Risk factors for pulmonary complications in patients with sarcoma after the resection of pulmonary nodules by thoracotomy*

Fatores de risco de complicações pulmonares em pacientes com sarcoma após toracotomia para a ressecção de nódulos pulmonares

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Abstract

Objective: To identify the risk factors for pulmonary complications after thoracotomy for the resection of pulmonary nodules in patients with sarcoma. **Methods:** A retrospective cohort study involving 68 consecutive patients diagnosed with sarcoma and submitted to a total of 174 thoracotomies for the resection of pulmonary nodules. The dependent variable was defined as the occurrence of any postoperative pulmonary complications. The independent variables were related to the patient, underlying diagnosis, and type of surgical procedure. We analyzed the data using a multivariate generalized estimating equations model with logistic link function and a symmetric correlation structure. **Results:** Complications were observed in 24 patients (13.8%, 95% CI: 9.0-19.8), and there was one death. The mean length of hospital stay was twice as long in the patients with postoperative complications as in those without (18.8 ± 10.0 days vs. 8.6 ± 6.0 days; $p < 0.05$). The variables that correlated with the outcome measure were the type of resection (wedge vs. anatomic; OR = 3.6; 95% CI: 1.5-8.8), the need for blood transfusion (OR = 9.8; 95% CI: 1.6-60.1), and the number of nodules resected (OR = 1.1; 95% CI: 1.0-1.1). The multivariate model showed an area under the ROC curve of 0.75 (95% CI: 0.65-0.85). **Conclusions:** Postoperative pulmonary complications were common after pulmonary nodule resection in patients with sarcoma, occurring in approximately 10% of the procedures. The occurrence of such complications can be expected when techniques other than wedge resection are employed, when blood transfusion is required, and when a great number of nodules are resected. Therefore, it is possible to identify patients at risk for pulmonary complications, who should be closely monitored in the immediate postoperative period. In such patients, all preventive measures should be taken.

Keywords: Sarcoma; Neoplasm metastasis; Risk; Thoracotomy; Thoracic surgery.

Resumo

Objetivo: Identificar os fatores de risco para complicações pulmonares em pacientes com sarcoma após serem submetidos a toracotomia para a ressecção de nódulos pulmonares. **Métodos:** Estudo de coorte retrospectivo com 68 pacientes consecutivos com diagnóstico de sarcomas e submetidos a 174 toracotomias para a ressecção de nódulos pulmonares. A variável dependente foi definida como a ocorrência de qualquer complicação pulmonar pós-operatória. As variáveis independentes foram relacionadas com o paciente, o diagnóstico de base e o tipo de procedimento cirúrgico. Os dados foram analisados segundo um modelo multivariado de estimação de equações generalizadas, com uma função de ligação logística e uma estrutura de correlação simétrica. **Resultados:** Houve 24 complicações (13,8%; IC95%: 9,0-19,8), incluindo um óbito. Os pacientes que apresentaram complicações pós-operatórias tiveram um tempo médio de internação duas vezes superior àqueles sem complicações (18,8 ± 10,0 dias vs. 8,6 ± 6,0 dias; $p < 0,05$). As variáveis que se correlacionaram com o desfecho foram o tipo de ressecção (em cunha ou anatômica; OR = 3,6; IC95%: 1,5-8,8), necessidade de transfusão sanguínea (OR = 9,8; IC95%: 1,6-60,1) e número de nódulos ressecados (OR = 1,1; IC95%: 1,0-1,1). O modelo multivariado obtido exibiu uma área sob a curva ROC de 0,75 (IC95%: 0,65-0,85). **Conclusões:** As complicações pulmonares pós-operatórias após a ressecção de nódulos pulmonares em pacientes com sarcoma não foram raras, ocorrendo em cerca de 10% dos procedimentos. A ocorrência dessas complicações pode ser antecipada pelo uso de ressecção não em cunha, necessidade de hemotransfusão e maior número de nódulos ressecados. Assim, já no pós-operatório imediato, é possível identificar pacientes de risco, que devem ser estritamente monitorizados durante o período pós-operatório imediato. Para esses pacientes, todas as medidas preventivas devem ser tomadas.

Descritores: Sarcoma; Metástase neoplásica; Risco; Toracotomia; Cirurgia torácica.

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Introduction

Sarcomas, notably osteosarcomas, are rare and aggressive tumors that metastasize rapidly.[1] Up to 20% of all patients with sarcoma present with metastases, predominantly in the lungs, at the time of diagnosis.[1,2] However, the mean five-year survival has increased, from 10-20% in the 1960s to 60-70% in the early 1990s.[1] This advance resulted from a multimodal treatment, which includes radiotherapy and chemotherapy, together with surgery for the resection of the primary tumor and metastases. Thoracotomy for the resection of metastases has been incorporated into the therapeutic armamentarium, and such resection is considered a major determinant of survival in patients with sarcoma, even in those with multiple metastases.[2]

After the resection of pulmonary metastases, up to 12% of sarcoma patients present with pulmonary complications, which prolong the hospital stay and result in an in-hospital mortality rate of up to 2%.[3-6] However, the risk factors for such complications have yet to be clearly defined. Such knowledge could contribute to the stratification of risk, optimizing the surgical decision-making process and defining preventive interventions.

The objective of the present study was to identify the independent variables associated with postoperative pulmonary complications in sarcoma patients undergoing thoracotomy for the resection of pulmonary nodules suspected of or confirmed as being metastatic.

Methods

This was a retrospective hospital cohort study involving 68 consecutive patients diagnosed with sarcoma and submitted to a total of 174 thoracotomies for the resection of pulmonary nodules between January of 2001 and October of 2008 at the SARAH-Brasília Hospital, located in the city of Brasília, Brazil. The project was evaluated and approved by the local human research ethics committee.

In all patients, the primary tumor was histologically diagnosed,[7] through biopsy or anatomopathological study of the surgical specimen. The pulmonary nodules were detected by a chest CT scan, which is routinely employed as a screening method. Surgical treatment of a probable pulmonary metastasis was considered based on the following basic principles: the primary tumor was controlled; there were no extrathoracic metastases; no other treatment modality was deemed effective; pulmonary function was compatible with the surgical treatment; clinical conditions were compatible with the surgical treatment; and clinical and radiological findings indicated that the metastasis was resectable.[8]

In order to sacrifice as little as possible of the normal adjacent parenchyma, wedge resection (minimum margin of 5 mm) was the method of choice for the resection of the pulmonary nodules. The patients included in the present study underwent laboratory evaluation and spirometry in the preoperative period. The surgical procedure proposed was not performed unless the patients presented with normal coagulation profile, normal red blood cell count, normal white blood cell count (particularly if undergoing chemotherapy), and acceptable pulmonary function test results.[9] The patients were prophylactically treated with antimicrobial agents and heparin. Depending on the circumstances, nonpharmacological interventions (early ambulation, pneumatic compression, or compression stockings) were also used. Depending on the case, one or two multiperforated chest tubes of various calibers were used and then removed after lung expansion, which was confirmed by means of physical examination and chest X-rays, as well as by the absence of air leak, together with clear fluid drainage (< 200 mL/day). For pleural or mediastinal drainage, we used a water-seal drainage system with a separate collection chamber and the possibility of continuous suction (Pleur-evac; Genzyme Surgical Products Corp., Fall River, MA, USA). In the postoperative period, all of the patients received continuous epidural or intravenous analgesia via a patient-controlled analgesia pump. Breathing exercises were practiced in the preoperative period and consisted of assisted cough, incentive spirometry, and deep breathing (sustained and spontaneous). Oxygen therapy and noninvasive mechanical ventilation were initially used in cases of complications accompanied by hypoxia or hypercapnia.

The dichotomous dependent variable was defined as the occurrence of any postoperative pulmonary complications prior to discharge.

Only the complications that were registered in the patient charts and motivated a clinical decision were considered.[10] Therefore, infectious complications, such as pneumonia and empyema, were computed only when the biochemical, clinical, and radiological data were consistent with such complications and an antimicrobial agent was prescribed. Pneumothorax and prolonged air leak were considered complications only if further drainage was required or if the drainage lasted more than five days, even when patients had previously undergone continuous suction. All episodes of dyspnea with hypoxia requiring invasive or noninvasive ventilatory support were considered to be cases of acute respiratory failure, the causes of which were investigated. Atelectasis, for instance, fit that description. Finally, postoperative bleeding was not considered a complication unless it required fluid resuscitation or surgical revision.

In addition to gender and age, other variables, related to the preoperative and perioperative periods, were considered. Preoperative variables included the histological type of the primary neoplasm, staging,[11] neoadjuvant chemotherapy, smoking history, the principal spirometric parameters, comorbidities, and previous thoracotomies. Perioperative variables included surgical time, type of surgery, number of nodules resected, blood loss, and blood transfusions.

The results were expressed as mean and standard deviation, median (interquartile range), or proportion (95% CI), extreme values being occasionally indicated. The Student's t-test, the chi-square test, Fisher's exact test, and the Mann-Whitney test were applied. The level of significance was set at $p < 0.05$, and all tests were two-tailed.

In the multivariate analysis, we considered the total numbers of patients (n = 68) and thoracotomies (n = 174). By doing so, we did not violate the principle of data independence, because certain outcome measures occasionally related to the same patients but to different surgical procedures. Therefore, we used a multivariate generalized estimating equations (GEE) model[12] with logistic link function and a symmetric correlation structure. Initially, a univariate analysis was performed when critical values of $p < 0.25$ were considered for the subsequent inclusion of the independent variable in the multivariate analysis.[13] The multivariate GEE model was constructed by consecutively excluding the independent variables through the likelihood ratio test.[13] Multicollinearity was also studied, with the objective of determining whether there were independent variables that showed correlations or associations. The final model was validated by the ROC curve.[14] The Statistical Analysis System, version 9.13 (SAS Institute, Cary, NC, USA), and the Statistical Package for the Social Sciences, version 13.0 (SPSS Inc., Chicago, IL, USA), were used for the statistical treatment of the data.

Table 1 - Absolute and relative distribution, in decreasing order of frequency, of all histological types of sarcomas diagnosed in the 68 patients investigated.[a]

Diagnoses	Sarcoma		Total, n (%)
	Bone, n (%)	Soft tissue, n (%)	
Osteosarcoma	34 (81.0)	-	34 (50.0)
Synovial sarcoma	-	11 (42.3)	11 (16.2)
Ewing's sarcoma	5 (11.9)	-	5 (7.4)
Undifferentiated sarcoma	-	4 (15.4)	4 (5.9)
Epithelioid sarcoma	-	3 (11.5)	3 (4.4)
Pleomorphic leiomyosarcoma	-	2 (7.6)	2 (3.0)
Chondrosarcoma	2 (4.8)	-	2 (2.9)
Fibrosarcoma	-	2 (7.7)	2 (2.9)
Liposarcoma	-	2 (7.7)	2 (2.9)
Malignant neurilemmoma	-	1 (3.8)	1 (1.5)
Small cell sarcoma	1 (2.4)	-	1 (1.5)
Embryonal rhabdomyosarcoma	-	1 (3.8)	1 (1.5)
Total	42 (100.0)	26 (100.0)	68 (100.0)

[a]The classification adopted was that of the World Health Organization.[7]

Table 2 - Absolute and relative distribution of the pulmonary complications of the 174 thoracotomies performed in 68 patients.

Complications	Patients	Thoracotomies, n (%)
Pneumonia[a]	5	6 (25.0)
Pneumothorax	4	4 (16.7)
Bleeding[b]	4	4 (16.7)
Atelectasis[c]	3	3 (12.5)
Bronchial fistula[d]	1	2 (8.3)
Chylothorax	2	2 (8.3)
Thromboembolism[e]	2	2 (8.3)
Empyema	1	1 (4.2)
Total[f]	22	24 (100.0)

[a]Two of the cases occurred in the same patient. [b]In each of the four patients, bleeding from the bronchial wall occurred due to coagulation disorder and hemothorax. [c]It was accompanied by acute respiratory failure. [d]The two cases occurred in the same patient. [e]The two cases occurred in different patients, one of whom died.[f]Four patients presented with more than one different complication. Therefore, the total was 22, although there were, in fact, 18 patients with at least one complication.

Results

A total of 68 patients were investigated. Of those, 44 were male (64.7%), and the male/female ratio was 1.8:1.0. The median age of the patients at the first surgical procedure was 21.5 years (range, 7-70 years). Bone sarcoma (62.0%) and soft tissue sarcoma (38.0%) were the most common underlying diagnoses, as established by histological examination. Osteosarcomas accounted for 81.0% of the cases of bone sarcoma. Among the soft tissue sarcomas, synovial sarcomas predominated (42.0%; Table 1).

Information regarding the smoking habit was retrieved from the medical charts of only 44 patients (65.0%), and those 44 patients had undergone a total of 90 surgical procedures. Of those 44 patients, 29 (66.0%) were nonsmokers, 9 (20.5%) were former smokers, and 6 (13.6%) were smokers.

All of the patients underwent extensive resection of the primary tumor, with the exception of 2 patients, whose primary tumors were located in the spinal column. In those cases, local control, prior to thoracotomy, was achieved with chemotherapy and radiotherapy. Regarding the staging of the tumor, 56 patients (82%) were classified as having stage IV tumors, because the histopathological examination of the nodules confirmed the presence of pulmonary metastasis. The remaining 12 patients (18%), who underwent 15 thoracotomies, were classified as having stage III tumors or lower, because the histopathological examination of the resected material was negative for metastasis (calcified fibrous nodules, bronchiolitis obliterans, fungi, desquamative interstitial pneumonia, and eosinophilic pneumonia).

The study period ended in March of 2009, and the mortality rate among the patients investigated in the present study was 29.4%, the median follow-up period being 20.3 months (range, 3.1-120.4 months). The survival curve (estimated by the Kaplan-Meier method) showed that 60% of the patients survived for 50 months

Table 3 - Univariate analysis involving the continuous independent variables and considering the 174 thoracotomies performed.

Variables	Respiratory complication			
	No (n = 150)		Yes (n = 24)	
	Mean ± SD	Median (II)	Mean ± SD	Median (II)
Age, years	26.1 ± 12.8	22.0 (17.0-33.0)	30.9 ± 14.5	24.0 (20.5-45.0)
Total of nodules, n	4.3 ± 5.7	2.5 (1.0-5.0)	5.6 ± 5.3	4.0 (2.0-7.0)
Central nodules, n	0.2 ± 0.9	0.0 (0.0-0.0)	0.3 ± 0.6	0.0 (0.0-0.5)
Peripheral nodules, n	4.2 ± 5.6	2.0 (1.0-5.0)*	6.0 ± 5.7	4.0 (1.5-9.5)
Surgical time, min	114.9 ± 69.6	92.5 (65.0-150.0)	140.0 ± 60.6	130.0 (92.5-182.5)
Blood loss, mL	214.8 ± 318.4	100.0 (50.0-220.0)*	434.0 ± 532.4	265.0 (85.0-455.0)
FVC, % of predicted[a]	77.7 ± 20.2	76.8 (65.9-87.8)	71.1 ± 21.7	68.7 (53.2-86.6)
FEV_1, % of predicted[a]	78.8 ± 17.2	81.8 (69.3-89.4)	74.5 ± 17.8	73.6 (53.8-88.4)
FEV_1/FVC, %	85.0 ± 8.1	86.7 (79.0-91.6)	85.1 ± 8.9	84.9 (77.3-93.3)

II: interquartile range. [a]Based on equations proposed in a study conducted in Brazil by Pereira et al.[15] *$p < 0.05$ between thoracotomies with and without postoperative pulmonary complication.

of follow-up, the first thoracotomy being the reference point.

The number of thoracotomies per patient varied greatly, from 1 (in 29.0%) to 8 (in only one case), one third having undergone 2 procedures, with no difference between the types of sarcomas (bone sarcomas or soft tissue sarcomas). The vast majority of the thoracotomies performed consisted of wedge resections (146 procedures, 83.9%), performed in isolation or in combination with other techniques. Lobectomies and segmentectomies were performed in 14.9% and 12.1% of all procedures, respectively, either in isolation or in combination with other techniques. No differences were found between the sides on which the thoracotomies were performed, only 1 procedure having been performed simultaneously on both sides. The median surgical time was 90 min (range, 70-150 min). In 132 thoracotomies (75.9%), the patient had undergone chemotherapy prior to the procedure.

A total of 815 nodules (central or peripheral) were resected, the median number of nodules resected being 3 (range, 1-54 nodules/thoracotomy).

Eighteen patients presented with at least one respiratory complication in the postoperative period (26.5%; 95% CI: 16.5-38.6). Considering the total number of thoracotomies performed, 24 patients exhibited at least one complication (13.8%; 95% CI: 9.0-19.8). As can be seen in Table 2, the most common complication was pneumonia—which accounted for 25.0% of all complications—followed by pneumothorax (7.0%) and bleeding (7.0%). One of the patients died after pulmonary thromboembolism, the mortality rate therefore being 1.5% (95% CI: 0.0-8.2). In addition, it is of note that the mean hospital stay was two times longer in patients who had at least one post-thoracotomy complication than in those who had none (8.6 ± 6.0 days vs. 18.8 ± 9.6 days; $p < 0.05$). Among the thoracotomies in which the excised nodules tested negative for metastasis, there were no complications.

Regarding the continuous variables, blood loss and the number of peripheral nodules resected were significantly greater for the thoracotomies that resulted in complications ($p < 0.05$; Table 3). There were no differences between the groups in terms of the preoperative spirometric values.

Of the categorical variables analyzed, three differed in terms of postoperative complications versus no postoperative complications (Table 4). Right thoracotomies, thoracotomies performed in patients who received blood transfusion, and thoracotomies that involved surgical techniques of greater complexities (i.e., those in which wedge resections were performed in combination with other procedures) were the procedures that resulted in the largest number of complications. We found no collinearity between bleeding and transfusions, because various losses were controlled without the use of blood products.

We tested models that included the preoperative variables alone, the intraoperative

Table 4 - Univariate analysis involving the dichotomous or polytomous independent variables and considering the 174 thoracotomies performed.

Variables	Complication	
	No, n (%)	Yes, n (%)
Previous chemotherapy		
No	36 (24.0)	6 (25.0)
Yes	114 (76.0)	18 (75.0)
Total	150 (100.0)	24 (100.0)
Smoking status		
Nonsmoker	48 (61.5)	4 (33.3)
Former smoker	14 (17.9)	2 (16.7)
Smoker	16 (20.5)	6 (50.0)
Total	78 (100.0)	12 (100.0)
Side*		
Bilateral	0 (0.0)	1 (4.2)
Right	72 (48.0)	13 (54.2)
Left	78 (52.0)	10 (41.7)
Total	150 (100.0)	24 (100.0)
Previous thoracotomies		
0	98 (65.3)	13 (54.2)
1	33 (22.0)	7 (29.2)
2	15 (10.0)	3 (12.5)
3	3 (2.0)	1 (4.2)
4	1 (0.7)	0 (0.0)
Total	150 (100.0)	24 (100.0)
Wedge resection exclusively**		
No	39 (26.0)	13 (54.2)
Yes	111 (74.0)	11 (45.8)
Total	150 (100.0)	24 (100.0)
Blood transfusion***		
No	147 (98.0)	21 (87.5)
Yes	3 (2.0)	3 (12.5)
Total	150 (100.0)	24 (100.0)

Table 5 - Final multivariate model obtained by consecutively excluding the independent variables through the likelihood ratio test.

Variables	Estimate	Standard error	χ^2	p	OR	95% CI
Intercept	−0.46	0.91	-	-	-	-
Procedure other than wedge resectiona	1.28	0.45	7.94	0.0048	3.59	1.48-8.75
Blood transfusionb	2.28	0.93	6.07	0.0137	9.79	1.60-60.06
Total of nodules	0.05	0.03	3.35	0.0670	1.05	1.00-1.11

[a]The procedures that involved exclusively wedge resection were used as a reference.[b]The procedures that did not require blood transfusion were used as a reference.

variables alone, and the preoperative and intraoperative variables together. In the univariate analysis, none of the preoperative variables showed a p value < 0.25. However, a p value < 0.25 was found for the following intraoperative variables: number of superficial nodules; total number of nodules; type of resection; surgical time; blood loss status; and blood transfusion status. From a pragmatic standpoint, we decided to include in the model only the total number of nodules resected. The multivariate GEE model employed identified blood transfusions, surgical techniques that were more complex than wedge resection (anatomical resection), and a high number of nodules resected as being independent risk factors (Table 5). The multivariate model obtained exhibited a significant area under the ROC curve (0.75; 95% CI: 0.65-0.85).

Discussion

In the present study, which involved 68 consecutive patients who had bone sarcoma or soft tissue sarcoma and underwent 174 thoracotomies for the resection of pulmonary nodules, we observed a proportion of 14% of postoperative pulmonary complications. The variables associated with those complications were the type of resection, the need for blood transfusion, and the number of nodules removed.

The present study has some limitations, which should be pointed out. This was a retrospective study based on patient charts. As such, it is subject to measurement, selection, and information biases.[16] We highlight the possibility of a centripetal bias,[16] because the study was conducted in a referral institution.[6,17] However, the sample investigated in the present study was similar to those investigated in other studies in terms of gender, age, histological type, survival, surgical approach, and criteria for the selection of patients who should undergo resection.[7,18] Comorbidities were uncommon, because the study sample was essentially composed of young individuals, which is why comorbidities were not taken into consideration in the present study. Because the patients were young and stable, with no clinical evidence of consumptive syndrome or hypoproteinemia, no other laboratory tests were requested, although the literature has demonstrated the prognostic importance of pre-albumin in postoperative complications of pulmonary resection.[19] Finally, another limitation of the present study was the small number of events in relation to the total number of independent variables investigated (overfitting).[20]

The present study investigated consecutive patients and involved variables that were easy to obtain. In addition, there was no loss to follow-up. The institution employs electronic medical records,[21] which guaranteed that clinical events of interest were registered in an objective, timely, and reliable manner. In addition, the interdisciplinary patient care protocols for the preoperative, perioperative, and postoperative periods were consistent throughout the study period. Finally, the statistical approach was robust, involving GEE models[10] and validation by the ROC curve.[12]

Only four other studies have reported the proportion of pulmonary complications after thoracotomy for the resection of pulmonary metastases from sarcomas; those proportions ranged from 0% to 12%, and the mortality rates were as high as 2%.[3-6] One of these studies was conducted in the 1990s, at the same institution at which the present study was conducted.[6] Although the morbidity and mortality rates found in the present study were within those limits, we observed different pulmonary complications.

In one of the most often cited studies, which reported a mortality rate of 1.5%, empyemas and fistulas accounted for 40% of the complications.[3] In the previous study conducted at our hospital, there was a predominance of fistulas (which were seen in 5 of the 7 cases in which complications occurred).[6] In the present study, pneumonia and pneumothorax accounted for 40% of the complications, and there were two cases of pulmonary thromboembolism. These variations might be due to differences in the diagnostic criteria, clinical course, and methods available for clinical assessment.[9]

Before discussing the risk factors that we identified in the present study, we will briefly discuss the variables that were found to be dependent. Regarding gender, no other predictive model for postoperative pulmonary complications has shown differences between males and females in terms of the risk of developing such complications, regardless of the location or diagnosis of the underlying disease. In the present study, age was found to have no influence on the risk of developing postoperative pulmonary complications, which might be due to the fact that the study sample was composed principally of young individuals. It has been suggested that the risk of developing postoperative pulmonary complications increases after 80 years of age.[22,23] In the present study, neoadjuvant chemotherapy, which was used in 80% of the patients, did not correlate with postoperative complications. It should be borne in mind that the patients underwent surgery only after the clinical parameters, hemoglobin levels, and hematocrit levels had returned to normal. Although the effectiveness of neoadjuvant chemotherapy in such cases has yet to be formally demonstrated, our results show that neoadjuvant chemotherapy had no negative postoperative effects. Finally, neither previous thoracotomies nor any of the spirometric parameters were found to be independent variables. Many of our patients had previously undergone pulmonary resection and presented with a significant reduction in pulmonary function. The evidence shows that the postoperative pulmonary function of patients should be assessed if FEV_1 is ≤ 1.5-2 L or ≤ 80% of predicted.[8] This estimate applies to major procedures and not to wedge resections or segmentectomies. Nevertheless, during the decision-making process, the surgeons and clinicians involved in the present study always took the spirometric parameters and the extent of the resection into consideration.

In the present study, the patients who received blood transfusions were shown to be 10 times more likely to exhibit at least one postoperative pulmonary complication than were those who did not. There were no correlations between blood transfusion and the type of procedure (wedge resection vs. other), between blood transfusions and perioperative blood loss, or between blood transfusions and the number of nodules resected. Blood transfusion is known to be associated with an increased risk of death in patients with severe disease; blood transfusion is also known to be associated with pulmonary complications in clinical or surgical patients.[24,25] Of the patients evaluated in the present study, those who received multiple blood transfusions were at greater risk for complications, because, as is well known in oncology practice, the use of blood products can increase the risk of infectious complications, human error, hemolytic reaction, and graft-versus-host disease.[26]

The multivariate analysis showed that any type of resection other than those that were exclusively wedge resections increased the risk of pulmonary complication by 260%. Therefore, the primary objective should be to excise as many nodules as possible and preserve the parenchyma as much as possible. Because these patients undergo serial resections, procedures that are more extensive, such as lobectomies and segmentectomies, were avoided whenever possible. The method of choice was wedge resection, which is ideally used for the resection of superficial nodules, although factors such as the location and size of the nodules, as well as the distance between nodules, greatly influence the choice of surgical technique.[2]

The final model showed that the risk of postoperative pulmonary complications increased by 5% for every nodule resected. This finding is consistent with the knowledge that the number of metastatic pulmonary nodules is intimately associated with the prognosis. The study conducted by the International Registry of Lung Metastases,[18] in which it was reported that 42% of the tumors were sarcomas, showed that the five-year survival rates among patients with a single metastasis, two to three metastatic

nodules, and more than three metastatic nodules were 43%, 34%, and 27%, respectively.

A study conducted at our institution in 2000 included 40 patients with sarcoma who underwent resection of pulmonary metastases.[6] The sample analyzed in that study had characteristics that were in various aspects similar to those of the sample analyzed in the present study. That study sample comprised young patients (mean age of 24 years). Of the total of patients, 60% were male, and 55% had osteosarcoma. The mean five-year survival rate was 65%, and the rate of post-thoracotomy complication was 11.7% (95% CI: 4.8-22.6). In the present study, the mean age of patients was 22 years. Males accounted for 65% of the patients, and 50% had osteosarcoma. The mean 50-month survival rate after the initial thoracotomy was 60%, and the rate of complication was 13.8% (95% CI: 9.0-18.0). However, in the nearly 10 years that elapsed between the aforementioned study conducted in our institution and the present study, the mean number of thoracotomies per patient in the institution increased from 1.5 to 2.6, whereas the mean number of nodules resected per thoracotomy decreased from 13.0 to 4.5, without an increase in postoperative morbidity. We found only nine other studies reporting similar information. Regarding the mean number of thoracotomies per patient, we found no values higher than 3, and the 1.5-1.9 range predominated.[2-5,27-29] Regarding the number of nodules resected per procedure, we found only two studies in which the mean values were reported to be lower than 3,[3,4] whereas the highest mean value reported was 12 nodules/thoracotomy.[2,5] Considering that the natural history of the disease has not changed in those 10 years, it is reasonable to conclude that the current patients underwent more thoracotomies, and fewer nodules were resected. It is reasonable to assume that these patients have come to be monitored more closely, through frequent clinical examination and imaging tests, thereby creating the necessary conditions for early detection of new pulmonary nodules.[18] Although a short disease-free interval is known to be an important prognostic factor, it is not a contraindication for sequential resections.[30]

The present study is particularly important because it involved a group of young patients with a rare type of tumor, the prognosis of which is poor. This profile has changed in recent decades, notably after the advent of chemotherapy and surgical strategies that are more aggressive.[1] No other study conducted in Brazil or any other country has specifically investigated the risk factors for complications after the resection of pulmonary metastases in such patients. A predictive model would ideally allow us to stratify patients by risk range, which in turn would allow us to adjust the treatment in function of the prognosis. In the case of controllable risk factors, preventive measures might be useful. The model that we devised in the present study involved three modifiable independent variables. Depending on the volume and circumstances of the bleeding, various resources are available in order to avoid transfusions. Regarding the surgical technique and the number of nodules, the results of the present study are consistent with the contemporary practice of systematic follow-up and serial, conservative, resections.

We conclude that pulmonary complications after the resection of pulmonary nodules in patients with sarcoma were not rare, having occurred in approximately 1 in every 10 procedures. The type of surgical resection, the need for blood transfusion, and the number of nodules resected were the variables that were found to correlate with these complications. Based on these results it is possible to identify, as early as in the immediate postoperative period, patients who are potentially at risk for complications and therefore redouble preventive and surveillance efforts. Theoretically, all of the independent variables identified can be directly or indirectly controlled, thereby minimizing the morbidity and mortality associated with such interventions.

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