MANAGEMENT OF MALIGNANT CENTRAL AIRWAY OBSTRUCTION

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Cancer can invade the airway, cause various degrees of obstruction and develop symptoms. We conducted this retrospective and prospective, descriptive study to evaluate causes and treatments of patients with malignant central airway obstruction (CAO). 37 patients were diagnosed with malignant CAO at the Respiratory Center of Bach Mai Hospital. Results show that average age was 53.8 ± 13.1 years. CAO occurred mainly in the 45 - 59 age group and in men more than women. No significant differences between the number of patients with cancer originated from in (group 1) and out (group 2) of the airway with regard to the number of patients, degree of stenosis and location of stenosis. In group 1, Non - small cell lung cancer accounted for the majority. In group 2, squamous - cell esophageal carcinoma had the highest proportion. The prevalence of patient having treatment was higher than not having treatment statistically. In the treatment group, the number of participants undergoing combination of airway stent insertion and balloon dilatation was predominant. There were no significant difference in causes or locations or degrees of stenosis respecting treatment modalities. Participants having comfort after treatment accounted for the majority. In no treatment group and treatment group, cumulative proportions surviving were 0% (at 11th month) and 44.3% (at 9th month), respectively. The survival time in treatment group (15.1 ± 3.4 months) was statistically longer than in no treatment group (4.4 ± 1.9 months) (p = 0.031). Conclusions: Malignant CAO has different causes, location and degree of stenosis, thereby leading to diverse treatments. Clinicians need to consider appropriate treatments for patients to increase their comfort and survival time.

Keywords: malignant central airway obstruction, bronchoscopy, treatment.

I. INTRODUCTION

Central airway obstruction (CAO) can be caused by various disease processes including malignancy as well as non-malignancy and is the cause of significant morbidity and mortality [1]. Malignant CAO has received much attention over the last several decades because of its increasing prevalence due to epidemiology of respiratory cancer. However, causes and treatments of malignant CAO are disparate among studies, thereby interfering with the practice of clinicians [2].

In Vietnam, the actual incidence of malignant CAO is unknown; moreover, there is no consensus for treatment for this condition. Few Vietnamese researchers have addressed these problems while research on these features will help physician to have more evidences to apply to clinical practice and improve the outcomes of patients [3]. Therefore, the aim of this study is to evaluate causes and treatments of patients with malignant CAO in Vietnam, specifically at the Respiratory Center of Bach Mai hospital.

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II. METHODS

1. Study population

This study was conducted from May 2015 to July 2019 with 37 malignant CAO who was diagnosed and treated at the Respiratory Center Bach Mai Hospital.

Inclusion criteria

- Diagnosed with malignant CAO.
- Agreed to participate in research and gave their inform consents.

Criteria for diagnosis of CAO: having at least 1 of the following diagnostic imaging reports [4]

- Chest CT scans: extraluminal 3-D rendering or intraluminal reconstructions
- Bronchoscopy

Criteria for diagnosis of malignant CAO: was diagnosed with CAO and evidence of malignancy on pathology reports [4].

Exclusion criteria

- Was diagnosed with nonmalignant CAO.
- Refused to participate into the study.

Classification of CAO: According to Freitag [4]

- *Location of stenosis:*

I. Upper third of the trachea
II. Middle third of the trachea
III. Lower third of the trachea
IV. Right main bronchus
V. Left main bronchus

- Degree of stenosis:

1. < 25% decrease in cross - sectional area
2. 26 - 50% decrease in cross - sectional area
3. 51 - 75% decrease in cross - sectional area
4. 76 - 90% decrease in cross - sectional area
5. > 90% complete obstruction

Treatment modalities applied for patients: According to the American Journal of Respiratory and Critical Care Medicine [1] and Interventional Bronchoscopy guideline – A Clinical Guide [6].

2. Methods

Study design: Retrospective and prospective, descriptive study. Sampling method: non-randomized, consecutive sampling. All with malignant CAO admitted to the Respiratory Center Bach Mai Hospital, who are eligible for study inclusion criteria. Statistical Analysis: Continuous variables are presented as mean ± SD or median; categorical data are presented as numbers and percentages. P values smaller than 0.05 were considered as statistically significant. Survival time of patients was estimated by using Kaplan-Meier. Analyses were performed with SPSS 16.0 (IBM, Inc, New York). Ethical approval provided by Bach Mai University hospital and Hanoi Medical University.

III. RESULTS

The study involved 37 inpatients diagnosed with malignant CAO at the Respiratory Center of Bach Mai Hospital from May 2015 to July 2019.

1. Demographic characteristics

Table 1. Demographic characteristics (n = 37)

Variables	n (%)	p
Maternal age		
< 45 years old	7 (18.9)	
45 to 59 years old	19 (51.4)	0.048
> 59 years old	11 (29.7)	

Variables	n (%)	p
53.8 ± 13.1 [17;79]		
Sex		
Male	30 (81.1)	p < 0.01
Female	7 (18.9)	

The study involved 7 women and 30 men, average age was 53.8 ± 13.1 years, CAO occurred mainly in the 45-59 age group in men more than women (p < 0.01) (Table 1)

2. Causes of malignant CAO

Group 1 (G1): Cancers originate at the airways

Group 2 (G2): Cancers metastasize to the airways

Table 2. Causes of malignant CAO (n = 37)

	Causes of malignant CAO		n (%)		p
G1	SCLC		3 (8.1)		0.035
	NSCLC	Adenocarcinoma	4 (10.8)	16 (32.4)	
		Squamous cell carcinoma	4 (10.8)		
		Uncategorized	4 (10.8)		
	Tracheal cancer		4 (10.8)		
G2	Squamous-cell thyroid carcinoma		2 (5.4)		0.186
	Squamous-cell esophageal carcinoma		6 (16.2)		
	Thymoma		1 (2.7)		
	Non-Hodgkin lymphoma		1 (2.7)		
	Malignant peripheral nerve sheath tumor		1 (2.7)		
	Hypopharyngeal cancer		1 (2.7)		
	Others*		6 (16.2)		
Overall			37 (100)		

Abbreviation: SCLC, Small Cell Lung Cancer; NSCLC, Non-Small Cell Lung Cancer.

**One case for each cause.*

The analysis did not reveal any significant differences between the number of patients with cancer originated from in (19 participants) and out (18 participants) of the airway (p = 1). In detail, in group 1, NSCLC accounted for the majority (32.4%), while only a small number of those recorded indicated that having SCLC and tracheal cancer (8.1% and 10.8%, respectively) (p = 0.035). In group 2, squamous-cell esophageal carcinoma had the highest proportion (16.2%), followed by squamous-cell thyroid carcinoma (5.4%), but no significant difference was identified in cancers metastasizing to the airways (Table 2)

The relationship between cause and degree of stenosis or location of stenosis

Table 3. The relationship between cause and degree or location of stenosis (n = 37)

Features	Code	n (%)		p
		G1	G2	
Degree of stenosis [4]	1	6 (16.2)	6 (16.2)	0.534
	2	3 (8.1)	6 (16.2)	
	3	4 (10.8)	2 (5.4)	
	4	4 (10.8)	4 (10.8)	
	5	2 (5.4)	0 (0)	
	Overall	19 (51.4)	18 (48.6)	37 (100)
Location of stenosis [4]	I	4 10.8)	9 (24.3)	0.196
	II	2 (5.4)	3 (8.1)	
	III	3 (8.1)	1 (2.7)	
	IV	8 (21.6)	3 (8.1)	
	V	5 (13.5)	2 (5.4)	
	Overall	22 (59.4)	18 (48.6)	40*

**In some cases, stenosis can be found at 2 locations*

The analysis did not identify any significant differences between group 1 and group 2 with regard to degree of stenosis (p = 0.534) or location of stenosis (p = 0.196) (Table 3)

3. Treatments of patients with malignant CAO

Table 4. The relationship between cause and treatment modalities (n = 37)

Treatment modalities		n (%)		p
		G1	G2	
No treatment		7 (18.9)	3 (8.1)	0.572
Therapeutic bronchoscopy	Electrocautery	4 (10.8)	4 (10.8)	
	Combination*	5 (13.5)	7 (18.9)	
Surgical resection		1 (2.7)	2 (5.4)	
No information		2 (5.4)	2 (5.4)	
Overall		19 (51.4)	18 (48.6)	

**Combination of airway stent insertion and balloon dilatation*

The prevalence of patient having treatment was higher than not having treatment statistically (p = 0.02). In group of patients receiving treatment, the number of participants undergoing combination of airway stent insertion and balloon dilatation was predominant, accounting for 32.4%, the rest was different but not one of these differences was statistically significant (p = 0.07). In group 2, patients

having combination of airway stent insertion and balloon dilatation accounted for the majority (18.9%) while patients with no treatment had the highest prevalence in group 1. No significant difference observed between group 1 and group 2 with regard to treatment modalities (p = 0.572) (Table 4)

The relationship between location of stenosis & treatment modalities

Table 5. The relationship between location of stenosis & treatment modalities (n = 37)

Treatment modalities		Location of stenosis [4]					p
		I	II	III	IV	V	
No treatment		2	0	0	5	3	0.104
Therapeutic bronchoscopy	Electrocautery	4	1	2	0	1	
	Combination*	5	1	1	2	2	
Surgical resection		0	2	0	1	0	
No information		9					
Overall		40**					

**Combination of airway stent insertion and balloon dilatation*

*** In some cases, stenosis can be found at 2 locations*

Wherever obstruction was located, treatment modalities were mostly applied (Table 5). Modalities were varied for locations, but there were no significant differences in these locations in regard to treatment modalities (p = 0.104)

The relationship between degree of stenosis & treatment modalities

Table 6. The relationship between degree of stenosis & treatment modalities (n = 37)

Treatment modalities		Degree of stenosis [4]					p
		1	2	3	4	5	
No treatment		6	1	1	1	1	0.539
Therapeutic bronchoscopy	Electrocautery	1	2	1	4	0	
	Combination*	3	4	2	2	1	
Surgical resection		1	1	1	0	0	
No information		4					
Overall		37					

**Combination of airway stent insertion and balloon dilatation*

Regarding the degree of stenosis, treatment modalities were also diverse (Table 6). The analysis did not identify any significant differences in these degrees in regard to treatment modalities (p = 0.539)

Change in comfort after treatment

Table 7. Comfort after treatment (n = 37)

Comfort after treatment		Treatment modalities				
		Therapeutic bronchoscopy		Surgical resection	Overall	p
		Electrocautery	Combination*			
Yes	n (%)	7 (18.9)	10 (27.0)	2 (5.4)	19 (51.4)	< 0.01
No	n (%)	0 (0)	2 (5.4)	0 (0)	2 (5.4)	
No information	n (%)		16 (43.2)		16 (43.2)	

**Combination of airway stent insertion and balloon dilatation*

There were 16 cases (43.2%) with no information about patients' comfort after treatment (Table 7). 21 participants reported their condition after treatment, in which participants having comfort after treatment accounted for the majority (51.4%, p < 0.01)

Survival time after treatment

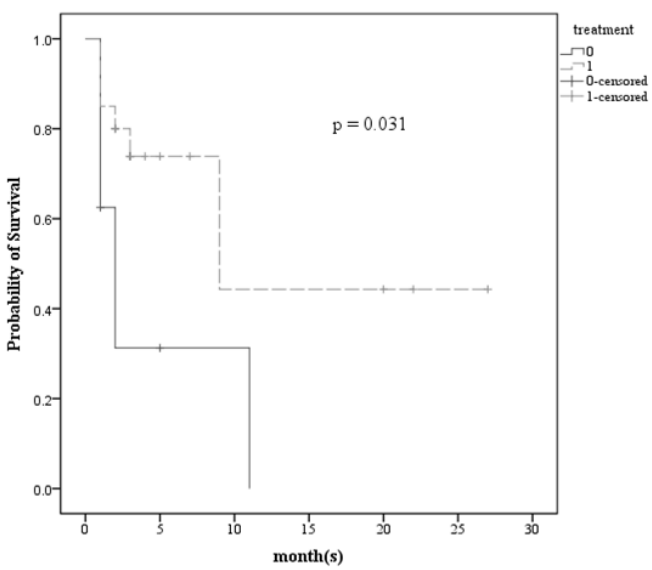

Figure 1. Kaplan-Meier curve showing overall survival of patients with treatment compared with patients without treatment

There were 28 patients being recorded for survival time (9 other cases with no information); the number of deaths was 13 (6 of 8 cases in the non treatment group, 7 of 20 cases in the treatment group). In the non- treatment group, 6 patients died at the 11th month, cumulative proportion surviving at this time was 0%. In the treatment group, 7 patients died at the 9th month, cumulative proportion surviving at this time was 44.3%. The mean survival time of the non treatment group

and treatment group were 4.4 ± 1.9 months and 15.1 ± 3.4 months, respectively. Log Rank test showed that Chi-square was 4.6, df was 1 and p was 0.031, meaning that the survival time in the treatment group was longer than in the non-treatment group; this difference was statistically significant (Figure 1).

IV. DISCUSSION

Demographic characteristics

Average age was 53.8 ± 13.1 years, of which the youngest was 17 years old, the oldest was 79 years old. This result is similar to Quach Thi Can [3] which had prevalence of male and female are 69% and 31%, respectively, possibly because Vietnam has a higher rate of smoking in men than in women. CAO occurred mainly in the 45 - 59 age group (p = 0.048) and in men (81.1%) more than women (18.9%) statistically (p < 0.01). This may be explained by the fact that older people are more likely to develop malignancy than other age groups [5].

Causes of malignant CAO

In group 1, NSCLC accounted for the majority (32.4%), while only a small number of those recorded indicated that having small cell lung cancer and tracheal cancer (8.1% and 10.8%, respectively) (p = 0.035). These results are consistent with the epidemiology of cancer, when squamous carcinoma usually occurs in male, smoking patients according to Hadique et al [6]. Wood et al [2] highlighted that esophageal carcinoma was the most common cause of malignant CAO in group 2, our study also showed similar data where squamous - cell esophageal carcinoma had the highest proportion (16.2%).

The relationship among relevant factors

The analysis did not identify any significant differences between group 1 and group 2 with regard to degree (p = 0.534) or location of stenosis (p = 0.196). These were mentioned in a research of Giap Van Vu and Tam Manh Mai however, their study did not focus on only malignant causes, thus, there is a need of more researches to analyze this relationship [7].

Treatments of patients with malignant CAO

The majority of patients (62.2%) had therapeutic bronchoscopy or surgical resection (p = 0.02). In these patients, the number of participants undergoing combination of airway stent insertion and balloon dilatation was predominant, accounting for 32.4%, the rest was different but not one of these differences was statistically significant (p = 0.07). Other studies also demonstrated the role of above modalities and all of them indicated that either interventions or surgery helped patients to improve symptoms as well as degree of stenosis [5; 8].

The relationship among relevant factors

There were no significant differences in causes (p = 0.572) or locations (p = 0.104) or degrees of stenosis (p = 0.539) in regard to treatment modalities. This showed that choice of treatment modalities depends on various factors and clinician should be careful when makes decision on treatment [8].

Change in comfort after treatment

In many previous studies on malignant CAO treatment, the authors evaluated life quality of patients after treatment, and they have demonstrated that interventions may improve symptoms and quality of life [5]. However, in this study, we only assessed the comfort of participants after treatment, specifically in group of participants reporting about their condition, participants having comfort after treatment accounted for the majority (51.4%, p < 0.01). This is a limitation of our study, unfortunately.

Survival time after treatment

In the treatment group and non - treatment

group, cumulative proportions surviving were 44.3% at 9th month and 0% at 11th month, respectively. Furthermore, the mean survival time of treatment group and without treatment group were 15.1 ± 3.4 months and 4.4 ± 1.9 months, respectively. Median overall survival of patients in our study was 9.0 ± 3.5 months, higher than results of Okiror et al (3.7 months); this can be explained by that the sample size of Okiror's study was higher than our study [8].

Log Rank test showed that Chi - square was 4.6, df was 1 and p was 0.031, it meant that the survival time in the treatment group was longer than in the non - treatment group, this difference was statistically significant (Figure 3.1). This is similar to results of Okiror [8], thereby indicating that the effectiveness of intervention was clear for patients with malignant CAO.

V. CONCLUSION

In patients with malignant CAO, the difference from etiologies, location and degree of stenosis lead to diverse treatments. Clinicians should consider having appropriate treatments for patients to increase their comfort and survival time.

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Conflicts of Interest: No potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Armin Ernst, David Feller - Kopman, Heinrich D. Becker, et al (2004). Central airway obstruction, *American journal of respiratory and critical care medicine*, **169(12),** 1278 – 1297.

2. Wood DE (2002). Management of malignant tracheobronchial obstruction, *Surgical Clinics*, **82(3),** 621 - 642.

3. Can Thi Quach (2006). Causes, clinical features and treatment results of laryngotracheal stenosis due to scar at National Otorhinorarynology Hospital of Vietnam, *PhD thesis.* Hanoi Medical Unviersity.

4. L. Freitag, A. Ernst, M. Unger, et al (2007). A proposed classification system of central airway stenosis, *European Respiratory Journal***, 30**, 7 - 12.

5. Honings J, Gaissert HA, van der Heijden HF, et al (2010). Clinical aspects and treatment of primary tracheal malignancies, *Acta Oto - Laryngologica*, **130(7),** 763 - 772.

6. Sarah Hadique, Prasoon Jain & Atul C. Mehta (2013). Therapeutic Bronchoscopy for Central Airway Obstruction, Interventional Bronchoscopy - A Clinical Guide, Rounds Sharon I.S., *Humana Press, New York.*

7. Giap Van Vu and Tam Manh Mai (2015). Clinical, paraclinical and causes of trachea stenosis, *Viet Med Jour,* **427(2)**, 172 - 178.

8. Okiror L, Jiang L, Oswald N, et al (2015). Bronchoscopic management of patients with symptomatic airway stenosis and prognostic factors for survival, *The Annals of thoracic surgery,* **99(5),** 1725 - 1730.