Study of Maximal Respiratory Pressures after Exposure to Breast Radiotherapy in Women: a Pilot Study

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Estudo das Pressões Respiratórias Máximas após Exposição à Radioterapia de Mama em Mulheres: um Estudo-Piloto

Estudio de las Presiones Respiratorias Máximas después de la Exposición a Radioterapia Mamaria en Mujeres: un Estudio Piloto

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Abstract

Introduction: Postoperative radiotherapy is widely used to reduce risks of locoregional recurrence of breast cancer. However, the radiation of the thoracic structures involves risks, especially to the lungs. **Objective:** To study the Maximal Respiratory Pressures (MRP) after exposure to breast radiotherapy in women. **Method:** Prospective observational study conducted at the Alfredo Abrão Cancer Hospital in Campo Grande, State of Mato Grosso do Sul – MS. The study sample consisted of women (n = 8) exposed to breast radiotherapy after quadrantectomy surgery. Respiratory muscle strength was assessed through Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP) using a portable device called manovacuometer. The exam was performed before the 1st session of radiotherapy and after the 25th session corresponding to the last day of radiotherapy treatment. It were also evaluated the weight and height to measure the body mass index (BMI), clinical respiratory symptoms of dyspnea using the Medical Research Council Dyspnea Scale and characterization of cough with the Common Lung Toxicity Criteria according to the clinical pneumonitis classification. **Results:** MIP values were 95.90 ± 23.86 and 81.20 ± 23.12 (mean ± standard deviation p = 0.035) in relation to the ideal percentage, characterizing a significant decrease when comparing before and after breast radiotherapy exposure. It was observed level of significance of p<0.05, t-student and paired test were applied. **Conclusion:** The study of MRP before and after exposure to breast radiotherapy showed a significant decrease in MIP.
Key words: Maximal Respiratory Pressures; Radiotherapy; Respiratory Muscles/radiation effects; Breast Neoplasms.

Resumo

Introdução: No câncer de mama, a radioterapia pós-operatória é amplamente usada para reduzir a incidência de recorrência local da doença. Entretanto, a irradiação das estruturas torácicas implica riscos, especialmente para os pulmões. **Objetivo**: Estudar as pressões respiratórias máximas (PRM) após exposição à radioterapia de mama em mulheres. **Método:** Estudo prospectivo observacional realizado no Hospital de Câncer Alfredo Abrão em Campo Grande, Estado de Mato Grosso do Sul – MS. A amostra deste estudo foi composta por mulheres (n = 8) expostas à radioterapia de mama após cirurgia de quadrantectomia. Avaliou-se a força dos músculos respiratórios por meio da pressão inspiratória máxima (Pimáx) e da pressão expiratória máxima (Pemáx), utilizando-se do aparelho portátil denominado manovacuômetro. O exame foi realizado antes da primeira sessão de radioterapia e após a 25ª sessão, correspondendo ao último dia de tratamento radioterápico. Também foram avaliados o peso e a altura para medir o índice de massa corporal, os sintomas respiratórios clínicos de dispneia com o uso da Escala de Dispneia *Medical Research Council* e a caracterização de tosse com os Critérios Comuns de Toxicidade Pulmonar, em classificação da pneumonite clínica. **Resultados:** Os valores da Pimáx resultaram em 95,90 ± 23,86 e 81,20 ± 23,12 (média ± desvio padrão da média – p = 0,035) em relação ao percentual ideal, caracterizando diminuição significativa ao se comparar antes e após a exposição à radioterapia. Observou-se nível de significância de p<0,05, teste *t-student* e pareado. **Conclusão:** O estudo das PRM antes e após a exposição à radioterapia de mama evidenciou diminuição significativa da Pimáx.
Palavras-chave: Pressões Respiratórias Máximas; Radioterapia; Músculos Respiratórios/efeitos da radiação; Neoplasias da Mama.

Resumen

Introducción: En el cáncer de mama, la radioterapia postoperatoria se usa ampliamente para reducir los riesgos de recurrencia locorregional de la enfermedad. Sin embargo, la radiación de las estructuras torácicas implica riesgos, especialmente para los pulmones. **Objetivo:** Estudiar las presiones respiratorias máximas (PRM) después de la exposición a la radioterapia de mama en mujeres. **Método:** Estudio observacional prospectivo realizado en el Hospital de Cáncer "Alfredo Abrão" en Campo Grande – MS. La muestra del estudio consistió en mujeres (n = 8) expuestas a radioterapia de mama después de una cirugía de cuadrantectomía. La fuerza muscular respiratoria se evaluó a través de la presión inspiratoria máxima (MIP) y la presión espiratoria máxima (MEP), utilizando un dispositivo portátil llamado manovacuómetro. El examen se realizó antes de la 1ª sesión de radioterapia y después de la 25ª sesión correspondiente al último día de tratamiento de radioterapia. También fueron evaluados el peso y la altura para calcular el índice de masa corporal; los síntomas clínicos de disnea respiratoria utilizando la Escala de disnea del "Medical Research Council", y la caracterización de la tos con los criterios comunes de toxicidad pulmonar según la clasificación de neumonitis clínica. **Resultados:** Los valores de MIP fueron de 95,90 ± 23,86 y 81,20 ± 23,12 en relación con el porcentaje ideal, caracterizando una disminución significativa (media ± desviación estándar de la media - p = 0,035) al comparar el antes y el después de la exposición a radioterapia mamaria. Se observó nivel de significancia de p <0,05, se aplicó t-student y prueba pareada. **Conclusión**: El estudio de PRM, antes y después de la exposición a radioterapia de mama, mostró una disminución significativa en la MIP.
Palabras clave: Presiones Respiratorias Máximas; Radioterapia; Músculos Respiratorios/efectos de la radiación; Neoplasias de la Mama.

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INTRODUCTION

The assessment of Maximal Respiratory Pressures (MRP) is performed to evaluate quantitatively the strength of the respiratory[1] muscles. It started in the 60s with the predictive studies performed by Black et al.[2,3] for the values of Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP). Since then, other authors have conducted researches of the MRP in different countries with healthy people[4-6] and in pathological conditions[7,8]. Considering the studies with breast cancer patients, scarce literature reporting postoperative strength assessments of the respiratory muscles in post-surgery[8-9] and after radiotherapy[10-14] were found.

Even knowing that the evaluation of MRP has great clinical relevance due to the dysfunction detection of the respiratory muscles that can lead to dyspnea, hypoventilation, decreased exercise tolerance, cough ineffectiveness accumulating pulmonary secretions and, in extreme cases, to respiratory failure[15] it is not yet routine in clinical practice for breast cancer patients. In addition, the measurement of the respiratory muscle strength may be helpful for the assessment of the impact of chronic diseases or its treatment in the respiratory muscles[15], as in the case of breast cancer treated with radiotherapy[16].

The examination of the Maximal Respiratory Pressures with the manovacuometer is easy to perform, low-cost, and non-invasive in the clinical practice. The pulmonary function test with spirometry is well known and it is expected the reduction of lung performance after radiotherapy for breast cancer[16]. In this context, the questions that need to be asked is whether respiratory muscle strength (RMS) can also be reduced in breast cancer patients knowing that the physiology and the mechanics of respiratory muscle function are interlinked with the lung and capacity volumes[15]. Furthermore, it is known that radiation therapy can result in various adverse effects, since it can cause biochemical changes and cell damage, despite its efficacy in the treatment of mammary neoplasm after conservative surgery[17], because patients submitted to chest radiation can develop muscle and lung toxicities[18,19]. Among these effects, pulmonary actinic changes are the second major group of complications developed in patients with breast cancer treated with radiotherapy[20].

Therefore, this study aimed to carry out the assessment of Maximal Respiratory Pressure in women exposed to radiotherapy to treat breast cancer after breast-conservative surgery, in order to detect possible changes in the respiratory muscle function.

METHOD

Observational and prospective study approved by the Institutional Review Board of UFMS – Universidade Federal de Mato Grosso do Sul, report CAAE 46913415.7.0000.002. In compliance with Resolution 466/2012 of the National Health Council of the Ministry of Health (CNS – MS) all the participants after being informed about the design and objectives of the study, signed the informed consent form.

A total of eight women exposed to breast radiotherapy after being submitted to quadrantectomy surgery (n = 8) who matched the eligibility criteria for age (45 to 70 years) and BMI participated in this study. Adjuvant therapy was indicated for the experimental group, after breast quandrantectomy surgery.

Women who did not present the following complications were eligible: metastatic cancer, chemotherapy and/or hormone therapy concomitant with radiotherapy, cognitive impairment, associated lung disease, central or peripheral neurological disorders.

Participants were consecutively selected among the patients who initiated radiotherapy treatment at Alfredo Abrão Cancer Hospital.

Research site

The research was conducted at the radiotherapy unit of Alfredo Abrão Cancer Hospital in Campo Grande, State of Mato Grosso do Sul, from December 2015 to February 2016.

Radiotherapy protocol

The group studied underwent adjuvant radiotherapy with linear accelerator, whose total dosage was 5000 centigrays (cGy), with a daily dose of 200 cGy, distributed in twenty-five sessions, during 25 days of treatment.

PROCEDURES

Assessment of maximal respiratory pressures (MRP)

Quantification of MIP and MEP was performed with the portable device called manovacuometer (WIKA brand with pressure scale ranging from -150 to 150 cmH_2O (0 to -150 to (0 to -150 for MIP; 0 to 150 for MEP). The mouthpiece attached to the device had a 2 mm diameter hole to function as a relief valve of the facial muscles. During the measurement of maximal respiratory pressures, the study participants remained in sedestation position with the trunk at a 90 angle with the lower limbs. It was requested the patients to force expiration until reaching the residual volume (RV) for MIP measurement, followed by a maximal inspiratory effort against the occluded airway (Maneuver Muller); this maneuver was kept for up to 2 seconds. For the evaluation of MEP, a maximum inspiration was requested to Total Lung Capacity (TLC), followed by a maximal expiratory effort against the

occluded airway (Muller maneuver), maintained for up to 2 seconds.

Data from Maximal Respiratory Pressures were collected at two moments: before the first session of radiotherapy and after the twenty-fifth session corresponding to the last day of the radiotherapic treatment.

According to the Brazilian Guidelines for Pulmonary Function Tests[21] the MRP was evaluated. The results were analyzed in line with the predictive values of Neder et al.[5] regression equations.

Complementary evaluations

The BMI was evaluated with the measurement of weight and height.

The modified Medical Research Council Dyspnea (MRC)[22] scale was utilized to evaluate symptoms of dyspnea and cough symptoms were evaluated with the Common Toxicity Criteria (CTC Version 2.0)[23] to classify the clinic pneumonitis according to CTC Version 2.0.

Statistic

Maximal respiratory pressures were classified as dependent variables and the independent, were gender, age, weight, height and BMI.

The comparison between the moments before and after radiotherapy in relation to MIP and MEP was performed using the paired t-Student test. The other results of this study were presented as descriptive statistics or as tables and graphs. It was utilized the statistical program SigmaPlot, version 12.5, considering a significance level of 5% for the statistical analysis.

RESULTS

In this study, it were evaluated eight women who underwent quadrantectomy surgery and received radiotherapy. The results of the variables age, height, weight and BMI for the patients evaluated in this study are presented in Table 1.

Table 2 shows the results of the comparison between the moments before and after radiotherapy, in relation to the ideal percentage of the MIP and MEP variables. Among women who underwent quadrantectomy, MIP (% of ideal) after radiotherapy was significantly lower than that observed prior to this treatment (paired Student t-test, p = 0.035). For MEP (% of ideal), no significant decrease was observed with radiotherapy treatment (p = 0.122). These results are shown in Figure 1.

Table 1. Results of the variables age, height, weight and BMI of the patients evaluated in this study

Variables	Mean ± MSD
Age (years)	54.40 ± 8.43
Height (m)	1.59 ± 0.08
Weight (Kg)	74.00 ± 9.04
BMI (Kg/m^2)	2,943 ± 4,12

MSD = Standard deviation of the mean.

Table 2. Results of the comparison between the moments before and after radiotherapy, in relation to the ideal percentage of MIP and MEP variables

Variable	Radiotherapy timing		P value
	Before	After	
MIP (% of ideal)	95.90 ± 23.86	81.20 ± 23.12	0.035
MEP (% of ideal)	72.48 ± 11.91	63.42 ± 12.60	0.122

MIP = Maximal Inspiratory Pressure; MEP = Maximal Expiratory Pressure (MEP).
Results are presented as mean ± standard deviation of the mean. P value in the paired Student t-test.

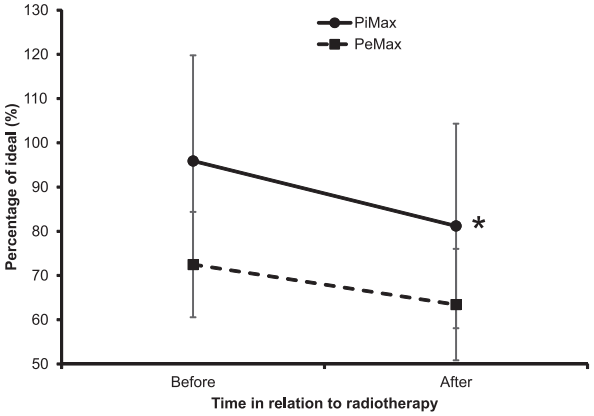

Figure 1. Graph showing MIP and MEP values, as a percentage of ideal, before and after radiotherapy, in patients who underwent quadrantectomy. Each symbol represents the mean and the bar the standard deviation of the mean. *Significant difference from the time before radiotherapy for MIP (paired Student t-test, p = 0.035)

Among patients who underwent quadrantectomy, the two most frequent staging observed were IIA (37.5% - n = 3) and IIB (25.0% - n = 2). Only one of the patients was a smoker (12.5%) and two of them had supraclavicular fossa (25.0%). Among the eight patients submitted to radiotherapy, 75.0% (n = 6) needed scar reinforcement and 87.5% (n = 7) of them underwent neoadjuvant chemotherapy. These results are presented in Table 3.

The degree of dyspnea according to MRC is 37.5% (n = 3) before radiotherapy and soon after, it increased to 62.5% (n =5) and 15 days after the treatment, it dropped to 25% (n = 2). According to the Common Toxicity Criteria, none of the patients presented cough before

Table 3. Distribution of patients who underwent quadrantectomy according to breast cancer staging, smoking, supraclavicular fossa, scar reinforcement treatment, and neoadjuvant chemotherapy

Variables	% (n)
Staging	
IA	12.5 (1)
IIA	37.5 (3)
IIA	12.5 (1)
IB	0.0 (0)
IIB	25.0 (2)
IIIB	12.5 (1)
Smoking	12.5 (1)
Supraclavicular fossa	**25.0 (2)**
Scar reinforcement	75.0 (6)
Neoadjuvant chemotherapy	87.5 (7)

radiotherapy, but after the treatment, 37.5% (n = 3) had this symptom and after 15 days, this symptom was not detected in any of these patients. Also, according to the Common Toxicity Criteria, dyspnea was not found in any of the patients before radiotherapy, but after, 25% (n = 2) had this symptom, and 15 days later, none of the patients presented dyspnea. These results are presented in Table 4.

Table 4. Distribution of patients who underwent quadrantectomy according to the degree of dyspnea and clinical pneumonitis (cough and dyspnea), at pre-radiotherapy (Pre-RT), post-radiotherapy (Post-RT) and 15 days after surgery radiotherapy (15 d post RT)

Variable	Before-RT % (n)	After-RT % (n)	15 days After-RT % (n)
Degree of dyspnea (MRC)			
0	62.5 (5)	37.5 (3)	75.0 (6)
1	25.0 (2)	37.5 (3)	12.5 (1)
2	12.5 (1)	12.5 (1)	12.5 (1)
3	0.0 (0)	12.5 (1)	0.0 (0)
Clinical pneumonitis degree (CTC)			
Cough			
0	100.0 (8)	62.5 (5)	100.0 (8)
1	0.0 (0)	37.5 (3)	0.0 (0)
2	0.0 (0)	0.0 (0)	0.0 (0)
3	0.0 (0)	0.0 (0)	0.0 (0)
Dyspnea			
0	100.0 (8)	75.0 (6)	100.0 (8)
1	0.0 (0)	25.0 (2)	0.0 (0)
2	0.0 (0)	0.0 (0)	0.0 (0)

MRC = Medical Research Council; CTC = Common Toxicity Criteria.

DISCUSSION

Postoperative chest radiotherapy is widely used in breast cancer to reduce the risks of locoregional recurrence and to improve overall survival. However, irradiation of thoracic structures involves risk, especially to the lungs. Therefore, the present study aimed to evaluate the impact of radiotherapy on respiratory function with manuovacuometry.

The mean age of the sample was 54.4 years. The literature indicates a relationship of major complications of actinic pulmonary functions over 61 years[24]. Overall, published studies report an association between changes in lung function and age in women undergoing breast cancer radiotherapy[23]. However, no publications on age-related respiratory muscle function were found in women undergoing radiotherapy after breast quadrantectomy. The BMI found in this study was 29,43 kg/m^2. Studies show that risk factors for development of radiation induced pneumonitis in breast cancer pactients are advanced age, body mass index indicating malnutrition or obesity (BMI less than 21 or above 27), and clinical staging and radiation dose (above20 Gy)[24,25]. Spirometry, used to evaluate changes in lung function in patients irradiated for breast cancer, has been previously described in the literature[17]. However, the majority of the researches do not include the use of manuovacuometry to detect respiratory muscle changes. As has been observed, few studies analyzed prospectively the functional modifications of the respiratory muscles using the evaluation of MRP before and after radiotherapy in breast cancer patients[10-14].

In the present study, there was a significant decrease in inspiratory muscle strength after radiotherapy in the women evaluated. A recent study[10] has shown that this reduction occurs and is associated with other respiratory changes: decreased thoracic and xiphoid mobility and reduced maximal expiratory pressure within three months of treatment termination in women with conservative breast surgery. The study of Santos et al.[13] showed a reduction in MRP measurements after radiotherapy, however its sample consisted of mastectomized women, unlike the present study, which analyzed only women who were submitted to conservative surgery.

Nevertheless, a study by Schettino et al.[12] shortly after the end of radiotherapy treatment and another by Vardar-Yağlı et al.[14] after five years of radiotherapy followed up women who underwent conservative and radical surgery. Both studies did not show a reduction of maximal respiratory pressures. This is because inspiratory pressures may possibly change after radiotherapy and return to normal levels after five years of follow-up. A similar study of Piazza et al.[11] found no significant difference in MIP values (p = 0.39).

Dunlap et al.[19] reported that radiation doses between 5000 cGy and 6000 cGy in the chest wall are strongly correlated with the development of toxicity that includes

muscle, connective tissue, the neurovascular bundle, and bone, consequently causing fibrosis of intercostal muscles[20], a fact that may explain the reduction of MIP. In addition, daily-fractionated radiation doses from 200 cGy in the treatment of breast cancer are biologically related to soft tissue alterations[26]. This muscle toxicity may be related to the application of radiation to the skeletal muscle that interacts with the muscle fiber; its oxidative capacity alters the muscle remodeling and regeneration response and can result in fatigue and weakness[27,28]. Even when the respiratory muscle is located outside the radiation field, it can often receive an off-target dose in chest radiotherapy, causing contractile dysfunction due to deoxyribonucleic acid (DNA) damage and oxidative stress to myofibrils[29], affecting muscle morphology, reactive oxygen species production and angiogenesis[30]. In this study, 87.5% of the evaluated patients underwent chemotherapy before surgery. Lee's studies[24] showed no relationship of pulmonary complications between neoadjuvant chemotherapy and radiotherapy. Similar to Bregagnol et al.[8] analysis, which showed no decrease in MRP values in patients undergoing neoadjuvant chemotherapy, however, no measurements were performed after radiotherapy.

Radiation pneumonitis is a pulmonary complication that can occur in patients treated with irradiation for breast cancer[24]. In the current study, there was remission of clinical respiratory symptoms that could show the presence of clinical pneumonitis defined according to CTC (version 2.0) 21 criteria 15 days after the end of radiotherapy, discarding the diagnosis of radiation pneumonitis. It is known that the signs and symptoms usually disappear spontaneously several weeks after the radiotherapic treatment[30]. Lingos et al.[31] concluded that radiation pneumonitis after breast-conservative surgery and radiotherapy breast cancer treatment is a rare complication, and is more likely to occur in patients treated with three radiation fields and undergoing chemotherapy concomitantly with radiotherapy treatment. This was not the case of the present study.

Based in the results found in this study, it is recommended to evaluate the maximum respiratory pressure in women who will be irradiated in the breast in order to track and detect early changes in respiratory muscle function. Since manovacuometer is a noninvasive, low cost and easy to perform exam, it may indicate the use of this equipament in clinical practice by physiotherapists to complement the physical assessment and follow up of these patients in order to detect changes and prevent pulmonary complications.

At the same time that the qualities of the study appear to be evident, its limitations should not be overlooked. Firstly, it is important to highlight that only participants who were in the period after quadrantectomy surgery with radiotherapy indication and without complications of another nature were included in the study, which restricted the sample. The exclusion of participants who underwent radical breast surgeries, and concomitant chemotherapy and/or hormone therapy treatment was due to the possibility of measuring respiratory alterations because of other than radiotherapy treatment. In addition, patients with pulmonary impairment were not included either, as respiratory problems prior to radiotherapy treatment could bias the results.

Secondly, we must emphasize that in clinical practice respiratory impairment is not always similar for all the patients, because of the irradiation. In this case it is essential to perform a broad respiratory assessment, emphasizing the dysfunctions present in each case.

CONCLUSION

The study of maximal respiratory pressure before and after exposure to breast radiotherapy showed significant decrease in maximal inspiratory pressure in women. The negative impact on the respiratory system was characterized by diaphragm muscle weakness. Manovacuometer may be used to assess the integrity of respiratory muscles by measuring their strength post thoracic radiotherapy in breast cancer patients.

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CONTRIBUTIONS

The authors contributed equally and substantially in all the phases of the study and approved the final version to be published.

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DECLARATION OF CONFLICT OF INTEREST

There is no conflict of interests to declare.

REFERENCES

1. Pessoa IMBS, Parreira VF, Fregonezzi GAF, et al. Reference values for maximal inspiratory pressure: a

systematic review. Can Respir J. 2014;21(1):43-50. doi: http://dx.doi.org/10.1155/2014/982374

2. Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. Am Rev Respir Dis. 1969;99(5):696-702. doi: https://doi.org/110.1164/arrd.1969.99.5.696
3. Black LF, Offord K, Hyatt RE. Variability in the maximal expiratory flow volume curve in asymptomatic smokers and in nonsmokers. Am Rev Respir Dis. 1974 Sep;110(3):282-92. doi: https://doi.org/10.1164/arrd.1974.110.3.282
4. Rosa GJ, Morcillo AM, Assumpção MS, et al. Predictive equations for maximal respiratory pressures of children aged 7-10. Braz J Phys Ther. 2017;21(1):30-36. doi: http://dx.doi.org/10.1016/j.bjpt.2016.04.002
5. Neder JA, Andreoni S, Lerario MC, et al. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. Braz J Med Biol Res. 1999;32(6):719-27. doi: http://dx.doi.org/10.1590/S0100-879X1999000600007
6. Simões RP, Deus APL, Auad MA, et al. Maximal respiratory pressure in healthy 20 to 89 year-old sedentary individuals of central São Paulo State. Rev Bras Fisioter. 2010;14(1):60-7. doi: http://dx.doi.org/10.1590/S1413-35552010000100010
7. Tilanus TBM, Groothuis JT, TenBroek-Pastoor JMC, et al. The predictive value of respiratory function tests for non-invasive ventilation in amyotrophic lateral sclerosis. Respir Res. 2017;18(1):144. doi: http://dx.doi.org/10.1186/s12931-017-0624-8
8. Bregagnol RK, Dias AS. Alterações funcionais em mulheres submetidas à cirurgia de mama com linfadenectomia axilar total. Rev Bras Cancerol. 2010;56(1):25-33.
9. Abreu APM, Endres D, Costa AB, et al. Função pulmonar e força muscular respiratória em pacientes submetidas à cirurgia oncológica de mama. Rev Bras de Cancerol. 2014;60(2):151-157.
10. Suesada MM, Carvalho HA, Albuquerque ALP, et al. Impact of thoracic radiotherapy on respiratory function and exercise capacity in patients with breast cancer. J Bras Pneumol. 2018;44(6):469-476. doi: http://dx.doi.org/10.1590/s1806-37562017000000120
11. Piazza CC, Guirro EOC, Costa D, et al. Avaliação da função pulmonar e muscular respiratória em mulheres com câncer de mama. Rev Bras Mastologia. 2006;16(4):143-149.
12. Schettino RC, Jotta N, Cassali GD. Função pulmonar em mulheres com câncer de mama submetidas à radioterapia: um estudo piloto. Fisioter Pesq. 2010;17(3):248-52. doi: http://dx.doi.org/10.1590/S1809-29502010000300011
13. Santos DE, Rett MT, Mendonça ACR, et al. Efeito da radioterapia na função pulmonar e na fadiga de mulheres em tratamento para o câncer de mama. Fisioter Pesquisa. 2013;20(1):50-55. doi: http://dx.doi.org/10.1590/S1809-29502013000100009
14. Vardar-Yağlı N, Şener G, Sağlam M, et al. Meme kanseri olan kadınlarda ve sağlıklı kişilerde pulmoner fonksiyonlar ve solunum kas kuvvetinin karşılaştırılması. Turk J Physiother Rehabil. 2014;25(3):37-41. doi: http://dx.doi.org/10.7603/s40680-014-0019-4
15. Troosters T, Gosselink R, Decramer M. Respiratory muscle assessment. Eur Respir Mon. 2005;31:57-71. doi: http://dx.doi.org/10.1183/1025448x.00031004
16. Bessa EJC, Lopes AJ, Rufino R. A importância da medida da força muscular respiratória na prática da pneumologia. Pulmão RJ. 2015;24(1):37-41.
17. AlSaeed EF, Balaraj FK, Tunio MA. Changes in pulmonary function tests in breast carcinoma patients treated with locoregional post-mastectomy radiotherapy: results of a pilot study. Breast Cancer (Dove Med Press). 2017;9:375-381. doi: https://doi.org/10.2147/BCTT.S114575
18. Javadinia SA, Dehghani M, Ferns GA, et al. Toxicity of adjuvant radiotherapy in patients with breast cancer: a review study. Rep Radiother Oncol. 2018;5(1):e89328. doi: https://doi.org/10.5812/rro.89328
19. Dunlap NE, Cai J, Biedermann GB, et al. Chest wall volume receiving >30 Gy predicts risk of severe pain and/or rib fracture after lung stereotactic body radiotherapy. Int J Radiat Oncol Biol Phys. 2010;76(3):796-801. doi: https://doi.org/10.1016/j.ijrobp.2009.02.027
20. Schmitz KH, DiSipio T, Gordon LG, et al. Adverse breast cancer treatment effects: the economic case for making rehabilitative programs standard of care. Support Care Cancer. 2015; 23(6):1807-17. doi: https://doi.org/10.1007/s00520-014-2539-y
21. Souza RB. Pressões respiratórias estáticas máximas. J. Pneumol. 2002;28(Supl3):S155-S165.
22. Kovelis D, Segretti NO, Probst VS, et al. Validation of the modified pulmonary functional status and dyspnea questionnaire and the medical research council scale for use in brazilian patients with chronic obstructive pulmonary disease. J Bras Pneumol. 2008;34(12):1008-1018. doi: http://dx.doi.org/10.1590/S1806-37132008001200005
23. Saad ED, Hoff PM, Carnelós RP, et al. Critérios comuns de toxicidade do Instituto Nacional de Câncer dos Estados. Rev Bras Cancerol. 2002;48(1):63-96.
24. Lee TF, Chao PJ, Chang L, et al. Developing multivariable normal tissue complication probability model to predict the incidence of symptomatic radiation pneumonitis among breast cancer patients. Plos One. 2015;10(7):e0131736. doi: https://doi.org/10.1371/journal.pone.0131736
25. Allen AM, Prosnitz RG, Ten Haken RK, et al. Body mass index predicts the incidence of radiation pneumonitis in breast cancer patients. Cancer J. 2005;11(5):390-8. doi: https://doi.org/10.1097/00130404-200509000-00006

26. Benk V, Souhami L, Faria SL. Complicações mais ligadas à radioterapia. In: Faria SL. Câncer de mama: diagnóstico e tratamento. Rio de Janeiro: Medsi; 1994.

27. Hardee JP, Puppa MJ, Fix DK, et al. The effect of radiation dose on mouse skeletal muscle remodeling. Radiol Oncol. 2014;48(3):247-56. doi: https://doi.org/10.2478/raon-2014-0025

28. Jurdana M, Cemazar M, Pegan K, et al. Effect of ionizing radiation on human skeletal muscle precursor cells. Radiol Oncol. 2013; 47(4):376-81. doi: https://doi.org/10.2478/raon-2013-0058

29. Hsieh CH, Lin YC, Chen YJ, et al. Diaphragm contractile dysfunction causes by off-target low-dose irradiation. Am J Transl Res 2016;8(3):1510-7.

30. Fix DK, Hardee JP, Bateman TA, et al. Effect of irradiation on akt signaling in atrophying skeletal muscle. J Appl Physiol 2016;121(4):917-94. doi: https://doi.org/10.1152/japplphysiol.00218.2016

31. Lingos TI, Recht A, Vicini F, et al. Radiation pneumonitis in breast cancer patients treated with conservative surgery and radiation therapy. Int J Radiat Oncol Biol Phys. 1991;21(2):355-60. doi: https://doi.org/10.1016/0360-3016(91)90782-y

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