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Original Article

Respiratory Emergency in Hospitalized patient with Intrathoracic Malignancy at H. Adam Malik General Hospital

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Abstract

Background: *Increased number of intrathoracic malignancy cases (Lung tumor, Mediastinum tumor, Secondary lung cancer and Chest wall tumor) contribute in increased complications of respiratory emergencies such as superior cava vein yyndrome (scvs), massive malignant pleura effusion (mpe), central airway obstruction (cao), massive hemoptysis, lung thromboembolism and pneumothorax. This study aims to look at the proportions, outcomes, and factors that influence respiratory emergency in intrathoracic malignancy cases.*
Methods: *This was a retrospective case series of inpatient respiratory emergencies in patients intrathoracic malignancy at H. Adam Malik Central General Hospital - Medan from 1 May 2011 to 30 April 2016.*
Results: *From 690 subjects intrathoracic malignancy, there were 137 (19.8%) patients with respiratory emergencies and mostly caused by lung tumors (83.9%). Massive MPE was is the most common emergency of 45 cases (6.5%) and massive haemoptysis of at least 4 cases (0.6%). The risk of death was higher in patients with respiratory emergencies. Mediastinum and location of tumor contribute in respiratory emergency appearance with respective OR of 3.9 and 1.5 (p value <0.005)*
Conclusions: *Increased of mortality rate in patients with respiratory emergency and MPE massive is the most cases. Type of the malignancy and Right lung tumor contribute of respiratory emergency in intrathoracic malignancy cases. (**J Respirol Indones 2022; 42(1): 1–8)***
Keywords: *respiratory emergency, intrathoracic malignancy, incidence, outcome*

Kegawatdaruratan Respirasi pada Pasien Rawat Inap dengan Keganasan Intratoraks di RSUP H. Adam Malik

Latar belakang: *Meningkatnya kasus keganasan rongga toraks (Tumor paru, Tumor mediastinum, Tumor paru metastase dan Tumor dinding dada) menyebabkan meningkatnya komplikasi berupa kegawatdaruratan respirasi seperti Sindroma vena kava superior (SVKS), Efusi pleura ganas (EPG) Masif, Central airway obstruction (CAO), Hemoptisis masif, Tromboemboli paru dan Pneumotoraks. Penelitian ini bertujuan untuk melihat proporsi, luaran, dan faktor yang mempengaruhi munculnya kegawatdaruratan respirasi pada keganasan rongga toraks.*
Metode Penelitian: *Penelitian ini merupakan laporan kasus serial yang dilakukan secara retrospektif terhadap kasus kegawatdaruratan respirasi pada pasien keganasan rongga toraks yang dirawat inap di RSUP H. Adam Malik Medan pada periode 1 Mei 2011 – 30 April 2016.*
Hasil: *Dari 690 subjek dijumpai sebanyak 137 (19.8%) dengan kegawatdaruratan respirasi dan penyebab terbanyak adalah tumor paru (83.9%). Efusi pleura ganas masif merupakan kegawatdaruratan terbanyak yaitu 45 kasus (6.5%) dan hemoptisis masif yang paling sedikit 4 kasus (0.6%). Risiko kematian lebih tinggi pada pasien dengan kegawatdaruratan respirasi. Tumor mediastinum dan tumor paru kanan lebih berisiko menimbulkan kegawatdaruratan respirasi dengan OR masing - masing 3.9 dan 1.5 (p-value <0.05)*
Kesimpulan: *Meningkatnya angka kematian pada pasien dengan kegawatdaruratan respirasi dan didominasi kasus EPG masif. Jenis keganasan dan letak tumor di kanan berpengaruh terhadap munculnya kegawatdaruratan respirasi. (**J Respirol Indones 2022; 42(1): 1–8)***
Kata kunci: *kegawatdaruratan respirasi; keganasan rongga toraks; angka kejadian; luaran*

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INTRODUCTION

Intrathoracic malignancy consists of lung cancer, mediastinal tumors, mesothelioma, secondary lung tumors and chest wall tumors.[1] Respiratory emergencies are one of the oncology emergencies due to complications or adverse reaction of the treatment that requires prompt immediate action to prevent death or serious organ damage.[2]

Lung cancer is a malignant disease with high mortality rate and the most cause of death due to cancer in the United States with 5 years survival rate only 17.7%.[3] Increase number of lung cancer and intrathoracic malignancy lead to increase oncology emergency cases especially respiratory emergencies. Minami et al, conducted a study of 245 lung cancer patients who came to the Emergency Room (ER) and found that respiration complaints were the most cases (37.6%).[4]

Respiratory emergency is a life-threatening condition, and require immediate attention due to disruption of gas exchange in the lung or failure of the respiratory system, which if it is not addressed immediately can lead to a condition called acute respiratory failure characterized by declining oxygen in the arteries (hypoxemia) or elevated levels of carbon dioxide (hypercarbia) or a combination of both. Respiratory emergency due to malignancy such as Superior vena cava syndrome (SVCS), malignant pleural effusion (MPE), massive hemoptysis, venous thromboembolism (deep vein thrombosis and pulmonary embolism), central airway obstruction (CAO) and pneumothorax.[5]

From previous studies found that the incidence of Massive pleural effusion about 11.2% of all pleural effusions and 53.7% caused by malignancy.[6] While the incidence SVCS about 3.8%, CAO as much as 13%, Venous thromboembolism 21%, Massive hemoptysis 3%, and pneumothorax was found as much as 0.03–0.05%.[7–11]

The risk of death will increase in patients intrathoracic malignancies with respiratory emergency. The aim of this study was to determine the proportions, outcomes, and factors that related to the respiratory emergencies in hospitalized intrathoracic malignancies patients.

METHOD

This study is a case series which was conducted retrospectively in intrathoracic malignancy patients with respiratory emergencies who were hospitalized at H. Adam Malik General Hospital in 5 years period (1st May 2011 to 30th April 2016).

The samples in this study are total sampling that fulfill the inclusion and exclusion criteria. The inclusion criteria were diagnosis of intrathoracic malignancy (lung tumor, mediastinal tumor, secondary lung tumor, chest wall tumor and mesothelioma) based on cytology or histopathology examination, and patients who were on treatment or not (e.g surgery, chemotherapy or radiotherapy). The exclusion criteria were patients with pulmonary tuberculosis or post tuberculosis, patients with blood clotting disorders and patients whose diagnose of malignancy was established from other hospital. The diagnosis of respiratory emergency based on the gold standard: (1) Massive MPE, defined by the present of malignant cells from pleural fluid examination on pleural biopsy with massive size of pleural effusion from CXR; (2) SVCS was diagnosed from clinical finding and Thoracic CT scan; (3) CAO was diagnosed by the presence of airway obstruction in the trachea or the main carina by bronchoscopy; (4) Massive hemoptysis, based on Bushro's criteria, is the discovery of bloody cough at least 600 mL/24 hours or bloody coughing <600 mL and ≥250 mL with Hb <10g% and still lasting 24 hours or bloody cough <600 mL and ≥250 mL with Hb >10g% and still continues within 48 hours;[12] (5) venous thromboembolism/pulmonary embolism, established from Ct angiography/VQ Scan and Well Score; (6) Pneumothorax was established clinically and radiologically.

All research procedures have been approved by the Health Research Ethical Commission. Data were obtained from the Medical Record Unit and data processing was performed

using the Statistical Package for Social Sciences (SPSS) where p value <0.05 was considered significant.

RESULTS

As much as 690 patients enrolled in this study from 5 years period. The characteristics of the subject (Table 1) mostly in age ranged between 50–59 years (38.4%), and male predominant (78.8%).

Majority of educational background was senior high school (50.4%) but mostly unemployed (47.5%). The proportion of intrathoracic malignancies found that lung tumors was the most cases about 626 cases (90.8%), mediastinal tumors 32 cases (4.6%) and secondary lung tumors as many as 32 cases (4,6%). While chest wall tumor and mesothelioma were not seen from the observation period. As many as 197 patients died during hospitalization and 493 patients discharge from hospital with outpatient treatment or by their own request.

Of the 690 cases of intrathoracic malignancy, 137 cases (19.8%) came with respiratory emergencies complication and 553 cases (80.2%) without respiratory emergency (Table 2). The distribution of respiratory emergencies every year can be seen in Figure.1, where the percentage of patients who present with respiratory emergencies is almost similar every year, with ranged 16.3% to 27.8%. The most common respiratory emergency was massive MPE about 45 cases (6.5%) followed by superior vena cava syndrome (svcs) (40; 5.8%), central airway obstruction (cao) (27; 3.9%), pneumothorax (11; 1.6%) and massive hemoptysis (4; 0.6%), which can be seen in Table 2. The annual distribution of respiration emergencies can be seen in Figure 2. In this study also found 10 (1.4%) patients who came with multiple emergencies (> 1 respiratory emergency) with annual distribution between 0–3.1%.

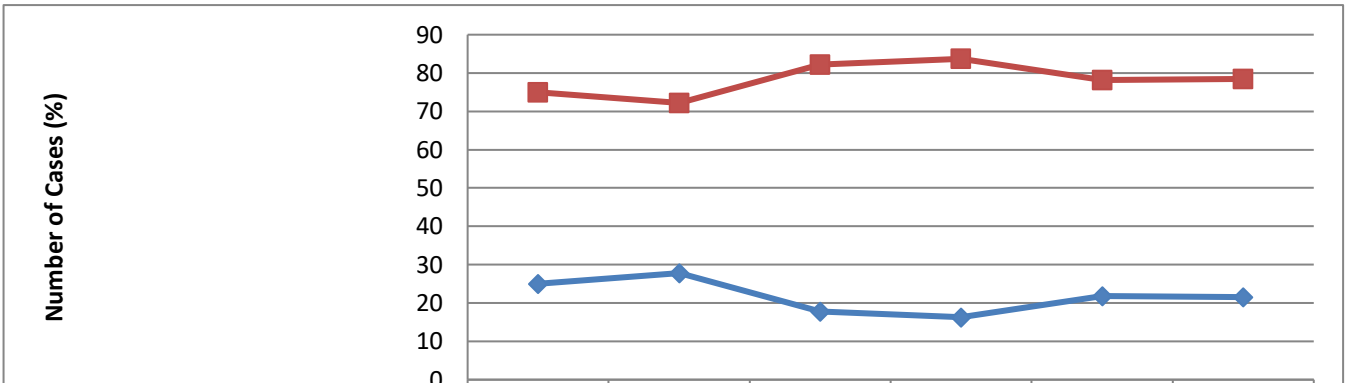
Table 1. Characteristic of Intrathoracic Malignancy Patients

Characteristic		n	%
Age (years)	<40	47	6.8
	40–49	120	17.4
	50–59	265	38.4
	60–69	186	27.0
	≥70	72	10.4
Gender	Female	146	21.2
	Male	544	78.8
Occupation	Civil Servant	49	7.1
	Private	313	45.4
	Unemployed	328	47.5
Education	Never school	1	0.1
	Primary School	152	22.0
	Middle High School	111	16.1
	Senior High School	348	50.4
	Diploma/Bachelor	78	11.3
Malignancy	Lung Tumor	626	90.7
	Mediastinal Tumor	32	4.6
	Secondary Lung Tumor	32	4.6
Outcome	Death	197	28.5
	Outpatient	493	71.5

Table 2. Distribution of Respiratory Emergency in Intrathoracic Malignancy Patient

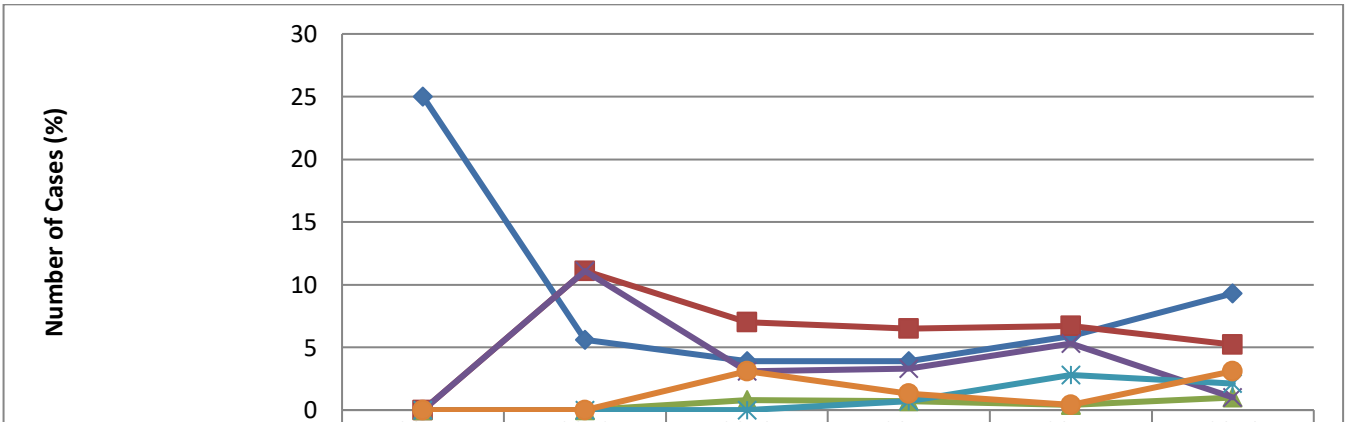
		2011		2012		2013		2014		2015		2016		SUM
		n	%	n	%	n	%	n	%	n	%	n	%	N (%)
Respiratory Emergency	With Respiratory Emergency	2	25	5	27.8	23	17.8	25	16.3	61	21.8	21	21.6	137 (19.8)
	Without Respiratory Emergency	6	75	13	72.2	106	82.2	128	83.7	224	78.2	76	78.4	553 (80.2)
Type of Respiratory Emergency	SVCS	2	25	1	5.6	5	3.9	6	3.9	17	5.9	9	9.3	40 (5.8)
	Massive MPE	0	0	2	11.1	9	7.0	10	6.5	19	6.7	5	5.2	45 (6.5)
	Massive Hemoptysis	0	0	0	0.0	1	0.8	1	0.7	1	0.4	1	1.0	4 (0.6)
	CAO	0	0	2	11.1	4	3.1	5	3.3	15	5.3	1	1.0	27 (3.9)
	Pneumothorax	0	0	0	0.0	0	0.0	1	0.7	8	2.8	2	2.1	11 (1.6)
	Multiple RE	0	0	0	0.0	4	3.1	2	1.3	1	0.4	3	3.1	10 (1.4)

Note: SVCS= Superior Vena Cava Syndrome, CAO = Central Airway Obstruction, RE=Respiratory Emergency



	2011	2012	2013	2014	2015	2016
Respiratory Emergency	25	27.8	17.8	16.3	21.8	21.6
Without Respiratory Emergency	75	72.2	82.2	83.7	78.2	78.4

Figure 1. Respiratory Emergency Chart from 2011–2016



	2011	2012	2013	2014	2015	2016
SVCS	25	5.6	3.9	3.9	5.9	9.3
Massive MPE	0	11.1	7	6.5	6.7	5.2
Massive Hemoptysis	0	0	0.8	0.7	0.4	1
CAO	0	11.1	3.1	3.3	5.3	1
Pneumothorax	0	0	0	0.7	2.8	2.1
Multiple RE	0	0	3.1	1.3	0.4	3.1

Figure 2. Distribution of Respiratory Emergency in 2011–2016

Table 3. Factors related to the Respiratory Emergency appearance

		Respiratory Emergency		Without Resp. Emergency		*P*	OR	95% CI
		n	%	n	%			
Age (years)	<40	15	21.7	32	46.3		1	1
	40–49	19	27.5	101	14.8		0.40	0.18–0.87
	50–59	53	38.7	212	38.3	0.22	0.53	0.26–1.05
	60–69	37	27.0	149	26.9		0.52	0.26–1.07
	≥70	13	9.5	59	10.7		0.47	0.19–1.10
Gender	Male	104	75.9	440	79.6	0.35	1	1
	Female	33	24.1	113	20.4		1.23	0.79–1.92
Type of Intrathoracic Malignancy	Lung Tumor	115	83.9	511	92.4	<0.001*	1	1
	Mediastinal Tumor	15	10.9	17	3.1		3.92	1.90–8.08
	Secondary Lung Tumor	7	5.1	25	4.5		1.24	0.52–2.94
Site of Tumor	Right Lung	78	67.8	293	57.5	0.04*	1	1
	Left Lung	37	32.2	217	42.5		0.64	0.41–0.98

Note: *) significant with Logistic Regression test with level of accuracy 5%

Factors that affected the respiratory appearance in intrathoracic malignancy had been analyzed using logistic regression, as can be seen in Table 3. Mediastinal tumors 3.9 times more likely related to respiratory emergency appearance with CI 1.90-8.08, while age and gender do not affect the occurrence of respiratory emergency. Factor that influences the respiratory emergency appearance in lung tumor is the location of the tumor, which is the right lung tumor 1.5 times more likely at risk of developing respiratory emergencies than the left lung tumor (Table 3).

DISCUSSION

From 690 subjects found that lung tumors cases were the most common types of intrathoracic malignancy, there are 626 lung tumor cases (90.7%), mediastinal tumors as many as 32 cases (4.6%), secondary lung tumors 32 cases (4.6%), whereas mesothelioma and chest wall tumors not found in 5 years of observation (Table 1). Male more common than women (78.8% vs 21.2%) and the highest age ranged between 50–59 years (38.4%) and 60–69 years (27%).

The results of this study are slightly similar from previous studies at H. Adam Malik General Hospital from 201 inpatient lung cancer patients were found as much as 86.1% were male with aged ≤ 60 years about 40.8%.[13] There were 137 (19.8%) intrathoracic malignancy patients presented with respiratory emergency (Table 2), these data not much different from previous studies in lung cancer patients who came to the emergency department because of respiratory complaints of 37.6%.[4]

In this study there were 45 patients (6.5%) with massive malignant pleural effusion (MPE), while the study at Persahabatan – Jakarta Hospital by Syahruddin et al. found 52.4% patients with MPE from lung cancer cases from 3 years obeservation.[14] This difference because of the sample using pleural fluid cytology that known has low sensitivity about 48.5%,[15] and also the MPE cases in this study should be a massive size pleural effusion, while other MPE sizes were excluded.

Jiminez et al. found the number of massive pleural effusions was 11.2% from all pleural effusions and 53.7% of the cases was massive pleural effusions due to malignancy.[6] Malignant pleural effusion in this study was mostly caused by lung tumors and metastatic lung tumors, this is consistent with the most common causes of MPE, which is lung cancer (36%), breast cancer (26%), lymphoma (13%), ovarian cancer (9.3%) and gastrointestinal malignancies (7.3%).[16] Sixteen patients died from 45 patients with massive MPE (35.5%), in a previous study had known that massive MPE related to poor prognosis with median survival rate of only 5 months[6]. The mortality rate due to massive MPE is quite high even though the therapy for malignancy already given (chemotherapy or radiotherapy). This is because in patients with MPE already in advance disease (stage IV) so the prognosis and survival rates are worse.

The second most common cause of respiratory emergency was Superior Vena Cava Syndrome (SVCS) from 40 patients (5.8%). This number is not much different from the study by Rowell & Gleeson (2002) who found the incidence of SVCS in lung cancer patients was 3.8%.[7] From a previous study found that malignancy was the most common cause of SVCS, which was around 94%, while mediastinal tumors 35.4% and lung tumors 22.5%.[17] In this study, as many as 14 of the 40 patients with intrathoracic malignancies hospitalized with SVCS were died (35%). Median survival rate in patients with SVCS from previous study was 5.5 months and radiotherapy emergency should be performed immediately to relief symptoms about 56–96% for 3–30 days.[18] The high mortality rate in SVCS patients is due to inappropriate management beside radiotherapy emergency, installation of endovascular stents, bypass surgery using graft from the innominate/jugular vein to the right atrium has been shown to alleviate SVCS symptoms and increase survival rates.[19]

The incidence of central airway obstruction in this study was 27 cases (3.9%), this number was lower than the previous study 13%.[8] The difference

due to the criteria of central airway obstruction (CAO) in this study was an obstruction of the main trachea and main carina whereas in previous studies included obstruction in the main bronchi. The mortality rate in patients with CAO is 37% (10/27), Similar result from prior studies whereas 44% of patients with malignancy with CAO died in one year after diagnostic.[8] Management of CAO with therapeutic bronchoscopy (such as stenting, electro cryotherapy, mechanical/thermal ablation, brachytherapy) has been shown to alleviate symptoms significantly, improve quality of life and survival rates more than twice compared with patients who were not underwent the therapy.[20]

The incidence of pneumothorax in this study was 11 patients (1.6%), this figure was slightly higher than the previous study by 0.03% to 0.05%.[11] It can be caused by other comorbidities such as COPD and previous lung infections not excluded. The mortality rate in patients with pneumothorax is 1 in 11 patients (9.09%), it shows that the management of pneumothorax cases already given such as thorax drainage (WSD) installation. Massive hemoptysis was found in 4 patient (0.6%), which was lower than the previous study (3%).[10] This condition because of patients with other comorbidities such as pulmonary tuberculosis and patients with blood clotting disorders were excluded. While in from Retno et al. Persahabatan Hospital found as many as 3.4% patient with bloody cough caused by lung cancer. In this study 50% (2/4) of patients with massive hemoptysis died, this result is consistent with studies of massive hemoptysis conservatively treated with a mortality rate of 50% to 100%.[21]

The high mortality rate of massive hemoptysis patients in this study was due to inadequate (conservative) therapy. Treatment of massive hemoptysis requires multidisciplinary collaboration where interventions such as therapeutic bronchoscopy are needed using rigid bronchoscopy and flexible bronchoscopy (with cold saline, instillation of vasoconstriction agents, forgaty balloon tamponade and stenting), cessation of bleeding using electrocautery, Nd-YAG laser and the main therapy is to embolize bronchial arteries. Study by Lee et al. (2012) in patients with massive hemoptysis who performed bronchial artery embolism reported the success rate of this treatment about 92.9%.[22]

Pulmonary thromboembolism was not found from this study due to lack of diagnostic modalities such as V/Q scan and pulmonary angiography and Well score data also incomplete. Therefore, the emergency respiratory rate may be higher considering the rate of venous thrombosis in malignant patients was 23.1%,[23] and pulmonary thromboembolism alone causes 5–10% of deaths in inpatient patients[9].

During observations, most patients died due to lung tumors and the risk of death increased in patients with respiratory emergency then patient without respiratory emergency. Increased of mortality in patients with respiratory emergency compared to those without emergencies makes it important to know what factors related to the respiratory emergency occurrence in intrathoracic malignancy. From Table 3 can be seen that the type of intrathoracic malignancy significantly affects the incidence of respiratory emergency (P<0.001). Also, can be seen that mediastinal tumors are 3.9 times more likely to cause respiratory emergency compare to lung tumors. This is due to a tumor in the mediastinal cavity (an imaginary cavity between the left and right lungs). This cavity is anatomically filled with important organs such as the heart, arteries, veins, trachea, thymus gland, nerves, connective tissue, lymph nodes and channels. This cavity is narrow and stiff, so that if there is a tumor in this area it will suppress the surrounding organs and cause life-threatening emergencies, such as suppression of the trachea (CAO), suppression of the superior vena cava (SVCS), suppression of lymph glands (pleural effusion).

Factors that influence the respiratory emergency appearance in lung tumors was the location of the tumor, where the right lung tumor is 1.5 times more likely to cause a respiratory emergency than the left lung tumor. From study observations, it was found that respiratory

emergencies that often appear in the right lung tumor, such as SVCS, this is because the location of the tumor in the right lung is anatomically close to the superior vena cava.

CONCLUSION

From 137 patients with respiratory emergency found that lung tumors were the most common causes (83.9%). The most common respiratory emergency was massive MPE (6.5%) and massive hemoptysis is the rarest cases (0.6%). Mortality rate was higher in patients with respiratory emergency. Factors related to the respiratory emergency occurrence in intrathoracic malignancy patients were the type of malignancy and the site of the tumor.

Mortality rate was higher in patients with respiratory emergency and patient with intrathoracic malignancy need immediate treatment collaboration between multidisciplinary to relief symptom and improve quality of life and survival rates.

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