# Daily Physical-Rest Activities in Relation to Nutritional State, Metabolism, and Quality of Life in Cancer Patients with Progressive Cachexia

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**Abstract**

**Purpose:** To evaluate daily physical-rest activities in cancer patients losing weight in relation to disease progression.

**Experimental Design:** Physical activity-rest rhythms were measured (ActiGraph, armband sensor from BodyMedia) in relation to body composition (dual-energy X-ray absorptiometry), energy metabolism, exercise capacity (walking test), and self-scored quality of life (SF-36, Hospital Anxiety and Depression Scale) in weight-losing outpatients with systemic cancer (71 $\pm$ 2 years, $n$ = 53). Well-nourished, age-matched, and previously hospitalized non–cancer patients served as controls (74 $\pm$ 4 years, $n$ = 8). Middle-aged healthy individuals were used as reference subjects (49 $\pm$ 5 years, $n$ = 23).

**Results:** Quality of life was globally reduced in patients with cancer ($P < 0.01$), accompanied by significantly reduced spontaneous physical activity during both weekdays and weekends compared with reference subjects ($P < 0.01$). Spontaneous physical activity declined over time during follow-up in patients with cancer ($P < 0.05$). However, overall physical activity and the extent of sleep and bed-rest activities did not differ between patients with cancer and age-matched non–cancer patients. Spontaneous physical activity correlated weakly with maximum exercise capacity in univariate analysis ($r = 0.41$, $P < 0.01$). Multivariate analysis showed that spontaneous physical activity was related to weight loss, blood hemoglobin concentration, C-reactive protein, and to subjectively scored items of physical functioning and bodily pain (SF-36; $P < 0.05$-$0.004$). Anxiety and depression were not related to spontaneous physical activity. Patient survival was predicted only by weight loss and serum albumin levels ($P < 0.01$), although there was no such prediction for spontaneous physical activity.

**Conclusions:** Daily physical-rest activities represent variables which probably reflect complex mental physiologic and metabolic interactions. Thus, activity-rest monitoring provides a new dimension in the evaluation of medical and drug interventions during palliative treatment of patients with cancer.

The understanding of the biological mechanisms behind cancer cachexia has improved considerably in recent years (1). This encouraging situation is explained by extended multidisciplinary efforts to improve patient care including palliative chemotherapy (2), nutritional support (3, 4), systemic anti-inflammatory treatment, and pain treatment (4–7), which are all founded on evidence-based medicine. Our earlier studies of host metabolism in response to progressive malignancy were usually carried out on hospitalized patients, in part due to the application of considerably invasive models (8–10). By contrast, recent randomized controlled studies on palliative support, including long-term nutrition as well as drug and hormonal treatment, were carried out on outpatients in whom measurements of health-related quality of life, body composition, and metabolic characteristics including exercise testing were evaluated (11, 12). Some limitations in such studies were discrepant information between subjective scoring of physical functioning and objective assessment of the patients' exercise capacity. This comparison implied that a number of patients did not entirely recognize significant changes in their physical performance (5). Similar discrepancies have been observed in young individuals operated on for inflammatory bowel disease (13). Therefore, it seems that subjective and objective evaluations of performance may deviate during disease conditions (14). Recent technical developments of convenient and valid instruments for the registration of physical-rest activities during a 24-h period have shown a great deal of promise in the documentation of out-hospital conditions and

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home monitoring (15–19). The aim of this study was therefore to evaluate spontaneous physical-rest activities in relation to disease status as evaluated by nutritional state, energy metabolism, exercise capacity, and health-related quality of life in unselected weight-losing cancer patients.

## Materials and Methods

***Patients.*** Fifty-three patients with cancer (71 ± 7 years: mean ± SD) were included. Thirty-nine of these patients agreed to perform repeated activity-rest measurements of spontaneous physical activity at our outpatient clinic (Table 1). Pancreatic carcinoma was the most common diagnosis. All patients had systemic disease with local, regional, and distant metastases; 54% of all patients underwent surgical exploration in which palliative resection was done in 33% of all patients, whereas 23% of all patients had no specific tumor treatment besides palliative care according to individual needs.

Average weight loss was >10% at the start and follow-up periods. Most patients had systemic inflammation indicated by slightly increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Kidney function and serum calcium were normal. Overall liver function tests were also within normal values or only occasionally above normal limits in most patients. Most patients had increased tumor markers (CEA, CA-125, CA 19-9; Table 2).

All patients that were included in the study ($n$ = 53) were followed up until death or until premortal state (Fig. 1). Reference groups were either recruited from our staff ($n$ = 23; 49 ± 5 years; mean ± SD) or among patients that were recently hospitalized for benign disease ($n$ = 8, 74 ± 4 years) in order to compare activity-resting levels to that in cancer patients in the home setting.

***Biochemical variables.*** Biochemical measurements were done upon inclusion into the study and every 4 months thereafter on a single day at the clinic. Blood tests (RBC and WBC counts, neutrophil, lymphocyte, platelet, and hemoglobin concentrations), serum electrolytes, serum creatinine, ESR, CRP, liver function tests (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and serum bilirubin), and serum albumin levels were all routine hospital tests. Serum CEA, CA-125 and CA19.9 were determined by RIAs as well as serum insulin (Linco Research, Inc.), insulin-like growth factor 1 (Mediagnost), leptin (Linco Research, Inc.), and total ghrelin (Phoenix Peptides).

**Table 1.** Diagnoses, metastatic involvement, and palliative treatment in cancer patients subjected to repeated activity-rest measurements (ActiGraph)

| Group | Follow-up period (mo) | | | |
|---|---|---|---|---|
| | 0 | 4 | 8 | >12 |
| Tumor | | | | |
| Pancreas | 18 | 10 | 6 | 5 |
| Esophagus/ventriculum | 13 | 13 | 5 | 11 |
| Colorectal | 4 | 3 | 2 | 1 |
| Unknown | 3 | 2 | 1 | 0 |
| Other | 1 | 1 | 1 | 5 |
| Metastases | | | | |
| Regional (all) | 19 | 13 | 7 | 15 |
| Liver | 7 | 6 | 1 | 3 |
| Lung | 1 | 3 | 2 | 3 |
| Peritoneum | 2 | 2 | 2 | 0 |
| Other metastases | 3 | 0 | 0 | 0 |
| Surgical exploration | 21 | 14 | 7 | 6 |
| Palliative resection | 7 | 8 | 4 | 12 |
| Chemotherapy | 1 | 1 | 1 | 3 |
| β-Blocker | 7 | 2 | 1 | 1 |
| Steroid | 8 | 4 | 3 | 3 |
| TPN at home | 3 | 2 | 2 | 2 |
| No treatment | 9 | 6 | 3 | 1 |

NOTE: Diagnoses and treatments were similar in this group compared with the entire patient cohort of 53 patients.

***Physiologic variables.*** Measurements at rest included heart rate, and systolic and diastolic blood pressure measured at follow-up every 4 months.

***Nutritional state.*** A diet record was kept to register food intake for 4 days, including one weekend day to account for variations in food intake that might occur between weekdays and weekends (20). Body weight and body composition were assessed every 4th month by the dual-energy X-ray absorptiometry technique as previously described (20).

***Energy expenditure.*** Resting energy expenditure was measured in the morning after an overnight fast by indirect calorimetry (Deltatrac; Datex) at inclusion and every 4 months thereafter, as previously described (21).

***Exercise capacity.*** Exercise testing on a treadmill was initiated with a warm-up period by asking the patient to remain in the standing position with all necessary equipment connected for 1 min followed by continuous walking at 1.5 km/h for 2 min and exponentially increasing the workload by changes in gradient at a 12% range elevation (sine $a$; 6.9 degrees) for 1 min; followed by changes in speed with increases at 0.1 km/h every 10 s. The patients were encouraged to provide maximal effort and to exercise for as long as possible until they were restricted subjectively or objectively. The patient could obviously terminate the test if desired. The speed at which the patient finished the test was defined as maximal exercise power. The maximal mechanical power (W) at exercise was calculated automatically by the software provided by the manufacturer (Cardionics, Inc.) and accounted for body weight, walking speed, and the elevation angle of the treadmill. Oxygen uptake and carbon dioxide production were measured from expired air with a Medical Graphics System CPX equipment (Medical Graphics Corp.) calibrated with 21% oxygen in nitrogen and 12% carbon dioxide in nitrogen before each test as described. Exercise testing was done every 4 months (11, 13, 14).

***Spontaneous physical activity.*** Patients wore an ActiGraph accelerometer (AM 71256, Activity Monitor; ActiGraph). ActiGraph is a small electronic device measuring 2 × 1.5 × 0.6 inches and weighing 1.5 oz placed noninvasively on the nondominant wrist. It continuously records the number of accelerations per minute. At least 3 days of recordings were done in all patients at all conditions. Data were transferred to a computer and analyzed by a program (Ambulatory Monitoring, Inc.). Patients were asked to remove the item only when in contact with water. ActiGraph recordings were analyzed at low, medium, and high activity threshold. Twenty-eight patients were registered several times for follow-up, whereas 25 patients did only one registration (Table 2).

***Sleep and resting conditions.*** Raw data, including movement, heat flux, skin temperature, near-body temperature, and galvanic skin response were measured by a SenseWear $PRO_2$ armband sensor from BodyMedia, body monitoring system (Sensor Medics Italia Srl). This monitoring system was used to measure sleep and resting conditions as important components of the activity-rest rhythm in cancer (22).

***Quality of life.*** Quality of life was estimated from patient scores of items related to daily life such as rest and activity. The SF-36 contains 36 questions assessing eight aspects of the patients' quality of life: physical functioning, role-physical functioning, bodily pain, general health, vitality, social functioning, role emotional functioning, and mental health. Responses to questions within scales were summed and linearly transformed to scale scores that range from 0 (representing poor health status) to 100 (representing optimal health status). The Swedish version

**Table 2.** Clinical characteristics during follow-up of all cancer patients subjected to one or several ActiGraph registrations at home (4-5 d)

| Group | Follow-up period (mo) | | | |
|---|---|---|---|---|
| | 0 | 4 | 8 | >12 |
| Total number of patients at risk | 53 | 38 | 25 | 13 |
| ActiGraph registrations | 39 | 29 | 15 | 22 |
| Age | 71 ± 2 | 70 ± 2 | 67 ± 2 | 61 ± 1 |
| Male/female | 28/11 | 20/9 | 10/5 | 14/8 |
| Weight (kg) | 70 ± 2 | 70 ± 2 | 70 ± 4 | 68 ± 2 |
| Weight loss (%) | 11 ± 1 | 13 ± 2 | 14 ± 2 | 13 ± 2 |
| Hemoglobin concentration (g/L) | 125 ± 2 | 124 ± 2 | 126 ± 4 | 129 ± 2 |
| ESR (mm/h) | 35 ± 3 | 34 ± 5 | 29 ± 5 | 16 ± 2 |
| CRP (mg/L) | 20 ± 5 | 24 ± 7 | 32 ± 12 | 7 ± 1 |
| Serum creatinine (μmol/L) | 89 ± 5 | 83 ± 5 | 73 ± 5 | 74 ± 3 |
| Serum calcium (mmol/L) | 2.3 ± 0.02 | 2.3 ± 0.02 | 2.3 ± 0.03 | 2.3 ± 0.02 |
| Serum ASAT (μkat/L) | 0.6 ± 0.07 | 0.6 ± 0.08 | 0.9 ± 0.2 | 0.6 ± 0.06 |
| Serum ALAT (μkat/L) | 0.6 ± 0.11 | 0.5 ± 0.06 | 0.9 ± 0.3 | 0.5 ± 0.08 |
| ALP (μkat/L) | 2.4 ± 0.2 | 2.5 ± 0.3 | 2.9 ± 0.4 | 2.2 ± 0.5 |
| Serum bilirubin (μmol/L) | 14 ± 2 | 13 ± 2 | 17 ± 4 | 13 ± 2 |
| CEA | 551 ± 344 | 1423 ± 851 | 723 ± 498 | 416 ± 410 |
| CA 125 | 95 ± 20 | 120 ± 38 | 310 ± 157 | 97 ± 37 |
| CA 19-9 | 1,022 ± 326 | 2,576 ± 1427 | 3,905 ± 1601 | 184 ± 155 |

NOTE: Tumor markers: CEA, CA-125, and CA 19-9 (normal values, <30, <5, and <25, respectively). ESR (normal values: <20 for females, <28 for male). CRP (normal value, <5). Liver function tests: serum bilirubin, alkaline phosphatase (ALP), aspartate amino transferase (ASAT), and alanine amino transferase (ALAT; normal values, <5, <1.8, <0.75, and <1.1, respectively). Mean ± SE.

has been validated and normative data have been presented for the general Swedish population as previously described (23, 24). Anxiety and depression were self-scored by the patients by means of the self-assessment Hospital Anxiety and Depression (HAD) scale instrument for use in general hospital outpatients (25, 26).

***Statistics.*** The results in the tables are presented as mean ± SE for the number of surviving and participating patients at each follow-up occasion. Values beyond 12 months were reported as pooled information. Repeated measures were tested statistically by the nonparametric log-rank technique. Univariate correlations were calculated by a *z*-test, and multivariate analyses were done by linear regression analysis; $P < 0.05$ with two-tailed test was regarded as statistically significant. The Committee for Ethics at the Faculty of Medicine, Göteborg University approved the study protocol and each patient provided informed consent.

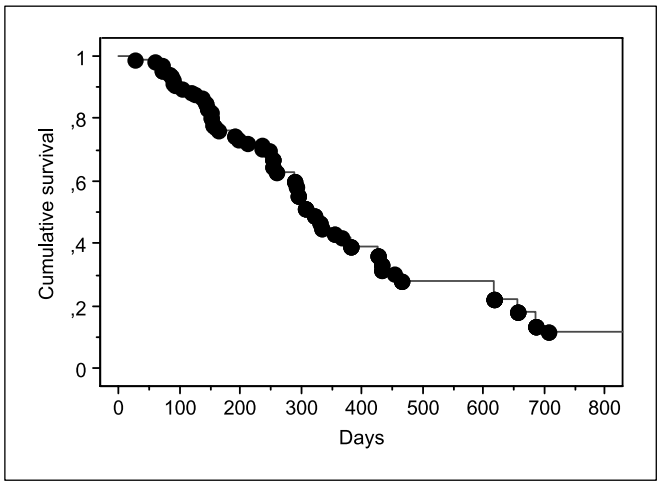


**Fig. 1.** Survival of cancer patients.

## Results

***Daily spontaneous physical activity.*** Self-scored quality of life was globally reduced in the present group of cancer patients compared with normative values in age-matched healthy reference individuals (Table 3). Spontaneous daily physical activity was also significantly reduced in patients with cancer compared with slightly younger and healthy individuals measured both at weekdays and weekends (Fig. 2A), whereas physical-rest activity did not differ from age-matched and recently hospitalized non–cancer patients.

Overall physical activity did not seem to decline in patients with cancer during follow-up (Table 4). This unexpected phenomenon was explained by the fact that patients with short survival had overall worse outcome, more severe status, and lower physical activity than cancer patients with longer survival. Thus, physical activity declined significantly over time when analyzed only in patients subjected to follow-up measurements ($P < 0.05$; Fig. 2B). Most patients showed hypoalbuminemia but had normal plasma glucose levels and subnormal insulin-like growth factor-I levels longitudinally (Table 4). The overall caloric intake was reasonable in most patients with the composition of macronutrients accounting for components of body status and energy expenditure (Table 4). Mean whole body fat and fat-free mass (FFM) remained stable overall during the entire follow-up period similar to physical activity levels (Table 4), but declined on an individual basis. Univariate correlation analyses with nonparametric statistics showed weak but significant correlations between daily spontaneous physical activity, weight loss, ESR, CRP, serum albumin, and whole body FFM in patients with cancer, whereas maximum exercise capacity was correlated with weight loss, ESR, serum albumin, and particularly, FFM (Table 5; Fig. 3A, B, C).

**Table 3.** Global self-scored health-related quality of life in all cancer patients determined by SF-36 and HAD scale (as described in Materials and Methods)

| | Cancer patients | Normative value (65-74 years old) |
|---|---|---|
| SF-36 | | |
| Physical functioning | 62 ± 3* | 70.9-74.2 |
| Bodily pain | 57 ± 4* | 67.4-71.0 |
| General health | 43 ± 3* | 64.4-67.6 |
| Vitality | 43 ± 3* | 67.4-70.7 |
| Social functioning | 62 ± 4* | 85.0-88 |
| Role of emotional functioning | 53 ± 7* | 74.9-79.8 |
| Mental health | 65 ± 3* | 79.9-82.7 |
| Role of physical functioning | 16 ± 5* | 62.5-68 |
| Physical component scale | 35 ± 1* | |
| Mental component scale | 42 ± 2* | |
| HAD scale | | |
| Anxiety | 7.5 ± 1 | 0-7 † |
| Depression | 7.2 ± 1 | 0-7 |

NOTE: Patients are $n = 53$. Subscale scores were measured on occasions when physical and sleep activities were registered. Patients' ages were 68 ± 11 (range, 44-89 years; mean ± SD).
*Significantly outside the 99% confidence limit for normative values.
†A score of 8 to 10 is conditionally bad; 11 to 21 is bad.

Significant univariate correlates (weight loss, blood hemoglobin concentration, ESR, CRP, serum albumin, maximum exercise capacity, and FFM) to spontaneous physical activity were used in the prediction of patient survival by multivariate analysis, in which weight loss ($P < 0.02$) and serum albumin ($P < 0.04$) predicted survival (data not shown). Multivariate stepwise forward regression analysis was done with daily spontaneous physical activity as the dependent variable versus weight loss, blood hemoglobin concentration, ESR, CRP, serum albumin, plasma glucose, serum insulin-like growth factor-I, serum insulin, serum FFA, whole body fat, whole body FFM, and daily caloric intake as independent variables chosen as potentially important to either explain or become changed during cancer progression (Table 6). Weight loss, blood hemoglobin concentration, and CRP explained the variability in daily spontaneous physical activity (Table 6). Multivariate stepwise forward regression analysis with daily physical spontaneous activity as the dependent factor versus all subjectively scored items in SF-36 and the HAD scale as independent factors showed that only subjectively scored physical functioning and bodily pain predicted objectively measured physical activity ($P < 0.0001$; data not shown). Anxiety and depression did not predict spontaneous physical activity. The same calculation with maximum exercise capacity as the dependent factor indicated that serum albumin and FFM predicted exercise capacity ($P < 0.0001$; Table 6).

***Sleep and rest activity.*** Cancer patients slept each night (at home) to the same extent as well-nourished age matched non–cancer patients (494 ± 23 versus 483 ± 58 min), whereas younger healthy individuals slept significantly less per night (399 ± l4 min; $P < 0.007$). Weight loss, systemic inflammation (CRP, blood hemoglobin concentration, SR, serum albumin), and caloric intake (kcal/d) predicted with borderline significance the extent of sleep in cancer patients ($P < 0.07$). Items used for self-scored quality of life (SF-36), anxiety (HAD, part 1), and depression (HAD, part 2) did not predict the extent of sleep in our patients with cancer (multivariate analysis), whereas bodily pain (BP, SF-36) showed a weakly significant correlation to extent of sleep in univariate analysis ($P < 0.05$).

## Discussion

The hallmark in the evaluation of treatment efficacy in medicine is disease-specific mortality or patient survival. Randomized studies powered to provide such information demands a large number of patients. Therefore, self-scored health-related quality of life has become increasingly important as surrogate markers, although quality of life measures are themselves necessary to judge the subjective perspective of medical treatments. It is however always important to add complementary objective measures on outcome (27). In our own studies, we relied on measurements of metabolism (hormones, energy expenditure, substrate flux, etc.), body composition, and exercise capacity as objective criteria in the palliative treatment of cancer cachexia (3–7, 11). A limitation

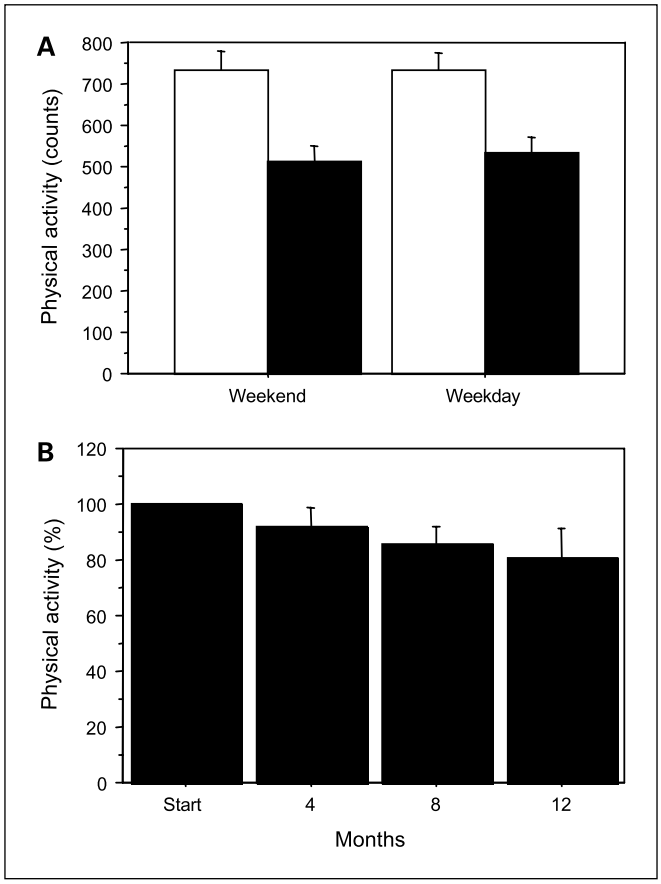


**Fig. 2.** *A,* average spontaneous daily physical activity in patients with cancer (*filled columns, n* = 53) during weekends and weekdays compared with the same measurements in the reference group of healthy volunteers (*empty columns, n* = 23; $P < 0.01$). *B,* alterations in the percentage of overall daily physical activity in those cancer patients who were subjected to more than two repeated measurements over time ($P < 0.05$, $n = 28$). All measurements were done by ActiGraph monitoring.

**Table 4.** Spontaneous physical activity and maximum exercise capacity in relation to body composition, blood biochemistry, and dietary intake during follow-up in cancer patients

| Group | Follow-up period (mo) | | | |
|---|---|---|---|---|
| | 0 | 4 | 8 | >12 |
| Daily physical activity (counts) | 627 ± 48 | 718 ± 80 | 513 ± 306 | 753 ± 88 |
| Maximum exercise capacity (W) | 103 ± 10 | 103 ± 12 | 133 ± 8 | 124 ± 11 |
| Resting heart rate ($min^{-1}$) | 71 ± 1 | 70 ± 2 | 73 ± 2 | 68 ± 2 |
| Blood pressure (mm Hg) | 137/78 | 138/77 | 132/76 | 133/76 |
| Resting energy expenditure | 1,503 ± 37 | 1,489 ± 49 | 1,509 ± 66 | 1,476 ± 63 |
| Caloric intake (kcal) | 1,859 ± 110 | 1,834 ± 195 | 2,077 ± 242 | 2,048 ± 384 |
| Protein intake (g/d) | 73 ± 4 | 67 ± 7 | 85 ± 13 | 67 ± 7 |
| Fat intake (g/d) | 77 ± 6 | 79 ± 10 | 89 ± 16 | 73 ± 7 |
| Carbohydrate intake (g/d) | 205 ± 12 | 211 ± 22 | 225 ± 18 | 180 ± 14 |
| Whole body fat (kg) | 14.1 ± 1.1 | 16.9 ± 1.9 | 32.8 ± 7.4 | 19.9 ± 3.2 |
| FFM (kg) | 50.2 ± 2.4 | 50.4 ± 3.4 | 63.7 ± 4.0 | 56.0 ± 3.2 |
| Serum albumin (g/L) | 35.1 ± 1 | 36 ± 1 | 33 ± 2 | 37 ± 1 |
| Plasma glucose (mmol/L) | 6.4 ± 0.3 | 7.3 ± 0.6 | 7.1 ± 0.7 | 5.9 ± 0.5 |
| Insulin-like growth factor-I (nmol/L) | 118 ± 9 | 125 ± 22 | 99 ± 13 | 110 ± 7 |

NOTE: Patients at risk are shown in Table 2 (mean ± SE).

of such measurements may be that in-hospital conditions are overemphasized, although changes in body composition reflect long-term alterations (3). Thus, it is of interest to apply recent techniques for monitoring daily physical-rest activities in cancer patients at their home environment. The ActiGraph and SenseWear Armband accelerometer techniques have been previously used for monitoring physical activity, physical functioning, rest-activity rhythms, and sleep-work cycles in a variety of clinical conditions (28–34). The present study was aimed at evaluating the relationships between overall daily physical-rest activities to whole body metabolism and nutritional state which is known to either explain or indirectly reflect the progression of cachexia in transsectional analyses. Repeated measurements were also done on patients willing to allow re-investigations. Our results confirm that unselected weight-losing cancer patients display decreasing spontaneous physical activity along with the progression of their disease, in line with previous reports (35, 36). This reduction was similar in magnitude across both weekends and weekdays compared with activities in healthy and younger individuals, but did not differ from physical-rest activities in age matched control patients without cancer.

Univariate correlations showed weak but significant relationships between a substantial number of variables reflecting systemic inflammation, nutritional state, and maximum exercise capacity in cancer (Table 5). Multivariate regression analysis was used to compare the prediction power of physical activity among such independent variables. These calculations show that weight loss was a major factor predicting variability in spontaneous physical activity, followed by blood hemoglobin concentration, and CRP. Self-scored physical functioning and bodily pain (items in SF-36) also predicted variations in overall daily physical activity (Table 6). This is important because self-scored physical functioning was not related to objectively measured exercise capacity in earlier studies on patients with and without cancer (5, 13), nor to blood hemoglobin concentration in the present multivariate evaluation. Maximum exercise capacity is a reliable measure of muscular and cardiovascular function, but it may also be dependent on other factors such as mental status to sustain relative hypoxia during exercise and corresponding translocation of acid metabolites across the blood-brain barrier (12, 37). Therefore, spontaneous physical activity was compared with maximum exercise capacity in univariate analyses (Fig. 3C). It was obvious that different independent variables predicted alterations in physical activity and exercise capacity, although a weak correlation between physical activity and physical capacity occurred. Thus, out-hospital measures of spontaneous physical activity, assessed by actigraphs, may or may not indicate alterations in the functional cardiovascular and organ capacities of patients.

It is unclear how spontaneous physical activity is controlled in daily life in health and disease (38–41). Tissue metabolism is dependent on the oscillation of afferent and efferent neuroendocrine signals of which a majority has been reported to be altered in progressive cancer. Many of these oscillating circuits are characterized by circadian periods and their

**Table 5.** Univariate nonparametric correlations between spontaneous physical activity and maximum exercise capacity, and measures of nutrition (weight loss, FFM) and inflammation (ESR, CRP, serum albumin) in cancer patients

| | SPA* | *P* | ME* | *P* |
|---|---|---|---|---|
| Weight loss (%) | -0.36 | <0.0002 | -0.30 | <0.02 |
| ESR (mm/h) | -0.27 | <0.006 | -0.37 | <0.003 |
| CRP (mg/L) | -0.28 | <0.004 | - | NS |
| Serum albumin (g/L) | 0.48 | <0.0001 | 0.29 | <0.02 |
| FFM (kg) | -0.35 | <0.0003 | 0.55 | <0.0001 |
| ME (W) | 0.41 | <0.009 | — | NS |

NOTE: Whole body FFM.
Abbreviations: SPA, spontaneous physical activity; ME, maximum exercise; NS, not significant.
*Spearman rank correlation coefficient based on results from 49 cancer patients.

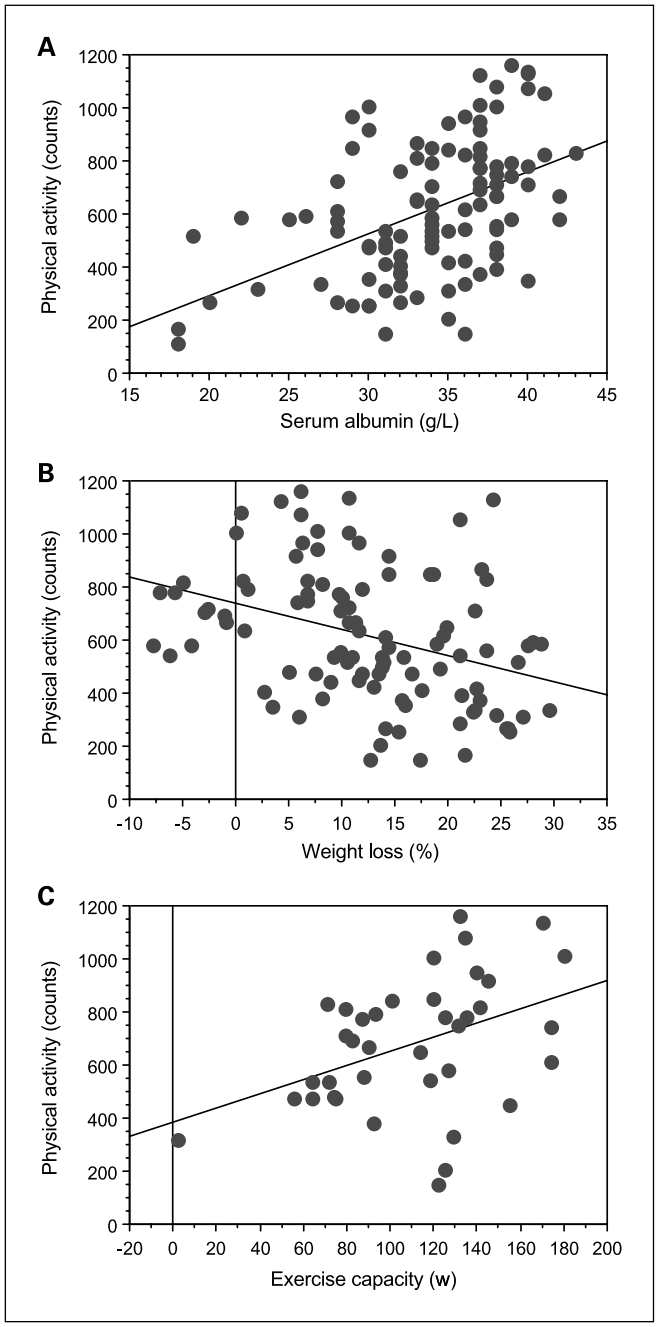


**Fig. 3.** *A – C,* the relationship between daily physical activity and serum albumin ($r = 0.47$; $P < 0.001$), weight loss ($r = 0.36$; $P < 0.0002$), and maximum exercise capacity ($r = 0.41$; $P < 0.01$) in patients with cancer.

synchronization integrates the many physiologic and behavioral processes required to meet the challenge of daily life (36, 42). Earlier actigraph studies have reported abnormal circadian function in hospitalized cancer patients on chemotherapy when compared with outpatients in their home setting (29, 43). Such investigations showed that daily sleep patterns were disturbed and translated into disruption of quality of life in patients with advanced lung cancer (43). Also, cancer-related fatigue in relapse-free patients with previous hematologic malignancies and depressed mood was related to decreased physical activity, rather than to anemia, endocrine, and immunologic alterations (39). Others have reported that cachexia-related fatigue may be correlated with and predicted by physical performance and body composition (44). Thus, clinical information on relationships between tumor growth, treatment response, cancer-related fatigue, the appearance of cachexia, and physical activity are certainly very complex but important to understand, particularly when information shows that palliative treatment attenuates symptoms and improves patient status (45). Thus, it is obvious that systemic inflammation, nutritional state, exercise, and living habits as well as stress factors are all relevant in mind-body medicine in patients with or without cancer (46–49). For example, we have recently used the accelerometer technique in monitoring cancer patients under treatment with insulin in a randomized study to attenuate cachexia (50), in which insulin treatment improved the metabolism and prolonged survival but without being related to increased spontaneous daily physical activity, which was unexpected. Therefore, more research is needed to better understand integrative physiologic changes including neurohumoral, mental, metabolic, and nutritional disorders in progressive cancer.

In conclusion, spontaneous physical activity seems to be an important reflector of complex physiologic interactions among organs and tissues in daily life, and the control of behavior by the central nervous system during health and disease. Activity-rest monitoring techniques provide additional tools for the evaluation of aspects on medical interventions in cancer disease. For example, it was obvious that different factors predicted alterations in spontaneous physical activity and physical capacity.

**Table 6.** Multivariate stepwise forward regression analysis with daily spontaneous physical activity or maximum exercise capacity as dependent factors versus measures of systemic inflammation (blood hemoglobin concentration, CRP, serum albumin) and nutritional state (weight loss, FFM) as independent variables in cancer patients

| Independent variables | | Coefficient | *P* |
|---|---|---|---|
| Weight loss (%) | SPA | -8.7 | <0.0006 |
| | ME | — | NS |
| Hb | SPA | -3.7 | <0.04 |
| | ME | — | NS |
| CRP | SPA | -1.4 | <0.04 |
| | ME | — | NS |
| Serum albumin | SPA | — | NS |
| | ME | 3.0 | <0.0001 |
| FFM | SPA | — | NS |
| | ME | 2.0 | <0.0001 |
| PF (SF-36) | SPA | 2.9 | <0.004 |
| | ME | 0.8 | <0.0001 |
| BP (SF-36) | SPA | 1.8 | <0.05 |
| | ME | -0.5 | <0.001 |

NOTE: The multivariate regressions were significant at $P < 0.001$. Abbreviations: SPA, spontaneous physical activity ($R = 0.56$, adjusted $R^2$ 0.27; $n = 98$ measurements in 49 cancer patients); ME, maximum exercise capacity ($R = 0.67$, adjusted $R^2$ 0.43; $n = 66$ measurements in 49 cancer patients); Hb, blood hemoglobin concentration (g/L); PF, physical functioning; BP, bodily pain.

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