



Risk factors and postoperative complications in oncologic surgeries

Fatores de risco e complicações pós operatórias em cirurgia oncológica

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Abstract

Introduction: Oncological patients who are submitted to surgical procedures might have postoperative pulmonary complications (PPCs). Thus, preoperative physical conditions must be considered, since it is an important predictor of postoperative development. **Objective:** The purpose of this study was to analyze the risk factors for postoperative pulmonary complications that might compromise the recovery after oncologic surgery. **Method:** The present observational transversal study was made between March and October of 2015. Patients diagnosed with cancer were analyzed to determine pulmonary and functional condition and to identify the risk factors for the development of PPCs. The post-surgery recovery was followed through medical records. Data collected from patients' analyses was correlated with post-surgery development. **Results:** Thirty patients were analyzed. A negative and moderate correlation was found between maximal inspiratory pressure (MIP) and PPCs ($r=-0.39$; $p=0.032$). A positive correlation between the time of permanence in the Intensive Care Unit (ICU) and hospitalization days ($r=0.40$; $p=0.02$) was observed. Correlations between PPCs and mechanical ventilation ($r=0.36$; $p=0.04$) and hospitalization days ($r=0.40$; $p=0.02$) were also noticed in the present study. **Conclusion:** PPCs might prejudice post-surgery outcome. The greater are physical condition and pulmonary functions of the patients before surgery, the better is their recovery.

Keywords: Surgery. Cancer. Post-Surgery Complications. Pulmonary Function. Physiotherapy.

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Resumo

Introdução: Pacientes oncológicos submetidos a procedimentos cirúrgicos podem apresentar complicações pulmonares no pós-operatório. A condição física pré-operatória deve ser considerada, pois é um importante preditor do desenvolvimento pós-operatório. **Objetivo:** Analisar os fatores de risco para complicações pulmonares pós-operatórias (CPPO) que podem comprometer a recuperação após a cirurgia oncológica. **Método:** O presente estudo observacional transversal foi realizado entre os meses de março e outubro de 2015. Pacientes oncológicos participaram de uma avaliação para determinação da condição pulmonar e funcional pré-operatória e identificação dos fatores de risco para desenvolvimento de CPPO. A evolução pós-operatória foi acompanhada por meio de prontuários. Os dados coletados da avaliação foram correlacionados com o desenvolvimento pós-operatório. **Resultados:** Trinta pacientes foram analisados. Foi encontrada correlação negativa e moderada entre a PImáx e as CPPO ($r=-0,39$; $p=0,032$). A permanência na UTI apresentou correlação positiva com os dias de internamento hospitalar ($r=0,40$; $p=0,02$). A ventilação mecânica ($r=0,36$; $p=0,04$) e os dias de internamento no hospital ($r=0,40$; $p=0,02$) tiveram correlação com o tipo de CPPO. **Conclusão:** CPPO podem prejudicar o desfecho pós-operatório. Bom estado físico e boa função pulmonar prévias à cirurgia oncológica possibilitam melhor desempenho para o paciente no pós-operatório.

Palavras-chave: Cirurgia. Câncer. Complicações Pós-Operatórias. Função Pulmonar. Fisioterapia.

Introduction

Neoplasia is a public health problem. The global cancer burden is estimated to have risen to 18.1 million new cases and 9.6 million deaths in 2018. Statistical data show that one in 5 men and one in 6 women worldwide develop cancer during their lifetime, and one in 8 men and one in 11 women die from the disease [1,2]. There are an estimated of 600 thousand new cases of cancer in Brazil between 2018 and 2019, for each year, excluding nonmelanoma skin cancer (about 170.000 new cases), 420.000 new cases of cancer will occur, and most of these patients will need surgery as treatment [3,4].

Although surgeries present high cure rate, post-op complications may occur, such as infections, skin injuries, lesions in the surgical incision, musculoskeletal and vascular alterations, and cardiac and pulmonary complications [5 - 7].

Surgical procedures may also be followed by respiratory dysfunctions. Anesthetics may cause hypoventilation, cough inefficiency (due to the pain), immobility and central nervous system impairment. These complications may trigger PPCs, such as diaphragmatic dysfunction, respiratory muscle weakness, post-surgery pain and alveolar collapse; these events cause a reduction of vital capacity and also,

pulmonary residual functional capacity, contributing to surgical morbimortality, including time of hospitalization and its costs [8 - 13].

PPCs development is associated with a decrease in functional capacity and, consequently, with a greater difficulty in rehabilitating. Therefore, functional and physical capacities of the patients before surgery are directly correlated with their post-surgery healing process [4,5,14]. Physical characteristics, healthy conditions, lifestyle and decreased pulmonary functions may be considered risk factors for PPCs development [15,16,17,6].

Pre-surgery evaluations of the patient's physical condition and the identification of factors that might trigger PPCs are necessary to help staff in decision-making, prevent complications, decrease morbidity and mortality rates, as well as provide a post-surgery recovery with effective treatments [15,4,16].

Considering oncologic post-surgery complications and knowing the importance of having an adequate rehabilitation, this study aimed to evaluate the risk factors that may compromise post-surgery recovery. Understandings these factors, these

complications could be prevented, and the patients would have an adequate functional recuperation.

Methods

The present observational transversal study was made at the Physiotherapy Educational Clinic of Universidade Estadual do Centro-Oeste (UNICENTRO) between March and October of 2015. The post-surgery recovery was followed through medical records.

Participants

The participants were recruited utilizing a list of surgery appointments which had the name, telephone number, date, and type of surgery of the patients. The triage occurred in the oncology unit of São Vicente de Paulo Hospital, located in Guarapuava city. Patients received a call in which the objectives of the present work were clarified, and the invitation to join the research was made.

Patients with neoplasia that would undergo an elective oncologic surgery for tumor resection at any surgical site, were included in the study. Some patients were excluded from the research, such as the ones who underwent surgical excision of melanoma, those for staging and diagnosis or emergency operations or/and were hemodynamically unstable. Patients that did not have physical or cognitive conditions to perform the tests were also excluded.

Procedures

Preoperative evaluations were performed, at least, 15 days before surgery. First, personal and anthropometric data were collected, as well as information about the patients' lifestyle habits and healthy conditions. Measurements of respiratory muscle strength, pulmonary function, and peripheral muscle strength were performed, as well as a six-minute walk test (6MWT).

Risk scores for PPCs development were evaluated based on Hulzebos et al. [16] system, which classifies this risk in high or low.

Patients' post-op conditions were verified using medical records, considering the necessity of staying

in ICU and utilizing mechanical ventilation (MV), the hospitalization time and the outcome (hospital discharge or death).

Evaluations

Pulmonary function

Values of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were analyzed. To perform these tests, the patients remain seated, breathing through the mouth (with the help of a nose clip) and utilizing a mouthpiece connected to the spirometer (MicroLab, Cardinal Health). Patients are instructed to exhale quickly after a deep breath. This procedure was performed three times, with free intervals, registering the best measurement [11].

Respiratory muscle strength

Respiratory muscle strength test was conducted with an analog manovacuometer (Comercial Médica, São Paulo, Brasil), calibrated in cmH₂O, with a -120 to +120 cmH₂O. Measurements were taken with the individuals in a seated position, wearing a nose clip and keeping a mouthpiece held firmly between the lips. Maximal inspiratory pressure (MIP) was obtained by a maximal inspiratory effort maneuver after a maximal expiration, close to the residual volume (RV). Maximal expiratory pressure (MEP) was achieved by a maximal expiratory effort, after a maximal inspiration, close to the total lung capacity (TLC) [9]. Maneuvers were performed for 2 seconds and repeated three times with free intervals, being registered the best measure. For statistical analysis, maximum values were considered. Values found for MIP and MEP were compared to those predicted by the equations of Neder et al. [18].

Physical capacity

The physical capacity test was obtained by 6MWT, performed according to American Thoracic Society [19]. The equations proposed by Enright and Sherrill [20] were utilized to estimate the distance to be covered during the 6MWT, considering gender.

Peripheral muscle strength

Peripheral muscle strength was estimated by hand-grip strength (HGS), measured in dominant upper limb utilizing a digital dynamometer (Camry - EH101), with kilogram/strength registration (kg/s).

Participants were asked to stand and hold the dynamometer with arms at their side. Next, it was requested for them to squeeze the dynamometer with as much force as possible during 3 seconds [21]. Three trials were made, and the best result was registered for a subsequent analyze. Normative reference values were obtained from Camry Instrument Owner's Manual, which classifies the strength according to the person's age and gender [22].

Determination of risk scores

Risk scores were calculated according to Hulzebos et al. [16] proposal. A sum of risk factors and protective factors presented by each patient must be made to obtain the final score. A punctuation between -4 and -2 indicates a low risk, and between -1 to 10 indicates a high risk of developing PPCs. The risk factors are age (≥ 70), productive cough, smoking, and diabetes mellitus. The protective factors are FVC and MEP $\geq 75\%$ of the predicted value.

Determination of postoperative complications

The determination of postoperative pulmonary complications (PPCs) was based on Hulzebos et al. [16] study, which classifies the PPCs according to postoperative findings. Type I PPCs are related to dry cough or microatelectasis and temperature higher than 37.5°C or dyspnea. Type II refers to PPCs which involve productive cough, bronchospasm, hypoxemia with signs and symptoms of wheezing and dyspnea or atelectasis confirmed by radiology associated with temperatures higher than 37.4°C . Type III is related to pleural effusion or suspected pneumonia, pneumothorax and reintubation with a mechanical ventilation period not greater than 42 hours. Lastly, patients with PPCs of type IV depend on the mechanical ventilator for more than 48 hours post-operation, with or without intubation.

Ethical aspects

This study was approved by the Research Ethics Committee of Universidade Estadual do Centro-Oeste (UNICENTRO) (protocol number 973.298). All participants were informed about the experiment characteristics and signed the Informed Consent Form.

Statistical Analysis

The data were expressed as mean \pm standard deviation with sample minimum, sample maximum or median, with first and third quartiles. Frequency distribution was utilized to present the characteristics of the sample.

Data normality was verified using Kolmogorov-Smirnov test. Once data were considered non-parametric, Spearman correlation was used to correlate the presence of PPCs with the variables evaluated before surgery, as well as the type of complication with post-operative monitoring and ICU days, mechanical ventilation, and hospitalization. After, it was assessed the correlation between the types of PPCs and the variables which presented significant correlation previously.

The correlation coefficient was measured according to Cohen [23], considering values between 0.10 and 0.29 a weak correlation, between 0.30 and 0.49 a moderate correlation and values between 0.50 and 1 a strong correlation.

Reference values of respiratory and peripheral muscle strength, spirometric variables, and 6MWT were calculated and compared to the results found in the present study by Wilcoxon test, which is a non-parametric test.

Data of this study were analyzed by the Statistical Package for the Social Sciences (SPSS) software for Windows, version 19 and GraphPad InStat 4.3. The statistical differences were determined with a significance level of 95% ($p \leq 0.05$).

Results

We identified 192 patients in a list of surgery appointments. From this group, 89 patients were excluded from the study for having skin cancer, 11 for

undergoing simple procedures for examination and 8 for not having physical conditions to perform the tests. Fifteen people did not accept to participate in this research. Also, 35 patients agreed but were not able to move to the Educational Clinic to perform the evaluation. Therefore, 34 patients completed the preoperative evaluation, and 4 canceled the surgery, resulting in a final sample of 30 patients.

The sample was composed of individuals of both genders, being the majority women. Regarding surgery indication 36.6% (n=11) were breast surgery, 33.3% (n=10) were abdominal surgery, 16% (n=5) were head and neck surgery, 6.6% (n=2) were thoracic surgery and 6.6% (n=2) were cases of lymph nodes resection. Anthropometric characteristics, lifestyle habits, associated diseases, and surgery background of patients are described in Table 1.

Table 1 - Patients characteristics

Variable	Mean \pm SD	(U.L.; L.L.)
Age	52.8 \pm 14.6	(58.3; 47.4)
Weight	68.3 \pm 18.8	(75.3; 61.3)
Height	163.6 \pm 9.0	(184; 150)
BMI	25.9 \pm 6.6	(28.3; 23.4)
<i>Characteristics of the individuals</i>	N (%)	
Gender		
Male	6(20.0)	
Female	24(80.0)	
Smokers	8(26.7)	
Ex-smokers	8(26.7)	
Productive cough	12(40.0)	
Respiratory diseases	9(30.0)	
Dyspnea without etiology	11(36.7)	
SAH	11(36.7)	
DM	3(10.0)	
Sedentarism	27(90.0)	
Previous surgeries	17(56.7)	

Note: SD: standard deviation; U. L.: Upper Limit; L.L.: Lower Limit; BMI: body mass index; SAH: systemic arterial hypertension; DM: diabetes mellitus.

Table 2 presents the values of the variables respiratory muscle strength, maximal expiratory pressure (MEP), maximal inspiratory pressure (MIP), pulmonary function, functional capacity and peripheral muscle strength. These values were obtained in the preoperative evaluation and are compared to normal reference values. All the analyzed variables showed a statistically significant reduction ($p < 0.001$) when compared to their reference values.

Table 2 - Functional parameters of preoperative evaluation

Variables	Mean \pm SD	Mean \pm SD Pred.	Pred. %	p-value
MIP	50.0 \pm 30.6	90.9 \pm 13.8	59.4	<0.001
MEP	66.7 \pm 19.7	90.5 \pm 18.2	80.0	<0.001
FVC	2.4 \pm 0.6	3.3 \pm 0.8	73.0	<0.001
FEV1	2.2 \pm 0.6	2.7 \pm 0.6	82.5	<0.001
FEV1/FVC	0.9 \pm 0.1		91.3	<0.001
6MWT	463.2 \pm 129.8	583.1 \pm 108.0	81.0	<0.001
Pulmonary pressure	27.4 \pm 8.8			<0.001

Note: MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; FVC: forced vital capacity; FEV1: forced expiratory volume in one second; 6MWT: six-minute walking test; Pred.: predicted.

Regarding handgrip strength (HGS), 76.7% of the patients (n=23) presented a normal muscle strength, 10% (n=3) demonstrate results above the predicted values for their age, and 13.3% (n=4) showed values lower than the expected.

Data obtained in preoperative evaluation, risk factors for postoperative pulmonary complications (PPCs) and the classification of PPCs are demonstrated in Table 3.

Table 3 - Preoperative information, risk factor and PPCs types

Variables	Median [1 ^o Q; 3 ^o Q]	N (%)
Hospitalization (days)	2[2; 3]	
ICU days	0[0; 0]	
MV days	0 [0; 0]	
Number of patients in ICU		2(6.7)
Number of patients in MC		1(3.3)
Risk score	0[-4; 5]	
High risk		19(63.3)
Low risk		11(36.6)
PPCs		
Without complications		7(23.3)
Type I		3(10.0)
Type II		19(63.3)
Type III		1(3.3)

Note: 1^o Q: first quartile; 3^o Q: third quartile; ICU: intensive care unit; MV: mechanical ventilation; PPCs: postoperative pulmonary complications.

In Table 4 significant correlations between preoperative evaluated parameters, postoperative pulmonary complications, and postoperative data.

Table 4 - Correlation between preoperative evaluation, PPCs and post-surgery outcome

	PPCs	MEP	PMS	6MWT	ICU
MIP	r=-0.39; p=0.032	r=0.59; p<0.001	r=0.42; p=0.01	r=0.40; p=0.02	-
MEP	-	-	r=0.62; p<0.001	-	-
PMS	-	-	-	r=0.36; p=0.04	-
MV	r=0.36; p=0.04	-	-	-	r=0.69; p<0.001
Hospitalization days	r=0.40; p=0.02	-	-	-	r=0.40; p=0.02

Note: MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; PPCs: postoperative pulmonary complications; PMS: peripheral muscle strength; 6MWT: six-minute walking test; MV: mechanical ventilation; ICU: intensive care unit.

Discussion

The inverse correlation between MIP and PPCs indicates that the lower is MIP, the greater is the risk of developing complications. This fact may be justified by the results of Hulzebos et al. [17] study, in which several risk factors for PPCs and respiratory muscle weakness were associated with a high incidence of PPCs and pneumonia, and with a prolonged postoperative hospitalization.

Morano et al. [4] observed a high incidence of PPCs, an extended time of intubation and hospitalization in patients that presented average MIP values of 67.6 ± 39.9 cmH₂O. In the present study, this average was 50.03 ± 30.59 cmH₂O. According to ATS/ERS [24] guidelines regarding pulmonary function tests, MIP values lower than 80 cmH₂O may indicate respiratory muscle weakness, therefore, increase the risk of developing PPCs and worsening postoperative recovery. The results of the present study demonstrate that, beyond respiratory muscle weakness, 63.3% of the patients present a high risk of developing PPCs.

Abreu and collaborators [25] evaluated 20 women before breast cancer surgery and reported a lower MIP average value when compared to the ones demonstrated in the present study (43.1% and 59.4% of the predicted value, respectively). The results of the MEP values were also lower than those found in the present study (40.1% and 80.0% of the predicted value, respectively). These results highlight the reduction of respiratory muscle strength of oncological patients.

Hulzebos et al. [16] evaluated patients that underwent myocardial revascularization surgery and defined some predictive factors for PPCs. Among them, MIP and MEP values similar or higher than 75% of the predicted value were considerate protective factors for PPCs. Also, it

was found a correlation between preoperative respiratory muscle strength with PPCs. Although the present study analyzed oncological patients, similar results were found. Another study made by Hulzebos et al. [17] showed a reduction of PPCs in patients who presented MIP average value of 95.6 cmH₂O.

When considering the risk factors for PPCs, Hulzebos et al. [16] demonstrate that most of the patients showed high chances of developing these complications. This result may be explained by patients' profile, once 53.4% of them had a smoking background, 30% had respiratory diseases, 40% presented a productive cough, 10% were diabetic, and 36.7% had BMI higher than 27.

Saad et al. [26] aimed to identify risk factor for PPCs in 145 patients that underwent thoracic cancer surgery. From 27 patients who presented pulmonary complications, 26 had a smoking background. Brooks-Brunn [27] defined BMI higher than 27 as a risk factor for PPCs and, among the patients of the present study, 36.7% presented this index. Riedi et al. [15] evaluated the relationship between respiratory muscle strength and PPCs in cardiac surgeries and observed that 41.6% of the patients presented overweight, which was considered a contributing factor for a low survival rate [28,29].

In the present study, mechanical ventilation and hospitalization time had a significant correlation with the type of PPCs. The most frequent complication was PPCs type II with 63.3% of the cases. Van Adrichem et al. [10] evaluated individuals who underwent an esophagectomy and had similar results, showing that 61.5% of the patients presented complications of type I and II. Therefore, it is suggested that the patients of this study

had less grave complications due to the fact they remained hospitalized for a short period and only a few of them was sent to ICU, once the majority of the surgeries were of low complexity.

Patients who spent more time in ICU and needed MV were the ones who presented the worst complications, also because they remained hospitalized for a longer time when compared to the ones of PPCs type I and II. These results were similar to the ones presented by a Dutch study, in which the patients who had complications of type I and II spent less time hospitalized when compared to the patients with PPCs type II and IV [10].

Reeve et al. [7] studied patients who underwent a pulmonary resection by thoracotomy. The researchers verified that patients with PPCs spent more time hospitalized than the patients who did not present PPCs, with an average of 17 and six days of hospitalization, respectively.

The time in ICU was also correlated with the days of hospitalization. Thus, it is suggested that this correlation is because ICU patients are usually in a critical condition, need special care and might present worse pulmonary complications, therefore, remain a longer time in hospital.

In a study published in 2011, patients who were exposed to pulmonary resection were analyzed. Individuals that presented better respiratory strength and pulmonary function spent less time in ICU (average of 14.9 ± 44.7) and stayed fewer days in the hospital (average of 6.3 ± 3.0) when compared to the time spent in ICU (average of 40.5 ± 75.2) and hospital (average of 11.0 ± 6.3) of patients with worse pulmonary conditions [14].

By the results of the present study and other scientific publications, it is possible to confirm that the incidence of PPCs requires a greater care at this time, increasing the risk of this patients to stay in ICU in postoperative and remain an extended time in the hospital [7,14,17,4,10].

Preoperative functional conditions may influence the rehabilitation process. In the present work, the average of respiratory muscle strength (MIP: 50.03 ± 30.59 ; MEP: 66.7 ± 19.66) and pulmonary function (FVC: 2.40 ± 0.56 ; FEV1: 2.17 ± 0.56) values demonstrated that these variables are lower in postoperative patients, and this fact is directly associated with PPCs increase.

Nakamura et al. [30] analyzed the factors that might contribute to the reduction of pulmonary complications incidence after esophagectomy. The researchers reported factors that are related to PPCs incidence, among them, preoperative respiratory physiotherapy. Studies demonstrated that preoperative respiratory physiotherapy increases FVC,

FEV1, respiratory muscle strength and functional capacity [4,5,10,14]. This kind of physiotherapy is also associated with the reduction of PPCs and hospitalization time [4,10,17], which corroborate the present results.

Some limitations were found in the present study. One of them was the sample number, which precluded the evaluations of patients by specific types of surgeries. The other was the lack of postoperative evaluations, which were not performed because patients were not able to move to the Educational Clinic, then the outcomes of surgeries were not analyzed.

Conclusion

The correlations found in the present study demonstrate that a healthy physical condition and a good pulmonary function before oncological surgery enable a better prognostic in postoperative.

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