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ORIGINAL ARTICLE

Outcome differences between recanalized malignant central airway obstruction from endoluminal disease versus extrinsic compression

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Abstract

We compared the outcome of Nd:YAG laser therapy with stent placement for malignant central airway obstruction (CAO) at our center over a 10-year period. This is a retrospective review of patients undergoing Nd:YAG laser therapy or self-expanding metal stent (SEMS) placement for malignant CAO between November 2007 and October 2017. Seventy-two patients were recanalized for malignant CAO. The median (range) age was 63 (23–86) years, with 49 (68%) males. Patients underwent either laser therapy alone ($N = 36$), stent placement alone ($N = 30$), or both ($N = 6$). The wavelength of Nd:YAG laser used was 1064 nm, and median (range) laser energy used was 25 (15–35) W, in 377 (115–1107) pulses. Fifty-one (71%) patients died with median survival of 7.2 months. In subgroup analysis, 21 (58.3%) vs. 25 (83.3%), $p = 0.03$ patients died in the "laser resection" vs. "stent placement" group with longer median survival of 12.4 months in the former vs. 4.5 months, $p = 0.0004$ in the later. Esophageal cancer and left main bronchus involvement were significantly more common (10 (33.3%) vs. 0, $p = 0.0001$, and 16 (53.3%) vs. 8 (22.2%), $p = 0.01$), in the stent placement vs. laser resection group, respectively. Trachea or main bronchi involvement and respiratory failure on presentation requiring mechanical ventilation correlated with poorer survival. The immediate restoration of luminal patency, complication rate, and 30-day mortality was similar among the two groups. The median (range) energy used for laser therapy was 25 (15–35) W. Median of 377 pulses was used for the duration of 287.5 s. The results were compared using a Wilcoxon two-sample test, and Fischer exact test with p values considered indicative of a significant difference if less than 0.05. In patients requiring recanalization of malignant CAO, the extrinsic compression from esophageal cancer, trachea or main bronchi involvement, respiratory failure on presentation requiring mechanical ventilation, and stent placement correlated with poorer survival. Interventional pulmonology training program should emphasize on dedicated training in laser therapy as it is associated with improved survival.

Keywords Bronchoscopy · Stent · Cancer (lung) · Esophagus · Trachea

Introduction

Endoluminal protrusion of the neoplastic tissue into the airway from primary bronchogenic carcinoma, extrinsic compression of the airway by local extension of lung, esophageal or thyroid cancer, and pulmonary metastasis from distant sites of origin such as colon are the common causes of malignant central airway obstruction (CAO) [1–3]. Due to advanced stage, the conventional anti-cancer treatment has limitations in these cases. Surgery is often contraindicated, chemotherapy is of uncertain benefit, and radiotherapy does not have immediate effect on relief of CAO [4]. Thirty to 40 % of lung cancer patients die due to complications resulting from locoregional disease [5, 6]. Only mechanical and thermal bronchoscopic techniques such as balloon dilatation, stent placement, and laser or argon plasma coagulation offer instantaneous benefit and have been shown to provide symptomatic, radiological, and survival benefit [7–9].

The airway abnormality suitable for stent placement is the extrinsic compression by a tumor growing adjacent to the airway [10]. Thermal ablation such as laser is recommended for lesion that occludes the airway by ingrowing neoplastic tissue into the lumen of the airway [10]. Stents either metal or

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silicone exert their effect by radial expansion of the airway. Silicone stents are preferable in benign diseases for their ability to be removed and replaced, while metal stent can be placed in malignant lesions [11]. Among thermal therapies, Nd:YAG laser is the commonly used modality and enables immediate restoration of a viable airway with satisfactory medium-term palliation [3]. Argon plasma coagulation is another form of thermal therapy that is used for non-contact electrocoagulation [12]. We reviewed patients who underwent Nd:YAG laser therapy and self-expanding metal stent placement for malignant CAO at our center over a 10-year period. We hypothesized that patients having cancer causing CAO from endoluminal disease and treated by laser therapy will perform poorly due to greater compromise of airway patency from intraluminal location of disease and risks associated with thermal therapy, compared to patients with CAO from extrinsic compression where patency can be reestablished fairly quickly by stent placement.

Methods

We retrospectively reviewed patients undergoing Nd:YAG laser resection and stenting between November 2007 and October 2017 at our center. Variables such as demographic data, indication of laser therapy and stent placement, sites of intervention, visible effect of intervention on luminal patency, radiological effect of intervention, effect on change in level of care, survival, and complications were collected.

Seventy-two patients were treated for malignant CAO with recanalization. Patients underwent laser resection ($N = 36$), stent placement ($N = 30$), or both ($N = 6$). Six patients who underwent both laser resection and stent placement were excluded from the subgroup analysis.

Nd:YAG laser (Medilas Fibertom 8100 Nd:YAG laser, Dornier Medtech Asia, Germany) resection was performed in the operating room. A rigid bronchoscope (Bryan Corporation, Woburn, MA, USA) was inserted in the airway under general anesthesia. Patients were ventilated using an automated jet ventilator (1990 Bronchton-1, Carl Reiner GmbH, Austria). Rigid telescope (Bryan Corporation, Woburn, MA, USA), flexible bronchoscope (BF-P190, Olympus Ltd., Tokyo, Japan), and other instruments like Alligator Jaw Grasping Forceps (FG-6L-1, Olympus Ltd., Tokyo, Japan) were inserted through the primary lumen of the rigid bronchoscope. In patient requiring stent placement, metal stents used were Ultraflex stent (Ultraflex Tracheobronchial stent system, Boston Scientific Corporation, Marlborough, MA, USA), and silicone stents were NOVATECH Dumon stents (Boston Medical Products, Inc., Westborough, MA, USA). Routine treatment including chemotherapy and radiation were provided to the patients under the supervision of their oncologists. Approval was obtained from the Institutional Review Board of National Health Care Group to review and publish patient records retrospectively (IRB No. 2017/01019). Informed consent was waived because of the retrospective nature of the study.

Statistical analysis

The software (SPSS, version 17; SPSS, Chicago, IL, USA) was used for all statistical analyses. Distribution of data was assessed by using the histogram function. The data was normally distributed. The results were compared using a Wilcoxon two-sample test and Fischer exact test. p values were two-sided and considered indicative of a significant difference if less than 0.05. The beta value for the sample size was 0.3 (study power = 99.7%).

Results

Seventy-two patients were treated for malignant CAO between November 2007 and October 2017 (Fig. 1) The demographic features, types of malignancies, and the location of CAO are presented in Tables 1, 2, and 3, respectively. Types of recanalization techniques and outcomes are presented in Table 4.

All patients experienced immediate restoration or improvement in the luminal patency after recanalization. In patients with respiratory failure requiring assisted mechanical ventilation ($N = 11$), 9 (81.8%) patients were successfully extubated after recanalization in median (range) 2 (1–60) days. Complications were seen in 14 (19.4%) patients mainly as escalation of level of care for hypoxemia and bleeding. Fifty-one (71%) patients died and median (range) duration of survival was 7.2 (0.32–76.4) months.

In subgroup analysis, there was no difference in the age, gender, race, number of patients receiving cancer-targeted therapy after recanalization, and complications among the two subgroups. However, greater proportion of patients had esophageal cancer in the "stent placement" group compared to "laser resection" group (10 (33.3%) vs. 0, $p = 0.0001$). The left main bronchus was the more commonly involved site of CAO in the former 16 (53.3%) vs. 8 (22.2%) in the "laser resection" group, $p = 0.01$ (Fig. 2). The patients requiring stent placement tended to be sicker requiring mechanical ventilation, $p = 0.06$ (Table 4).

Fewer patients died, 21 (58.3%) vs. 25 (83.3%) $p = 0.03$, and median survival was longer, 12.4 (0.3–76.4) months, in the patients treated with "laser resection" compared to 4.5 (0.3–52) months in the "stent placement" group, $p = 0.0004$ (Table 4). The esophageal cancer, respiratory failure from CAO at initial presentation, and the involvement of trachea and main bronchi correlated with the mortality in the stent placement group (Fig. 3).

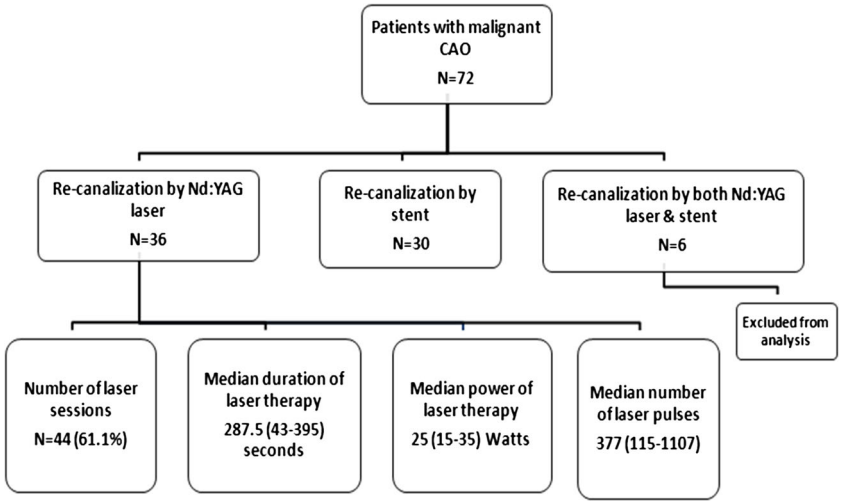

Fig. 1 Flow diagram of patients

Greater number of rigid bronchoscopies (57 vs. 34, $p = 0.43$) or total number of bronchoscopies (131 vs. 67, $p = 0.33$) were done in the "laser resection" group compared to group receiving stent placement but did not reach statistical significance.

The median (range) energy used for laser therapy was 25 (15–35) W. Median of 377 pulses was used for the duration of 287.5 s (Table 5).

The complication rate was similar among the two groups although greater proportion of patients in the laser resection group required escalation of level of care to ICU (11% vs. 3.3%, $p = 0.36$) and experienced significant bleeding (8.3% vs. none) without reaching statistical significance (Table 6).

Discussion

We found that "malignant CAO from endoluminal lesions recanalized using Nd:YAG laser" carried better prognosis than "malignant CAO from extrinsic compression recanalized with SEMS." CAO from esophageal cancer, obstruction located at the trachea or main bronchi, and respiratory failure requiring mechanical ventilation at the time of initial presentation correlated with the poorer survival.

Esophageal cancer and left main bronchus obstruction were more common in the "stent placement" group. These findings suggest that esophageal cancer may manifest more frequently as "extrinsic compression" of the trachea or left main bronchus compared to endoluminal obstruction. This can be explained by the anatomical location of the esophagus behind the trachea and left main bronchus. Similar association with the greater use of stent alone for esophageal cancer has been described by Chhajed et al. [13]. Seven (77%) patients were treated with stent alone whereas 2 (22%) required both stent and laser [13]. In our cohort, 10 (71.4%) were treated with stent alone whereas 4 (28.5%) required both stent and laser.

Death rate was significantly high, and median survival with 1-year survival was significantly low in the group undergoing stent placement. This was attributable to following reasons. First, two patients had anaplastic thyroid cancer, and one third

Table 1 Demographics of the patients ($N = 72$)

Variables	Malignant, $N = 72$	Laser only, $N = 36$	UFS only, $N = 30$	p value	Both laser and UFS, $N = 6$
Age, median (range)	63 (23–86)	63 (23–86)	63 (42–86)	0.49	72.5 (49–83)
Gender					
Male	49 (68)	21 (58.3)	22 (73.3)	0.29	6 (100)
Female	23 (32)	15 (41.7)	8 (26.7)		–
Race					
Chinese	54 (75)	26 (72.2)	23 (76.7)	0.78	5 (83.3)
Malay	4 (5.6)	2 (5.6)	2 (6.7)	1.0	–
Indian	8 (11.1)	5 (13.9)	2 (6.7)	0.44	1 (16.7)
Others	5 (6.9)	3 (8.3)	2 (6.7)	1.0	–

Data presented as number (%) or median (range)

UFS Ultraflex stent

Table 2 Type of malignancy ($N = 72$)

	Malignant, $N = 72$	Laser only, $N = 36$	UFS only, $N = 30$	p value	Both laser and UFS, $N = 6$
Primary airway		15 (41.6)	5 (16.6)		
Adenoid cystic carcinoma	1 (1.3)	1 (2.7)	0		–
Mucoepidermoid carcinoma	1 (1.3)	1 (2.7)	0		–
Squamous cell carcinoma	16 (22.2)	9 (25)	5 (16.6)	0.54	2 (33.3)
Carcinoid	2 (2.7)	2 (5.5)	0		–
Granular tumor of trachea	2 (2.7)	2 (5.5)	0		–
Local extension					
Lung	35 (48.7)	21 (58.3)	12 (40)	0.21	2 (33.3)
Esophageal cancer	14 (19.4)	0	10 (33.3)	0.0001	4 (66.6)
Thyroid cancer	1 (1.3)	1 (2.7)	0		–
Anaplastic thyroid carcinoma	2 (2.7)	0	2 (6.6)	0.20	–
Metastasis					
Gastric cancer	1 (1.3)	1 (2.7)	0		–
Colon carcinoma	3	3 (8.3)	0		–
Renal carcinoma	1 (1.3)	1 (2.7)	0		–
Breast carcinoma	2 (2.7)	1 (2.7)	1 (3.3)		–
Nasopharyngeal carcinoma	1 (1.3)	0	1 (3.3)		–
Others					
LELC	1 (1.3)	0	1 (3.3)		–
Sarcomatoid tumor	2 (2.7)	1 (2.7)	1 (3.3)		–
Glomus tumor	1 (1.3)	1 (2.7)	0		–
Neuroendocrine cancer	1 (1.3)	0	1 (3.3)		–
Unidentified	1 (1.3)	0	1 (3.3)		–

Data presented as number (%)

LELC lymphoepithelial carcinoma, *PITS* post-intubation tracheal stenosis, *PTTS* post-tuberculosis tracheal stenosis, *FB* foreign body, *TEF* tracheo-esophageal fistula, *UFS* Ultraflex stent

Table 3 Location of central airway obstruction ($N = 72$)

Location	Malignant, $N = 72$	Laser only, $N = 36$	UFS only, $N = 30$	p value	Both laser and UFS, $N = 6$
Trachea	29 (40.2)	14 (38.8)	10 (33.3)	0.79	5 (83.3)
Left main bronchus	24 (33.3)	8 (22.2)	16 (53.3)	0.01	–
Right main bronchus	20 (27.7)	10 (27.7)	8 (26.6)	1.0	2 (33.3)
Mixed	7 (9.7)	1 (2.7)	5 (16.6)	0.08	1 (16.6)
Left lower lobe	2 (2.7)	2 (5.5)	0	0.49	–
Right upper lobe	1 (1.3)	1 (2.7)	0	1.0	–
Right middle lobe	1 (1.3)	1 (2.7)	0	1.0	–
Right bronchus intermedius	1 (1.3)	1 (2.7)	0	1.0	–
Right lower lobe	1 (1.3)	1 (2.7)	0	1.0	–

Data presented as number (%)

UFS Ultraflex stent

Table 4 Outcomes in terms of reversal of respiratory failure, ICU length of stay, and mortality ($N = 72$)

	Malignant, $N = 72$	Laser only, $N = 36$	UFS only, $N = 30$	p value	Both laser and UFS, $N = 6$
Resource utilization					
Number of rigid bronchoscopies	98	57	34	0.43	7
Rigid bronchoscopies per patient	1.36	1.58	1.13		1.16
Patients requiring repeat interventions	7 (9.7)	4 (11.1)	2 (6.6)	0.36	1 (16.6)
Total number of bronchoscopies	216	131	67	0.33	18
Recanalization technique					
Balloon dilatation (sessions)	4 (5.5)	–	2 (6.6)		2 (33.3)
Definitive treatment	21 (29.1)	13 (36.1)	9 (30)	0.79	4 (66.6)
Number of deaths	51 (70.8)	21 (58.3)	25 (83.3)	0.03	5 (83.3)
Survival (months), median (range)	7.2 (0.32–76.4)	12.4 (0.32–76.4)	4.6 (0.32–52.1)	0.004	5.9 (0.99–56.2)
Survival in trachea and main bronchi group	6.3 (0.32–76.4)	12 (0.32–76.4)	4.6 (0.32–52.1)	0.01	5.9 (0.99–56.2)
Survival in lobar bronchi group	45.6 (4.8–67.2)	45.6 (4.8–67.2)	–		–
Survival in patients requiring single rigid bronchoscopy	6.7 (0.32–76.4)	11.2 (0.32–76.4)	3.9 (0.32–52.1)	0.01	4.8 (0.99–8.8)
Survival in patients requiring multiple rigid bronchoscopy	18.5 (0.52–64.5)	27.5 (4.2–64.5)	6.3 (0.52–19.5)	0.38	56.3
Survival in patients with definitive treatment	11.2 (0.99–62.1)	12 (4.2–62.1)	9.9 (1.2–42.3)	0.20	8 (0.99–56.3)
30-day mortality	8 (11.1)	3 (8.3)	4 (13.3)		1 (16.6)
1-year mortality	40 (55.5)	14 (38.9)	21 (70)	0.01	5 (83.4)
Intensive care unit patients					
Patients in intensive care unit	11 (15.2)	2 (5.5)	7 (23.3)	0.06	2 (33.3)
Prompt successful extubation	9 (81.8)	1 (50)	6 (85.7)	0.04	2 (100)
ICU length of stay (days), median (range)	9 (1–70)	4	7 (1–70)	0.84	11.5 (11–12)
Post-intervention ICU length of stay (days), median (range)	2 (1–60)	2	1 (1–60)	0.66	2.5 (2–3)

Data presented as number (%) or median (range)

ICU intensive care unit, *UFS* Ultraflex stent

(10) of patients had esophageal cancer in the "stent placement" group compared to none in the "laser resection" group. The reported median duration of survival in anaplastic thyroid cancer is about 4 months [14]. The reported median survival in advanced esophageal cancer with CAO is 2.5 and 2.8 months [13, 15]. Greater proportion of patients with cancers associated with shorter survival undergoing stent placement could be the likely reason for poor survival in this group. Poor survival in patients with malignant CAO from extrinsic compression and correspondingly undergoing stent placement has also been reported by Chhajed et al. [13]. Median survival reported in this study in the stent alone, laser alone, and both stent and laser group is 2.7, 10.4, and 3 months, respectively [13]. This is similar to 4.5 in stent

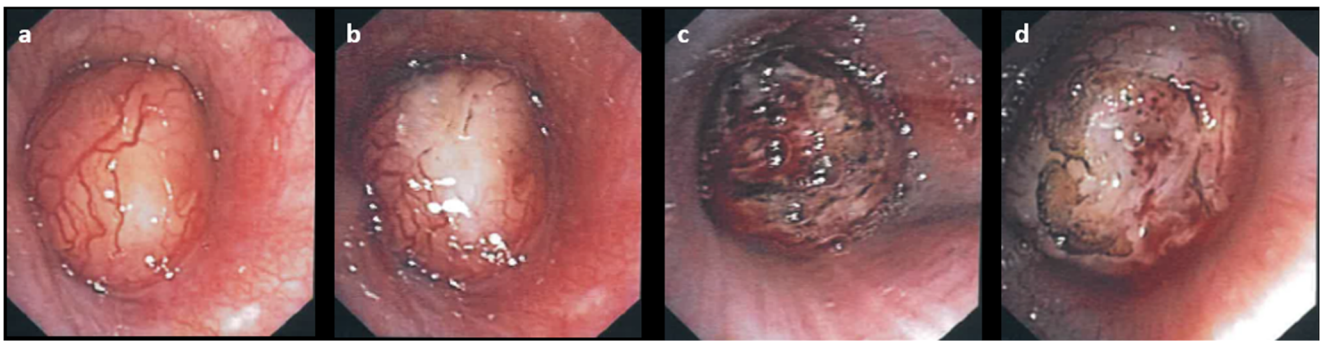

Fig. 2 Representative case of endobronchial mucoepidermoid carcinoma in the distal left main bronchus. **a** Endobronchial lesion. **b** Laser coagulation of the surface. **c** Charring effect of the laser. **d** Laser resection

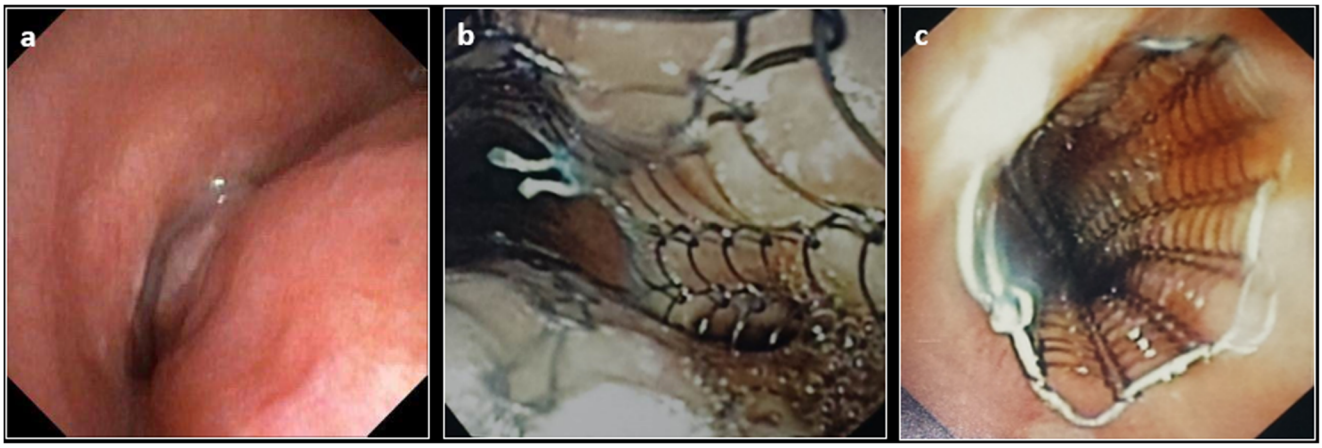

Fig. 3 Representative case of esophageal cancer causing extrinsic compression of the distal trachea. **a** Extrinsic compression of distal trachea. **b** Distal end of the Ultraflex stent placed in the trachea. **c** Proximal end of the Ultraflex stent placed in the trachea

alone, 12.4 in laser alone, and 5.9 months in both laser and stent groups in our cohort.

The second reason for poorer survival in the stent placement group could be the severity of illness. The patients undergoing stent placement were sicker as 7 (23%) were requiring assisted mechanical ventilation for respiratory failure in the ICU prior to intervention, compared to only 2 (5.5%) in those undergoing laser resection. Third, patients with trachea and bronchi involvement had poorer survival compared to those with the involvement of lobar bronchi. This finding is similar to reported earlier [13]. Chhajed et al. have reported median survival of 1.6 months compared to 1.8, 4.8, and 4.7 months with the involvement of trachea alone or right or left main bronchi alone, respectively [13].

Lastly, the longer survival in laser resection group could be owing to the fact that more patients, 15 (41.6%), in the laser resection group had malignancy associated with longer life expectancy such as adenoid cystic carcinoma, mucoepidermoid cancer, and carcinoid. The reported 5-year survival in adenoid cystic carcinoma and mucoepidermoid cancer is 84.7% and 79.3%, respectively [16, 17]. The reported 5-year survival rate in atypical and typical pulmonary carcinoid is 50–70% and 85–90%, respectively [18].

Greater number of rigid bronchoscopies or total number of bronchoscopies were done in the laser resection group compared to group receiving stent placement but did not reach statistical significance. This could be due to longer survival of these patients creating need for surveillance bronchoscopy to assess for, and therapeutic bronchoscopy to manage, any reocclusion or complications, respectively.

The rate of complication observed was 19.4%. The AQuIRE Registry, which involves multiple centers with 947 patients, reported 3.9% (0.9–11.7%) complications in therapeutic bronchoscopy in malignant CAO [19]. Although our rate of complications was higher than these reports, most complications were self-limiting and easily manageable, such as oral bleeding, tooth breakage, transient oxygen desaturation, and failure of stent to open. Unexpected escalation in level of care was seen in 8.3% patients in our cohort, higher than 4.4% (0.5–4.2%) reported by the AQuIRE Registry [19]. No significant difference in the rate of complications was seen among the two groups; however, bleeding and escalation of the level of care to ICU was more frequently seen in the laser resection group without reaching statistical significance.

This way, we were able to reject our hypothesis that patients having cancer causing CAO from endoluminal disease

Table 5 Recanalization techniques ($N = 72$)

	$N = 72$	Laser energy					
		Time (s)	Watt	Pulses			
Number of Nd:YAG	44 (61.1)	287.5 (43–395)	25 (15–35)	377 (115–1107)			
		Stent type and dimension (mm)					
Number of Ultraflex stents	39 (54.1)	40 × 10	40 × 12	40 × 14	40 × 16	60 × 16	60 × 18
		4	20	4	4	3	4
Number of silicone (Y-stent)	2 (2.7)	–	–	–			

Data presented as number (%) or median (range)

Table 6 Procedural complications ($N = 72$)

	Malignant, $N = 72$	Laser only, $N = 36$	UFS only, $N = 30$	p value	Both laser and UFS, $N = 6$
Any complication	14 (19.4)	7 (19.4)	7 (23.3)	0.76	–
Escalation of level of care	13 (18)	6 (16.6)	6 (20)	0.75	–
Escalation of level of care to intensive care unit	6 (8.3)	4 (11.1)	1 (3.3)	0.36	–
30-day mortality	8 (11.1)	3 (8.3)	4 (13.3)	0.69	–
Significant bleeding	2 (2.7)	2 (5.5)	–	0.49	–
Unexpected respiratory failure in 24 h	2 (2.7)	1 (2.7)	1 (3.3)	1.0	–
Complication requiring CPR	2 (2.7)	2 (5.5)	–	0.49	–

Data presented as number (%)

CPR cardiopulmonary resuscitation, *UFS* Ultraflex stent

and treated by laser therapy perform poorly compared to patients with CAO from extrinsic compression.

Our study has limitations. It is a retrospective single-center study. However, the strength of our study is that it supports and confirms the findings of the only one other study demonstrating the survival difference between thermal versus mechanical recanalization techniques in malignant CAO.

In conclusion, "malignant CAO from endoluminal lesions recanalized using Nd:YAG laser" carries better prognosis than "malignant CAO from extrinsic compression recanalized with SEMS." CAO from esophageal cancer, obstruction located at the trachea or main bronchi, and respiratory failure requiring mechanical ventilation at the time of initial presentation may correlate with the poorer survival. Interventional pulmonology training program should emphasize on dedicated training in laser therapy as it is associated with improved survival.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval Approval was obtained from the Institutional Review Board of National Health Care Group to review and publish patient records retrospectively (IRB No. 2017/01019).

Informed consent Informed consent was waived because of the retrospective nature of the study.

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