




# PREOPERATIVE PHYSICAL ACTIVITY LEVELS AND POSTOPERATIVE BURDEN IN CANCER PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

## NÍVEIS DE ATIVIDADE FÍSICA PRÉ-OPERATÓRIA E PROGNÓSTICO PÓS-CIRÚRGICO EM DOENTES ONCOLÓGICOS: UM ESTUDO OBSERVACIONAL PROSPETIVO

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### ABSTRACT

**Introduction:** There is a growing interest to understand the impact of preoperative physical activity (PA) levels in postoperative morbidity and mortality. The aim of this study is to assess the levels of PA in patients with head/neck or gastric cancer through accelerometry and compare postoperative burden among those “complying” or “not complying” with PA recommendations. **Methods:** We conducted an observational, longitudinal and prospective study in newly diagnosed patients with gastric or head/neck cancer, recruited at IPO-Porto. The levels of PA were evaluated through accelerometry. Data about postoperative burden (complications, length of hospital stay and mortality) were collected from clinical records. **Results:** A total of 81 patients were recruited, mostly men (76.5%), with an average age  $61.8 \pm 11.55$  years,  $69.08 \pm 15.55$  kg of weight and a BMI of  $25.82 \pm 5.29$  kg/m<sup>2</sup>. Fifty-four patients had a diagnosis of gastric cancer (66.7%) and 27 had head/neck cancer (33.3%). Patients spent 54% of their wearing time in sedentary behavior, 42% in light PA, and 4% in moderate to vigorous PA. Their median weekly MVPA was 132 (3-1860) min, and only 46.9% of patients accomplished the minimum amount of MVPA/week recommendations. No differences were noted among gastric and head/neck cancer patients. Regarding postoperative burden, 23.4% of patients had minor complications and 12.5% had major complications. The length of hospital stay was  $13.86 \pm 15.58$  days and 9.9% deaths occurred after surgery. Postoperative mortality was superior among those patients “not complying” with international recommendations of PA (7 vs. 1 death). **Conclusion:** Our data suggests that high preoperative PA levels may decrease the risk of postoperative mortality. Assessing preoperative levels of PA could bring value to identify those patients at greater risk of surgical burden and guide them to intervention designed to mitigate that risk by increasing their physical activity, such as prehabilitation.

**Keywords:** *preoperative physical activity levels; cancer; postoperative complications; length of stay; mortality.*

### RESUMO

**Introdução:** Há um interesse crescente em entender o impacto dos níveis de atividade física (AF) pré-operatória na morbimortalidade pós-operatória. O presente trabalho teve como objetivo avaliar os níveis de AF em doentes com cancro da cabeça/pescoço ou estômago e comparar o desfecho pós-operatório entre aqueles que “aderem” ou “não aderem” às recomendações de AF.



**Métodos:** Foi realizado um estudo observacional, longitudinal e prospectivo em doentes recém-diagnosticados com cancro da cabeça/pescoço ou estômago, recrutados no IPO-Porto. Os níveis de AF foram avaliados por acelerometria. Os dados sobre o desfecho pós-operatório (complicações, tempo de internamento e mortalidade) foram consultados nos registos clínicos. **Resultados:** Foram recrutados 81 doentes, a maioria homens (76,5%), com idade média de  $61,8 \pm 11,55$  anos, peso de  $69,08 \pm 15,55$  kg e IMC de  $25,82 \pm 5,29$  kg / m<sup>2</sup>. Cinquenta e quatro doentes tinham diagnóstico de cancro do estômago (66,7%) e 27 tinham cancro da cabeça/pescoço (33,3%). Os doentes passaram 54% do tempo de uso em comportamento sedentário, 42% em AF leve e 4% em AF moderada a vigorosa (AFMV). A mediana semanal de AFMV foi de 132 (3-1860) min, e apenas 46,9% dos doentes cumpriram as recomendações mínimas de AFMV / semana. Não foram observadas diferenças entre os doentes cancro da cabeça/pescoço ou estômago. Em relação ao desfecho pós-operatório, 23,4% dos doentes apresentaram complicações menor e 12,5%, complicações maior. O tempo de internamento hospitalar foi de  $13,86 \pm 15,58$  dias e ocorreram 9,9% mortes no período pós-operatório. A mortalidade pós-operatória foi superior entre os doentes que ou “não aderem” as recomendações internacionais de AF (7 vs. 1 óbito). **Conclusão:** Os nossos dados sugerem que níveis elevados de AF no pré-operatório reduzem o risco de mortalidade pós-operatória. A avaliação dos níveis de AF pré-operatória poderá auxiliar na identificação dos doentes com maior risco cirúrgico e orientá-los para intervenções de otimização pré-operatória, como a pré-habilitação.

**Palavras-chave:** nível de atividade física pré-operatória; cancro; complicações pós-operatórias; tempo de hospitalização; mortalidade.

## INTRODUCTION

It is estimated that approximately 80% of cancer patients, at some point in their journey, will need surgical treatment, with some of them undergoing multiple surgical interventions<sup>1</sup>. Despite its key role in cancer management, surgery is not free of adverse effects, being a significant source of morbidity and mortality, largely because of postoperative complications (POC)<sup>2</sup>. The occurrence of complications in the postoperative period severely limits the prognosis of the cancer patient undergoing surgery. It may weaken the patient, delay subsequent treatments and reduce its potential beneficial effects, prolong the hospital stay, increase the risk of hospital readmission and the need for continued care, increase costs, decrease the quality of life and precipitate premature death<sup>3-8</sup>. There is also evidence that POC can induce a long-lasting suppressive effect on patients' immune systems, making them more susceptible to recurrence of the neoplasia<sup>9-11</sup>. An association between POC (major and minor) and disorders of the patient's psychosocial well-being, namely with high levels of stress and depression, was also demonstrated up to 12 months after surgery<sup>12</sup>. Thus, preventing postoperative burden is imperative for

the delivery of high quality-care and improvement of patient outcomes.

Significant epidemiologic evidence supports the negative impact of physical inactivity and sedentary behavior on the health of cancer survivors, while being physically active has been associated with lower risk of all-cause and cancer-specific mortality for breast, colorectal and prostate cancer<sup>13,14</sup>. Several other cancer-related health outcomes also seem to be positively modulated by physical activity (PA), particularly structured exercise training, such as anxiety, depression, fatigue, health-related quality of life, lymphedema, physical function, bone health and sleep<sup>15</sup>. In addition, many cancer patients have concomitant comorbidities such as cardiovascular, metabolic, musculoskeletal and psychological disorders and PA may have a role in the management of these conditions<sup>16</sup>. These beneficial effects of PA/exercise have been mainly observed when PA/exercise was performed during systemic/adjuvant treatment or survivorship (after ending treatments)<sup>17</sup>. However, there is a growing interest to understand the impact of PA levels/exercise training to optimize patients to better support treatments, particularly surgery. A recent meta-analysis found that higher levels of PA in cancer patients undergoing surgery were associated



with shorter length of hospital, better postoperative quality of life, but not with reduced postoperative complications<sup>18</sup>. Nevertheless, this study also highlighted the lack of high-quality evidence on the association between preoperative PA levels and postoperative outcomes in cancer patients undergoing surgery. This was attributed in part to the heterogeneity between included studies in terms of PA assessment, which was mainly through questionnaires. It has been shown that cancer patients overestimate their self-reported PA level by 366% when compared to objective measures<sup>19</sup>.

Thus, the association between objectively measured PA levels and postoperative outcomes needs to be further explored. Small and wearable PA monitors, particularly accelerometers, are continually being refined as potentially very useful techniques in the accurate and detailed measurement of free-living PA<sup>20</sup>. Such information would help health care providers to better predict the risk of postoperative burden and thus guide on patient selection, to determine which thresholds of preoperative PA levels are associated with a greater risk of postoperative morbidity and mortality, and to identify those patients who need to be optimized before surgery with a prehabilitation program. The purpose of this work was to characterize preoperative PA levels (measured by accelerometry) in patients with gastric or head and neck cancer and compare postoperative burden among those “complying” or “not complying” with PA recommendations.

## METHODS

### Study Design

This is an observational, longitudinal and prospective study. The data were collected at the Instituto Português de Oncologia, Porto (IPO-Porto), in the departments of Head and Neck Cancer and Gastrointestinal Cancer. The study has been approved by the ethical committee of the IPO-Porto (CES-IPOP 03,193/016).

## Participants

Consecutive patients were recruited every Monday morning, between December 2018 and July 2019. All participants were informed about the aim of this investigation. Inclusion criteria were: i) patients diagnosed with gastric or head and neck cancer; ii) in the preoperative phase; iii) aged 18 years or older; iv) both sexes; v) returning the signed informed consent.

## Measurements

All patients were assessed in the preoperative period for general characterization (age, gender, weight, height, body mass index, marital status, educational level, and type of cancer) and PA assessment using accelerometry. Patients were instructed to wear an accelerometer (Actigraph GT3X model; Pensacola, FL, USA), on the right hip for seven consecutive days. They were instructed to maintain their daily routine and to remove the device only at the time to sleep, for showering or for activities that involved water. All physical active minutes during all valid wearing time were divided by the number of valid wear days, in order to calculate the mean number of minutes of PA per day. Accelerometers were programmed to record data in 1-second epochs (counts/min) and subsequently converted to 60-second epochs. The following cutoff points were used to differentiate PA levels: sedentary time (0 – 200 counts/min), Light PA (200 – 2689 counts/min) and Moderate to Vigorous PA (MVPA) ( $\geq 2690$  counts/min)<sup>21,22</sup>. We also measured the number of daily steps. The data were downloaded and analyzed using the software ActiLife (Actigraph, Florida, EUA, version 6.13.4).

The following postoperative data was collected from clinical records in May 2020 by an experienced outcome researcher from the IPO-Porto, with no previous involvement on the project and no knowledge about the purpose of the study: postoperative



complications and its severity according to Clavien-Dindo classification<sup>23</sup>, length of hospital stay (number of days), postoperative mortality (number of deaths that occurred after surgery).

## Data Analysis

The data were organized in Microsoft Office Excel software and analyzed using SPSS (version 26, USA). Kolmogorov-Smirnov and Shapiro-Wilk test were used to assess normality of the data. Data are presented in frequency (%), mean (SD) or median (min-max) as appropriate. To analyze the difference

between groups, the T-student test and Mann-Whitney test were used as appropriate. Results were considered statistically significant when  $p < 0.05$ .

## RESULTS

### General features of our sample and postoperative burden

Table 1 summarizes the general baseline features and postoperative burden. We assessed a total of 81 patients, mostly men (76.5%), with an average age  $61.8 \pm 11.55$  years,  $69.08 \pm 15.55$  kg of weight and a

TABLE 1 – General baseline features and postoperative burden

		Total	Gastric	Head and Neck	p
Patients, n (%)		81(100)	54 (66.7)	27 (33.3)	
Gender, n (%)	Male	62 (76.5)	38 (70.4)	24 (88.9)	0.064
	Female	19 (23.5)	16 (29.6)	3 (11.1)	
Age (years)		$61.8 \pm 11.55$	$62.85 \pm 12.37$	$59.74 \pm 9.582$	0.336
Weight (kg)		$69.08 \pm 15.55$	$70.87 \pm 15.80$	$65.81 \pm 15.03$	0.172
Height (m)		$1.64 \pm 0.08$	$1.64 \pm 0.07$	$1.63 \pm 0.09$	0.824
BMI	median $\pm$ DP	$25.82 \pm 5.29$	$26.49 \pm 5.48$	$24.68 \pm 4.81$	0.031
	< 18.5	3 (3.7)	0	3 (11.1)	
	18.5 – 24.9	32 (39.5)	19 (35.2)	13 (48.1)	
	25 – 29.9	33 (40.7)	25 (46.3)	8 (29.6)	
	30 – 34.9	10 (12.3)	8 (14.8)	2 (7.4)	
	> 35	1 (1.2)	0	1 (3.7)	
Surgery, n (%)		64 (79)	41 (75.9)	23 (85.2)	0.335
Postoperative complications	Without, n (%)	41 (64.1)	26 (48.4)	15 (65.2)	0.465
	Minor, n (%)	15 (23.4)	9 (16.7)	6 (26.1)	
	Major, n (%)	8 (12.5)	6 (11.1)	2 (8.7)	
Length of hospital stay	Number of days, median (min-max)	9 (1-105)	9 (1-61)	8 (2-105)	0.129
	$\leq 5$ , n	10	4	6	0.087
	> 5, n	54	37	17	
Postoperative mortality, n (%)		8 (9.9)	2 (4.9)	6 (26.1)	0.012



BMI of  $25.82 \pm 5.29$  kg/m<sup>2</sup>. Fifty-four patients had a diagnosis of gastric cancer (66.7%) and 27 had head/ neck cancer (33.3%). Body mass index was significantly different among patients with gastric and head/ neck cancer.

From the 81 patients that were initially scheduled for surgery, only 64 (41 patients with gastric cancer and 23 with head/ neck cancer) were indeed submitted to surgical treatment. Exclusion from surgery was due to disease progression and deterioration of medical condition (n=7) or death (n=10). From those submitted to surgical treatment, 41 (64.1%) had no postoperative complications (26 patients with gastric cancer and 15 with head/ neck cancer), 15 (23.4%) had minor complications (9 patients with gastric cancer and 6 with head/ neck cancer) and 8 (12.5%) had major complications (6 patients with gastric cancer and 2 with head/ neck cancer). On average, the length of hospital stay was  $13.86 \pm 15.58$  days (12.73 days for patients with gastric cancer and 15.87 days for patients with head/ neck cancer). A total of 8 deaths (9.9%) occurred after surgery (2 patients with gastric cancer and 6 with head/ neck cancer).

## Characterization of physical activity levels

Table 2 shows the preoperative levels of PA. On average, participants wore the accelerometer for an average of  $6.78 \pm 0.73$  days, with a daily use of  $12.47 \pm 1.86$  hours per day. An average of  $5730.06 \pm 3395.01$  steps per day have been recorded by pedometer. No significant changes were detected between patients with gastric cancer and patients with head/ neck cancer. The total sample spent a mean of  $2708.20 \pm 743.18$  minutes/week,  $2160.75 \pm 921.26$  minutes/week, 132 (3-1851) minutes/week and 1 (0-144) minutes/week in sedentary, light, moderate and vigorous activity, respectively. Thus, participants spent the majority of their wearing time in sedentary behavior (54% of their time), followed by light PA (42% of their time) and lastly in MVPA (4% of their time). Their mean weekly MVPA was 132 (3-1860) min, which is below the recommended levels, and only 38 participants (27 patients with gastric cancer and 11 patients with head/ neck cancer) accomplished the PA recommendations of MVPA. When patients were classified by their PA levels, we observed that 53% were considered “insufficiently active”, 24% as “active” and 23% as “highly active”. No significant changes were noted between patients with gastric or head/ neck cancer.

TABLE 2 – Characterization of preoperative physical activity levels

	Total	Gastric	Head and Neck	p	
<b>Accelerometer use, days/week</b>	7 [3-7]	7 [3-7]	7 [4-7]	0.149	
<b>Accelerometer use, hours/day</b>	$12.47 \pm 1.86$	11.93 [10-15.89]	$12.49 \pm 1.7$	0.535	
<b>Daily steps, n/day</b>	$5730.06 \pm 3395.01$	$6058,64 \pm 3485.15$	$5072,91 \pm 3167.41$	0.155	
<b>Physical Activity Level, min/week</b>	Sedentary	$2708.20 \pm 743.18$	$2676.85 \pm 766.71$	0.595	
	Light	$2160.75 \pm 921.26$	$2221.70 \pm 913.53$	0.403	
	Moderate	132 [3-1851]	150 [3-1190]	130 [5-1851]	0.314
	Vigorous	1 [0-144]	1 [0-144]	1 [0-17]	0.920
<b>MVPA (min/week)</b>	132 [3-1860]	150.50 [3-1219]	131 [6-1860]	0.302	
<b>Complying with PA Guidelines, n (%)</b>	38 (46.9)	27 (50)	11 (40.7)	0.437	



## Characterization of postoperative burden by physical activity levels

For this analysis, we categorized patients by “complying” or “not complying” with the international recommendations of PA (150 min/MVPA/week). In addition, because no differences were noted between gastric and head/ neck cancer patients, we combined their data to increase the sample size for analysis. Postoperative mortality, postoperative complications and length of stay hospital were superior among those patients not complying with international recommendations, but statistical differences were found only for postoperative mortality (Table 3).

## DISCUSSION

The aim of this observational, longitudinal and prospective study was to characterize preoperative levels of PA, measured by accelerometry, and compare postoperative burden among those “complying” or “not complying” with PA recommendations. The results of this study indicate that those patients complying with PA recommendations are at lower risk of postoperative death.

In the current study, 35.9% of the patients had postoperative complications, mostly minor. The complication rate among patients with gastric cancer was 16.7% for minor and 11.1 for major, while in

head/ neck patients the rate was 26.1 for minor and 8.7 for major complications, which is in the range of the values described in the literature for these patients<sup>24-27</sup>. Postoperative mortality rate was 9.9% when considering the overall sample, 4.9% when just considering gastric cancer patients and 26.1% when just considering head/ neck cancer patients, which is higher than published values<sup>28-31</sup>. We believe that this could be due to clinical differences. For instance, cachexia is a major risk factor for postoperative complications<sup>32</sup>. Despite we did not evaluate this variable, we found significant differences in BMI among head/ neck and gastric patients, with the former presenting a higher rate of patients in the underweight category. Also, unhealthy lifestyle habits like smoking and alcohol drinking are highly prevalent in this type of cancer and are also major risk factors for postoperative complications<sup>33</sup>. The average length of hospital stay was 13.86 days for the entire cohort and ranged from an average of 12.73±1.28 days (for gastric patients) to 15.87±22.29 days (for head/ neck patients), with a greater proportion of gastric cancer patients spending more than 5 days in hospital. This might be explained in part by the greatest postoperative mortality rate that was observed among head/ neck cancer patients.

We found that 53% of our patients did not comply with the amount of MVPA recommended by the international guidelines on PA<sup>34</sup> and thus were classified as insufficiently active, spending 61% of their weekly time in sedentary behavior, 31% in

TABLE 3 – Comparison of postoperative outcomes between patients complying and not complying with the recommendations of physical activity

	Not complying	Complying	P value
Postoperative mortality, n (%)	7 (87.5)	1 (12.5)	<b>0.019</b>
<b>Postoperative complications, n (%)</b>			
<b>Total</b>	18 (62.1)	23 (65.7)	0.798
<b>Minor</b>	9 (31)	6 (17.1)	0.193
<b>Major</b>	2 (6.9)	6 (17.1)	
<b>Length of hospital stay, median(min-max)</b>	9 [2-61]	9 [1-105]	0.485



light activity and only 1% in MVPA. This is in line with previous reports in newly diagnosed cancer patients, before starting their treatment<sup>35,36</sup>. We also found that postoperative mortality occurred less frequently in patients performing >150 min/week of MVPA, as previously reported for major oncological abdominal surgery<sup>37</sup>. This finding suggests that increasing PA levels during the preoperative period may be of benefit. Thus, preoperative PA levels should be assessed, and those patients with poor preoperative PA levels should be instructed to increase their activity levels. Such an intervention could be encouraged in the weeks before surgery. This is known as prehabilitation and several studies support the efficacy of this intervention to improve physical capacity and to reduce postoperative morbidity and mortality in cancer patients submitted to abdominal or thoracic surgery<sup>38-41</sup>.

We did not find any differences for postoperative complications or length of hospital stay among patients complying or not complying with PA guidelines. A previous meta-analysis suggested that higher levels of preoperative PA in patients undergoing cancer surgery were associated with shorter length of hospital stay, but not postoperative complications<sup>18</sup>. We believe that this deserves further attention in future studies as in addition to its severity, complications must be interpreted according to their type (surgical vs. non-surgical). Surgical complications are related to surgical procedures or techniques (e.g. bleeding, leaks, sepsis due to leaks etc.) while non-surgical complications are related to the patient's physiological health or comorbidities (e.g., acute kidney injury, acute respiratory failure, preexisting sepsis, etc.)<sup>42</sup>. We could not discriminate which type of complications were more frequent in our study population. If surgical complications were the most prevalent, it is conceivable that a higher PA level could do little to prevent them, as these are not related to the patient's physiological reserve. A previous study using prehabilitation in high-risk patients for undergoing elective major abdominal surgery

showed that the intervention reduced the number of medical complications but had no effect on surgical complications<sup>43</sup>.

## LIMITATIONS

This study has some limitations. First, the small sample size limited the analysis, particularly the comparisons between cancer type. Second, this was a single-center study, which can limit the generalization of the results. Third, the relationship between preoperative PA and postoperative outcomes may be influenced by factors such as age, gender, frailty, comorbidities, cancer stage. This should be investigated in future studies. Fourth, while the use of accelerometry should be preferred over self-reported questionnaires, accelerometers are expensive and require technical expertise, specialized hardware, software, and individual programming. Future studies should test the utility of less expensive and broadly available wearable devices for monitoring and tracking PA (e.g. smartphone apps, smart watches, fitness band, pedometers). Finally, a better characterization of postoperative complications (e.g., rate of surgical and non-surgical) would be of additive value to understand which were more prevalent and which were associated with physical inactivity.

## CONCLUSION

Our data suggests that having a high preoperative PA level may decrease the risk of postoperative mortality. Assessing preoperative levels of PA could bring value to identify those patients at greater risk of surgical burden. In addition, it could provide guidance to identify those patients who could benefit most from optimization programs (e.g. prehabilitation). At the minimum, patients should be encouraged by their clinicians to increase/maintain their PA levels in the weeks before surgery.



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