



THE INCIDENCE OF RADIATION PNEUMONITIS IN BREAST CANCER PATIENTS WHO RECEIVED RADIOTHERAPY USING 3-DIMENSIONAL TECHNIQUES

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ABSTRACT

Background: According to the 2018 Global Cancer Observatory from the World Health Organization (WHO), breast cancer was the most common cancer in Indonesia. 3-dimensional conformal radiotherapy (3D-CRT) is one of the breast cancer treatment planning. Effect of radiation on the lungs can cause radiation pneumonitis. The incidence rate of pneumonitis in breast cancer patients who received radiotherapy using 3D-CRT techniques from several researchers were still varied and there was no accurate data yet at RSUP Dr. Kariadi. **Objective:** To determine the incidence of pneumonitis in breast cancer patients undergoing breast cancer 3D-CRT. **Methods:** Cross-sectional was used as research design in this study. The subject was chosen by consecutive sampling methods. The independent variables of this study was 3D breast cancer radiation therapy, while the dependent variable was radiation pneumonitis. The hypothesis test on this study was analyzed using chi-square test. **Results:** Forty one subjects were included in this study, two subjects were found with a picture of pneumonitis on chest radiographs. The incidence of radiation pneumonitis in breast cancer patients who received radiotherapy using 3-dimensional techniques was 4.9%. The research also found that there was no significant relationship between breast cancer radiation therapy 3-dimensional techniques on the incidence of pneumonitis. **Conclusion:** The incidence of radiation pneumonitis in breast cancer patients who received radiotherapy using a 3-dimensional technique was 4.9%.

Keywords: 3 Dimensional Technique Radiotherapy, Breast Cancer, Radiation Pneumonitis

INTRODUCTION

According to the 2018 Global Cancer Observatory data from the World Health Organization (WHO), it is reported that breast cancer is the most common cancer in Indonesia, approximately 58,256 cases or 16.7% of the total 348,809 cases of cancer. The highest incidence rate in Indonesia for women is breast cancer, which is 42.1 per 100,000 population with an average 17 deaths per 100,000 population followed by cervical cancer, approximately 23.4 per 100,000 population with an average death rate 13.9 per 100,000 population. The incidence of breast cancer in Dr. Kariadi General Hospital ranks second.^{1,2}

Treatment of breast cancer depends on the stage and expression of the biomolecular agent or biomolecular-signaling. Main therapy for breast cancer are surgery, systemic therapy (chemotherapy), hormonal therapy, targeted therapy, and radiotherapy. Radiotherapy is one of the important modalities in breast cancer management. Radiotherapy in the management of breast cancer can be given as an adjuvant and palliative curative therapy.³

External radiotherapy techniques that are allowed are conventional 2-dimensional radiotherapy, 3-dimensional conformal radiotherapy, and Stereotactic Body Radiotherapy (SBRT). 3-dimensional conformal radiotherapy (3D-CRT) is a radiation therapy planning concept using volumetric data from CT-Scan. The use of CT-Scan in determining the target volume is useful in reducing geographic inaccuracies. With the development of diagnostic imaging technology and radiotherapy, the combination of 3-dimensional radiation planning with the use of more complex beam arrangements can produce a beam coverage that is fit to the shape of the tumor. So that it will reduce radiation exposure to normal tissue.⁴

The effects of radiation on the lungs can cause radiation pneumonitis. Capillary endothelial cells are very sensitive to radiation, and play an important role in the development of radiation pneumonitis. Damage to the endothelium can include detachment of cells from the basal membrane, obstruction of the lumen by thrombus, and rupture of capillaries. Furthermore, fibrin exudate fills the stromal cavity and alveolar lumen, edema and hyaline membrane formation will interfere with the gas exchange process.



Inflammatory processes such as acute pneumonitis may resolve completely or progress towards a fibrotic process resulting in obstruction of the alveolar lumen. Collagen deposition in fibrosis, also causes thickening of the alveolar wall and reduces the presence of pneumocytes. Then the alveoli become collapse and obliterated by connective tissue. When pulmonary fibrosis occurs, lung function will decrease, depending on the volume area of the lung exposed to radiation, and if the volume is small the other parts of the lung may compensate and significantly prevent clinical manifestations.⁵

The diagnosis of radiation pneumonitis is usually based on clinical symptoms and a chest x-ray examination. Several studies have analyzed the occurrence of early-phase radiation pneumonitis based on chest x-rays, approximately within 1-6 months (more often within 3 months) and the advanced phase become fibrosis. Radiation pneumonitis is difficult to diagnose clinically. This is because most patients are asymptomatic. Changes in the X-ray are characterized by an increase in opacity in the radiation-affected area.⁶

Some of the factors that increase the risk of radiation pneumonitis are lung volume exposed to radiation, radiation dose, timedose factor / fractionation, use of chemotherapy, underlying diseases and administration of corticosteroids.⁶

The 3-dimensional radiotherapy technique is expected to reduce the incidence of radiation pneumonitis. In addition to obtaining a beam coverage that is adapted to the shape of the tumor, the use of a more complex beam can increase homogeneity and reduce the dose to normal tissue, so that a better therapeutic ratio is obtained. A low radiation dose to healthy tissue and a homogeneous dose distribution aims to reduce both acute and chronic toxicity, so that a better quality of life is obtained. In addition, with a low dose of healthy tissue, it can be possible to do a dose escalation, with the hope that an increase in therapeutic response can occur.⁴

The incidence of pneumonitis in breast cancer patients undergoing radiotherapy using 3-dimensional techniques from several researchers is still varied and there is no accurate data yet at RSUP Dr. Kariadi, this study will analyze the incidence of pneumonitis in breast cancer patients undergoing breast cancer 3D-CRT.

METHODS

The research design used in this study was cross sectional. The subject is chosen by consecutive sampling methods. The independent variables of this study was 3D breast cancer radiation therapy, while the dependent variable was radiation pneumonitis. This hypothesis test on this study is analyzed with chi-square test.

RESULTS

During the period 2015-2019, 11765 patients were subjected to radiation therapy at RSUP Dr. Kariadi, and 2723 patients among them diagnosed with breast cancer. After recording medical records for 2019-2020 with consecutive sampling, 139 breast cancer patients received 3D radiation therapy, but those who met the inclusion criteria were 41 patients with post-radiation chest x-ray with data distribution in table 1.

Table 1. Distribution data of breast cancer patients

Variable	n	%
Age		
≤ 50 years	24	58,5
> 50 years	17	41,5
Gender		
Male	1	2,4
Female	40	97,6
Breast cancer location		
Right	14	34,1
Left	23	56,1
Bilateral	4	9,8
Type of surgery		
MRM	33	80,5
BCS	5	12,2
No surgery	3	7,3
Metastases		
Yes	10	24,4
No	31	75,6
Radiation pneumonitis		
Yes	2	4,9
No	39	95,1

Based on gender classification, almost all women, 97.6%, and 1 male patient were diagnosed with breast cancer. Most of them tend to be younger, the youngest age is 30 years, up to 50 years, as much as 58.5%. Based on the location of the malignancy, the left breast was mostly in 23 subjects (56.1%). 80.5% of patients referred for radiation therapy received MRM surgery, 3 patients did not receive surgery, and 12.2% received BCS. Based on metastasis or not to other organs, most were not metastases, 31 subjects (75.6%), and metastases were 10 subjects (24.4%). The results of post-



radiation chest x-rays, 4.9% of subjects developed pneumonitis. The ages of the subjects with the pneumonitis were all less than 50 years. The characteristics of the subjects evaluated after radiation associated with pneumonitis are presented in Table 2.

Table 2. Characteristics of radiation pneumonitis

Variable	Radiation pneumonitis				p
	Yes		No		
	n	%	n	%	
Age					
≤ 50 years	2	8,3	22	91,7	0,337
> 50 years	0	0	17	100	
Gender					
Male	0	0	1	100	0,951
Female	2	5	38	95	
Breast cancer location					
Right	1	7,1	13	92,9	0,830
Left	1	4,3	22	95,7	
Bilateral	0	0	4	100	
Type of surgery					
MRM	1	3	32	97	0,057
BCS	0	0	5	100	
No surgery	1	33,3	2	66,7	
Metastases					
Yes	0	0	10	100	0,567
No	2	6,5	29	93,5	

*Significance (p<0,05)

Table 2 presents the incidence of radiation pneumonitis based on age group, sex, location of breast cancer, type of surgery, and metastasis. Post-radiation pneumonitis occurred in 2 of 24 subjects (8.3%) aged ≤ 50 years, and out of 17 subjects aged > 50 years did not have post-radiation pneumonitis. The sex of research subjects, 98% female, only 1 person (2%) male. Pneumonitis occurred in 2 people (4.9%) subjects, all of them were female. Radiation pneumonitis occurred in 1 subject (7.1%) of 14 subjects with radiation area of right breast cancer, as well as in subjects who received radiation to the left breast area, 1 subject (4.3%) of 23 study subjects developed pneumonitis, while 4 subjects who received radiation bilateral, there was no pneumonitis. Subjects who received surgery was 37, whereas 1 subject did not receive surgery and 2 subjects had no history of surgery. Pneumonitis occurred in 1 subject (3%) of 33 who received Modified Radical Mastectomy (MRM), and no pneumonitis was found in all subjects who received Breast Conserving Surgery (BCS). Pneumonitis occurred in 1 of 3 subjects with no known history of

surgery. Post-radiation pneumonitis was not found in 10 subjects who had lung metastases, but was found in two (6.5%) of 31 subjects who did not develop lung metastases.

The results showed no significant difference in the occurrence of post-radiation pneumonitis based on the type of surgery (p = 0.057), radiation area (p = 0.830), age (p = 0.337), gender p = 0.951), or subjects with pulmonary metastases (p. = 0.567).

DISCUSSION

From a study conducted on 41 breast cancer patients at RSUP Dr. Kariadi, who received 3-dimensional radiation therapy techniques during the 2015-2019 period, two subjects were found with a pictures of pneumonitis on chest radiographs, so that the incidence of radiation pneumonitis in breast cancer patients undergoing radiation therapy using 3-dimensional techniques was 4.9%. This is in accordance with the hypothesis that there is a minimal incidence of pneumonitis in breast cancer patients undergoing 3-dimensional radiation therapy techniques. The results of this study are in accordance with the objectives of the 3D radiation technique which has a minimal impact on the occurrence of radiation pneumonitis compared to conventional techniques, such as the results of the study by Fatchoerchman et al. with the results of the incidence of radiation pneumonitis, stage II-III breast carcinoma patients who received chemoradiation therapy using conventional technique at RSUP Dr. Kariadi tends to be high at 40.6%, and research from Jeba J et al. It was found that radiation pneumonitis clinically occurs in almost one-fifth of breast cancer patients who undergo conventional radiotherapy.^{5,7}

Although the results of this study cannot accurately answer the relationship of 3-dimensional technique of breast cancer radiation therapy, to the incidence of post-radiation pneumonitis both from sex, age, area of radiation and surgery, only 2 (4.9%) of 41 subjects were found with pneumonitis. This result is much smaller than research using 2-dimensional techniques.

The incidence of radiation pneumonitis was almost the same as the percentage of right breast cancer, 1 subject out of 14 subjects (7.1%), 1 subject out of 23 subjects (4.3%) with left breast cancer, and 0 of 4 subjects (0%) with bilateral breast cancer. So there is no significant difference in the proportion of radiation pneumonitis incidence based on the location of breast cancer (p = 0.830). The results of



this study are consistent with research from Jeba J et al. where there was no significant difference in the proportion of radiation pneumonitis in patients with right and left breast cancer ($p = 0.246$).⁷

CONCLUSION

From a study conducted on 41 breast cancer patient subjects at RSUP Dr. Kariadi, who received 3-dimensional radiation therapy during the 2015-2019 period, two subjects were found with a picture of pneumonitis on chest X-rays so that the incidence of radiation pneumonitis in breast cancer patients undergoing radiotherapy using 3-dimensional techniques was 4.9%, much smaller than the study in patients subjected to radiation using conventional 2D techniques.

ETHICAL APPROVAL

Ethical Clearance (No: 61/KEPK/FK-UNDIP/V/2020) has been obtained from Komisi Etik Penelitian Kedokteran (KEPK), Faculty of Medicine, Diponegoro University

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, S.L., Y.W., F.H, C.H. Methodology, S.L., Y.W., F.H, C.H. Software, S.L. Writing—review and editing, S.L., Y.W., F.H, C.H.

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