomy continued to have significantly lower mean activity level and a dampened rhythm compared to the reference group 4 months post-surgery.

These findings are consistent with those from a study examining actigraphic rest–activity patterns in a variety of patients receiving either open abdominal or laparoscopic surgery during the 4 days before and after surgery [20]. Results from this study revealed decreased stability and increased fragmentation of rest–activity rhythms for both groups after surgery, but significantly decreased stability in the open abdominal versus laparoscopic surgery group. Our study extends these findings, indicating that the disparities persist at 4 months post-surgery in endometrial cancer patients who receive a laparotomy. While laparotomy is known to prolong recovery compared to laparoscopy, most women are cleared for full activity and resume full time work 6 weeks post-surgery. Our findings of significantly lower activity and dampened rhythms 4 months post-surgery are surprising and may suggest a need for improved pre-operative counseling regarding recovery in those requiring laparotomy. Results of the current study are also similar to those found in other cancer populations showing links between impaired rhythms and higher BMI [5,12]. The current study confirms this relationship in endometrial cancer patients over a 4-month course of surgical recovery and also may imply a need for enhanced counseling prior to surgery for those who are obese.

The current study identifies risk factors (i.e., obesity and more invasive surgery) for a more challenging recovery that are easily

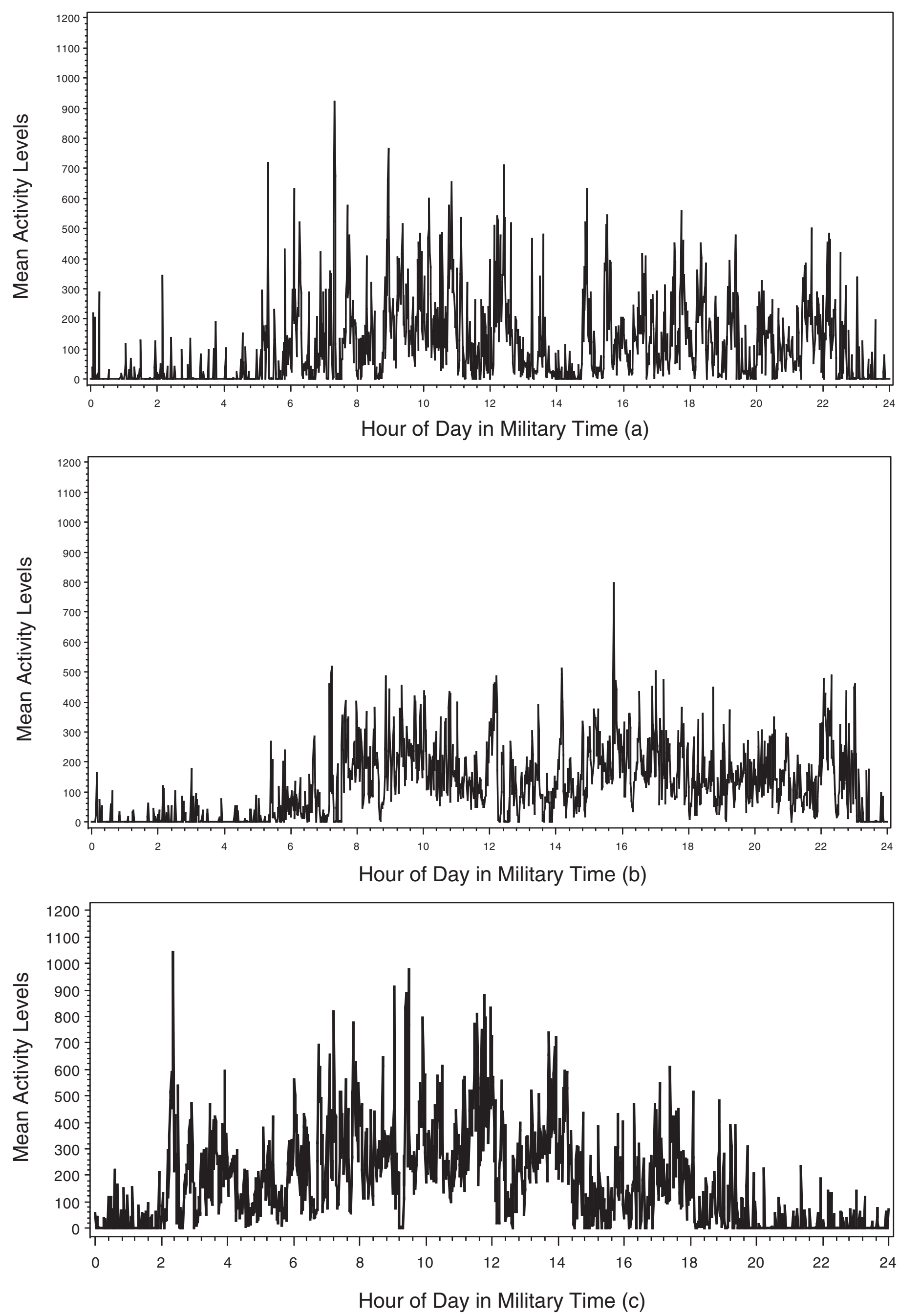

Fig. 2. a–f. Mean activity levels by hour of day for a participant with a more challenging rest–activity recovery pattern as demonstrated by less activity overall and less differentiation between night and day (a–c, mesor = 108.9, 120.7, and 173.8 and amplitude = 62.5, 82.5, and 152.9, at 1 week, 1 month, and 4 months, respectively) and another participant with a more favorable rest–activity recovery pattern as seen by greater activity level and more differentiation between night and day (d–f, mesor = 140.6, 224.8, and 271.5 and amplitude = 140.9, 258.0, and 285.2 at 1 week, 1 month, and 4 months, respectively).

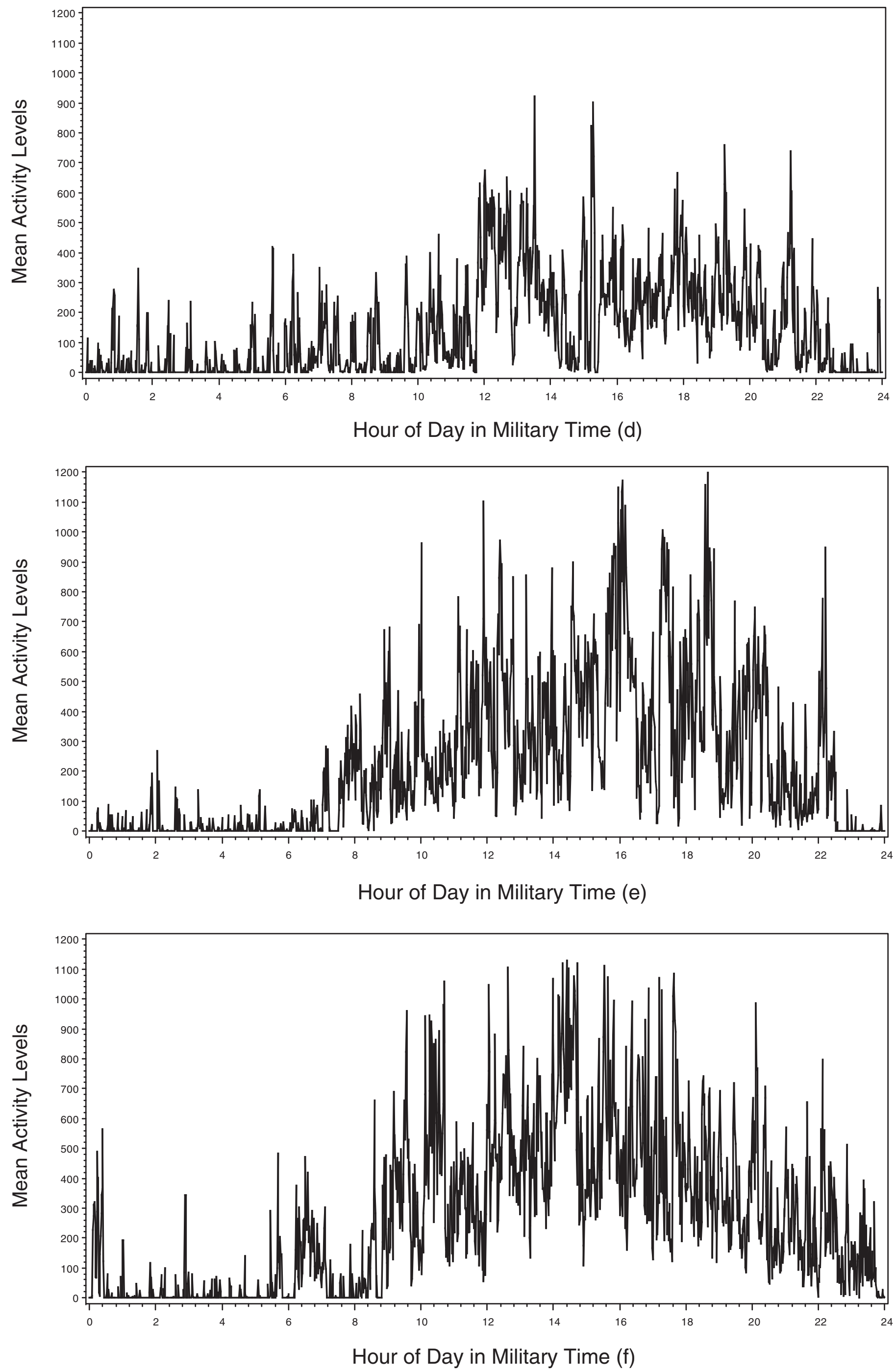

Fig. 2 (*continued*).

assessed at the start of endometrial cancer treatment. The mechanisms for these effects are not clear, but it may be that patients who are obese and/or who undergo more invasive surgery have more significant physical symptoms (e.g., greater pain, fatigue, and depressive symptoms) that could impact rest–activity patterns. Other potential mediators may include health comorbidities that affect sleep and activity as well as inflammation, which is often elevated in obese individuals, and has been associated with sleep patterns [21,22]. Future research investigating biological and behavioral pathways underlying the relationships seen is needed.

Surprisingly, age, cancer stage, adjuvant chemotherapy, and adjuvant radiation therapy did not predict rest–activity patterns. These findings stand in contrast to studies showing that chemotherapy negatively impacted rest–activity rhythms among women with breast and gynecologic cancers [11,17]. The relatively small number of patients who had adjuvant therapy (about 30%) and had more advanced disease (20%) may have made it more difficult to detect effects. Nonetheless, it is remarkable that BMI and surgery type appear to be more robust predictors of the recovery of rest–activity patterns, highlighting the importance of considering obesity and extent of surgery in understanding post-surgical recovery in this patient population.

Acrophase (i.e., the time of day the rhythm peaks) did not change significantly over time and was not associated with any of the health or treatment variables. This is similar to other studies of actigraphic rest–activity patterns within cancer populations [13]. It may be that

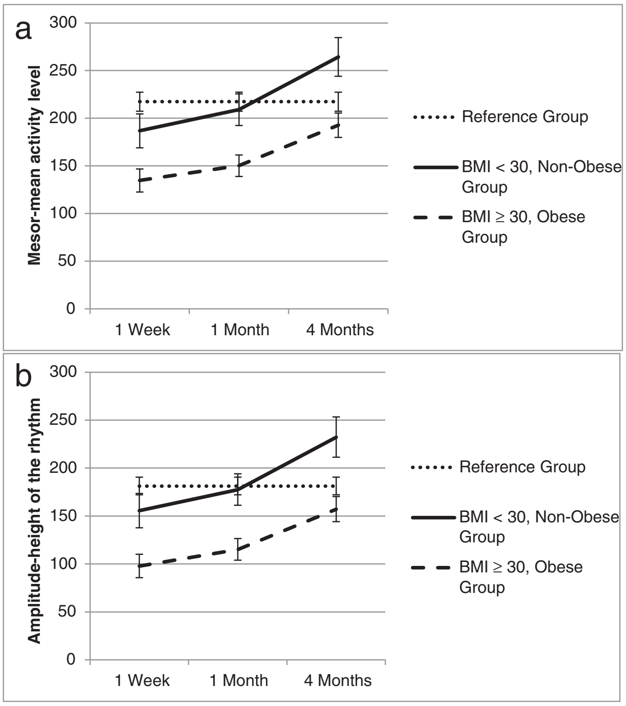

Fig. 3. a–b. BMI category predicted mean activity level (mesor) and rhythm height (amplitude) in linear mixed models controlling for surgery type and weekend or non-weekend collection. The mean of the reference group's one-time assessment of mesor and amplitude is shown in each graph. Mean scores for obese and non-obese participants differed significantly at all time points for both mesor and amplitude (all $p < .05$). At all time points, the non-obese group had scores commensurate with the reference group. At 1 week and 1 month, the obese group demonstrated significantly lower mesor and amplitude values than the reference group (all $p = .0001$), but had scores similar to the reference group at 4 months post-surgery (both $p = .1$).

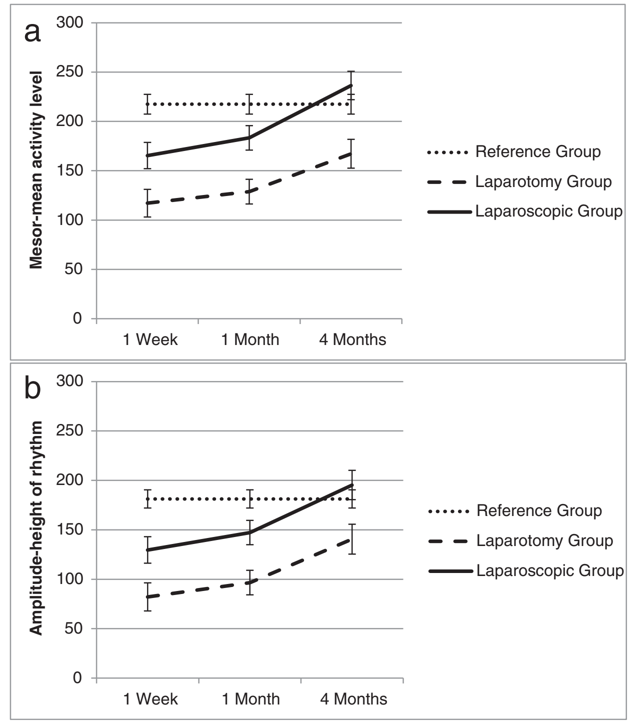

Fig. 4. a–b. Surgery type predicted mean activity level (mesor) and rhythm height (amplitude) in linear mixed models controlling for BMI category and weekend or non-weekend collection. The mean of the reference group's one-time assessment of average mesor and amplitude is displayed in each graph. Mean scores for participants who had a laparoscopic procedure differed significantly from those who had a laparotomy at all time points for both mesor and amplitude (all $p < .05$). At 1 week and 1 month, both surgical groups demonstrated mesor and amplitude values significantly lower than the reference group (p values ranged from .0001 to .04). By 4 months post-surgery, women who had laparoscopic surgery did not differ significantly from the reference group, but those who had a laparotomy continued to have significantly lower values for mesor and amplitude (both $p < .05$).

acrophase is a more stable aspect of rest–activity patterns that is not as easily disrupted by cancer treatment.

It is important to note some limitations of the study. As previously noted, a larger sample size could be of benefit when exploring predictors with lower base rates such as adjuvant chemotherapy. In addition, participants were not assessed prior to surgery, so we were unable to compare rest–activity rhythms pre- and post-surgery. At our center, endometrial cancer consultation, diagnosis, and surgery often occur in a very short time span, which made this logistically difficult. We were, however, able to compare scores with those from a historical age-matched reference group that was also similar with respect to education and race, providing information about the extent to which rest–activity patterns were dysregulated. It is noted that the reference group differed significantly from the cancer group in terms of BMI; however, BMI was controlled for in all primary analyses comparing these groups. A final limitation is the lack of a diagnostic testing for breathing- or movement-related sleep disorders or structured diagnostic interviews for insomnia, circadian rhythm disorders, or restless legs syndrome. Future studies could include such measures to understand the contribution of any specific sleep disorder to rest–activity patterns above and beyond the cancer treatment process investigated thoroughly within the current study. Strengths of the study include the prospective, longitudinal design, the inclusion of a reference group of women without cancer, and the use of an objective measurement of rest–activity patterns.

Further research is warranted to understand how rest–activity pattern trajectories relate to outcomes to better understand the significance of a more challenging rest–activity recovery pattern in this patient population. It is already known that disrupted circadian rest–activity patterns can contribute to quality of life impairments, including sleep disturbance, fatigue, depression, and anxiety symptoms in both cancer and non-cancer populations [4–8,11–14,17]. In addition, disrupted circadian rhythms have been implicated in cancer development, metastasis, and survival [3]. Moreover, rest–activity patterns are modifiable by both behavioral and biological interventions, including cognitive behavioral therapy and bright light therapy. Given the relatively high survival rate, but also the significant co-morbidities seen among women with endometrial cancer, this is a potentially fruitful and clinically important avenue for future investigations.

In summary, this is the first study to examine rest–activity patterns among endometrial cancer patients. The findings highlight initial significant dysregulation in rest–activity patterns followed by marked recovery 4 months post-surgery. Nonetheless, some patients showed more persistently dysregulated rhythms, including obese women and those who had laparotomies. Thus, the current study provides empirical support for the notion that surgical recovery will likely take more than 6 weeks before reaching more typical rest–activity patterns. These results also support improved pre-operative counseling regarding prolonged recovery for obese patients or those requiring laparotomy. In addition, our findings lay the groundwork for perioperative behavioral and biological interventions targeting rest–activity patterns that may be beneficial in endometrial cancer patients.

Conflict of interest statement

Dr. Rumble reports grants from UW Carbone Cancer Center, during the conduct of the study and grants from Merck, Inc., outside the submitted work. Dr. Gehrman reports grants from Merck, Inc., outside the submitted work. Dr. Benca reports grants and personal fees from Merck, Inc. and personal fees from Jazz, outside the submitted work. Dr. Costanzo and Ms. Moore report grants from NIH — National Cancer Institute and grants from University of Wisconsin Carbone Cancer Center, during the conduct of the study. Drs. Rose and Hanley have nothing to disclose.

Acknowledgments

This research was supported by grants K07 CA136966 (to ESC) and P30 CA014520 (UW Carbone Cancer Center Support Grant) from the National Cancer Institute, which funded the investigator-initiated trial award for the current study. We would like to acknowledge the UW Center for Sleep Medicine and Research for donating wrist actigraphs for data collection within the cancer sample. We would also like to acknowledge Gayle Love, PhD, Kristofer Hansen, and Carol Ryff, PhD for their collaboration on this project in terms of sharing MIDUS actigraphy data. The MIDUS II research was supported by a grant from the National Institute on Aging (P01-AG020166) to conduct a longitudinal follow-up of the MIDUS I investigation. The research was further supported by the following grants: M01-RR023942 (Georgetown) and M01-RR00865 (UCLA) from the General Clinical Research Centers Program and 1UL1RR025011 (UW) from the Clinical and Translational Science Award (CTSA) program of the National Center for Research Resources, National Institutes of Health. Finally, we would like to thank the patients who participated in this study for their time and effort.

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