eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Argon Plasma Coagulation in Bronchoscopy: A Safe and Effective Treatment for Airway Obstruction

Anggi Rizki Utami Nasution[1*], Indra Yovi[2], Sri Indah Indriani[2]

[1]Specialized Residency Training Program, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia

[2]Medical Staff Group/Department of Pulmonology and Respiratory Medicine, Arifin Achmad General Hospital/Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia

ARTICLE INFO

Keywords:
Airway obstruction
Argon plasma coagulation
Bronchoscopy
Meta-analysis

***Corresponding author:**
Anggi Rizki Utami Nasution

E-mail address:
anggirizkiutaminasution@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v9i6.1293

A B S T R A C T

Background: Airway obstruction can significantly impair a patient's quality of life and even become life-threatening. Traditional treatment options, such as surgery or laser therapy, can be invasive and associated with significant complications. Argon plasma coagulation (APC) has emerged as a minimally invasive alternative for treating airway obstruction. APC uses ionized argon gas to deliver controlled thermal energy, allowing for precise tissue coagulation and ablation. This meta-analysis aims to evaluate the safety and efficacy of APC in treating airway obstruction. **Methods:** A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science databases. Studies published between 2013 and 2024 that evaluated the use of APC in bronchoscopy for airway obstruction were included. The primary outcomes were the success rate of APC in achieving airway patency and the incidence of complications. **Results:** Seven studies (n=342 patients) met the inclusion criteria. The pooled success rate of APC in achieving airway patency was 91% (95% CI, 87-94%). The overall incidence of complications was 8% (95% CI, 5-11%), with minor bleeding being the most common. **Conclusion:** This meta-analysis demonstrates that APC is a safe and effective treatment for airway obstruction. It offers a high success rate in restoring airway patency with a low risk of complications. APC is a valuable tool for pulmonologists in managing patients with airway obstruction.

1. Introduction

Airway obstruction represents a significant clinical challenge, capable of substantially diminishing a patient's quality of life and, in severe cases, posing a direct threat to life. The compromise of the airway lumen can arise from a diverse spectrum of etiologies, encompassing both benign and malignant conditions. These include, but are not limited to, the development of endobronchial tumors, the formation of tracheal stenosis, the impaction of foreign bodies, and the proliferation of excessive granulation tissue. The diverse nature of these causes underscores the complexity of managing patients presenting with airway obstruction. Historically, the therapeutic strategies employed to alleviate airway obstruction have often involved invasive surgical procedures. These traditional approaches, while sometimes necessary, are not without inherent limitations and risks. Surgical interventions can be associated with significant morbidity, prolonged recovery periods, and the potential for substantial complications. Similarly, laser therapy, another modality frequently utilized in the management of airway obstruction, also carries a risk profile that includes the potential for complications such as bleeding, perforation, and damage to surrounding tissues. The need for less

invasive and safer treatment modalities has long been recognized in the field of pulmonology and thoracic medicine.[1-3]

In response to the limitations of traditional treatments, argon plasma coagulation (APC) has emerged as a minimally invasive technique that holds significant promise for the treatment of airway obstruction. APC represents a novel approach that utilizes ionized argon gas to deliver controlled thermal energy to the target tissue. This targeted energy delivery results in tissue coagulation and ablation, effectively reducing or eliminating the obstructive tissue. The APC procedure is performed through a bronchoscope, a flexible tube equipped with a camera that allows for direct visualization of the airway. This real-time visualization enables the clinician to precisely apply the argon plasma to the site of obstruction, maximizing therapeutic effect while minimizing damage to adjacent healthy tissues. The ability to deliver controlled thermal energy with precision is a key advantage of APC, allowing for targeted treatment of the obstructive lesion while preserving the structural integrity of the surrounding airway. The application of APC has been investigated across a range of airway obstruction scenarios. Studies have explored its use in the management of endobronchial tumors, both benign and malignant, the treatment of tracheal stenosis of varying etiologies, and the ablation of excessive granulation tissue that can compromise the airway lumen. These investigations have generally reported promising outcomes, demonstrating the potential of APC to effectively restore airway patency and consequently improve patient outcomes.[4-7]

The restoration of airway patency is of paramount importance in patients with airway obstruction. Effective treatment not only alleviates the immediate symptoms of respiratory distress but also prevents the development of potentially life-threatening sequelae such as respiratory failure. Furthermore, the improvement in respiratory function can lead to a significant enhancement in the patient's overall quality of life, allowing for increased activity levels and a reduction in the burden of respiratory symptoms. While individual studies have suggested the benefits of APC in treating airway obstruction, there remains a need for a comprehensive evaluation of the overall evidence. A systematic review and meta-analysis can provide a more robust assessment of the safety and efficacy of APC by pooling the results of multiple studies. Such an analysis can also help to identify potential sources of heterogeneity between studies and to determine the overall strength of the evidence supporting the use of APC.[8-10] This meta-analysis aims to address the existing gap in the literature by systematically reviewing and synthesizing the available evidence on the use of APC in bronchoscopy for the treatment of airway obstruction.

2. Methods

This meta-analysis was conducted in accordance with established guidelines for systematic reviews and meta-analyses. A comprehensive and systematic approach was employed to identify, select, appraise, and synthesize relevant studies evaluating the use of argon plasma coagulation (APC) in bronchoscopy for the treatment of airway obstruction. A systematic literature search was performed to identify all relevant studies. The following electronic databases were searched: PubMed, Scopus, and Web of Science. The search strategy was designed to be comprehensive, utilizing a combination of keywords and Medical Subject Headings (MeSH) terms. These terms were related to the key concepts of APC, bronchoscopy, and airway obstruction. The search strategy was tailored to each database to maximize the yield of relevant articles. To ensure a focused analysis, the search was limited to studies published in the English language, spanning the period from January 1st, 2013, to December 31st, 2024.

The studies retrieved from the electronic database searches were subjected to a rigorous selection process to determine their eligibility for inclusion in the meta-analysis. The selection process was conducted in a two-stage approach, involving the initial screening of titles and abstracts followed by a

full-text review of potentially relevant articles. In the first stage, two independent reviewers screened the titles and abstracts of all identified studies. This initial screening aimed to exclude obviously irrelevant studies, such as those not related to the topic of interest or those clearly not meeting the inclusion criteria. Studies were included if they met the following inclusion criteria; Studies evaluating the use of APC in bronchoscopy for the treatment of airway obstruction. This criterion ensured that the analysis focused specifically on the application of APC in the management of airway obstruction using bronchoscopic techniques; Studies reporting on the success rate of APC in achieving airway patency. Airway patency, defined as the restoration of an unobstructed airway lumen, was a primary outcome of interest in this meta-analysis; Studies reporting on the incidence of complications associated with APC. The safety profile of APC was a key consideration, and therefore, studies reporting on complications were included; Studies published in English between 2013 and 2024. This criterion ensured that the analysis included studies published within the specified timeframe and in the English language. Studies were excluded if they met any of the following exclusion criteria; Case reports, case series, and review articles. These types of studies were excluded as they typically do not provide the same level of evidence as controlled studies; Studies with fewer than 10 patients. Studies with very small sample sizes may not provide reliable estimates of treatment effects; Studies not reporting on the primary or secondary outcomes of interest. Studies that did not report on the success rate of APC in achieving airway patency or the incidence of complications were excluded. In the second stage of the selection process, the full text of all potentially relevant articles that passed the initial screening was retrieved. The study selection process is illustrated in a PRISMA flow diagram, providing a clear and transparent overview of the number of records identified, screened, and included or excluded at each stage.

Data extraction was performed using a standardized data extraction form. This form was designed to capture all relevant information from the included studies in a consistent and organized manner. The following data were extracted from each study; Study characteristics: This included information such as the study design, the country where the study was conducted, and the publication year; Patient demographics: This included data on the characteristics of the study population, such as the mean age, gender distribution, and the underlying cause of airway obstruction; Intervention details: This included information on the APC procedure, such as the settings used (e.g., power, flow rate), the technique employed, and any concomitant treatments; Outcomes: This included data on the primary and secondary outcomes of interest, such as the success rate of APC in achieving airway patency, the incidence of complications, and any other relevant clinical outcomes.

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS) for cohort studies. The NOS is a widely used and validated tool for evaluating the quality of observational studies. It assesses the quality of studies based on three main domains; Selection of study groups: This domain evaluates the representativeness of the exposed cohort, the selection of the non-exposed cohort (if applicable), and the ascertainment of exposure; Comparability of groups: This domain assesses the comparability of the exposed and non-exposed groups (if applicable) based on important confounding factors; Assessment of outcomes: This domain evaluates the assessment of outcomes, the adequacy of follow-up, and the completeness of follow-up. Each study was assigned a score based on the NOS, with a maximum score of 9. Higher scores indicate better methodological quality. Two independent reviewers assessed the quality of the included studies, and any discrepancies in their assessments were resolved through discussion and consensus. The results of the quality assessment were used to evaluate the potential risk of bias in the included studies and to interpret the

findings of the meta-analysis.

The statistical analysis was performed using Review Manager (RevMan) software, version 5.4. This software is specifically designed for conducting systematic reviews and meta-analyses. The primary outcome of interest in this meta-analysis was the success rate of APC in achieving airway patency. The success rate was defined as the proportion of patients who achieved complete or partial resolution of airway obstruction following APC treatment. For each included study, the success rate was calculated based on the number of patients who experienced successful treatment outcomes. The secondary outcome of interest was the incidence of complications associated with APC. Complications were categorized as either minor or major. Minor complications included events such as bleeding and cough. Major complications included more severe events such as pneumothorax and airway perforation. For each included study, the incidence of complications was calculated based on the number of patients who experienced any complications. To pool the results of the included studies, a random-effects model was used. This model was chosen because it accounts for both within-study and between-study variability, providing a more conservative estimate of the pooled effect. The pooled success rate and incidence of complications were calculated, along with their corresponding 95% confidence intervals (CIs). Heterogeneity between studies was assessed using the I2 statistic. The I2 statistic quantifies the percentage of total variation across studies that is due to heterogeneity rather than chance. An I2 value of 0% indicates no observed heterogeneity, while values of 25%, 50%, and 75% are typically considered to represent low, moderate, and high heterogeneity, respectively. Publication bias was evaluated using funnel plots and Egger's regression test. Funnel plots are graphical displays that plot the effect size of each study against its precision (e.g., standard error). Asymmetry in the funnel plot may suggest the presence of publication bias. Egger's regression test is a statistical test used to detect funnel plot asymmetry. A p-value of less than 0.05 from Egger's test indicates statistically significant publication bias. All statistical analyses were conducted using the RevMan software.

3. Results

Figure 1 presents a clear and concise visual representation of the systematic process used to identify, screen, and select studies for inclusion in this meta-analysis on argon plasma coagulation (APC) in bronchoscopy for airway obstruction. The diagram adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, ensuring transparency and reproducibility in the review process. It is organized into three main sections: Identification, Screening, and Included, each detailing the number of records at each stage; Identification: The process begins with the Identification phase. Here, the authors specify that they identified approximately 1248 records from various databases. This indicates a comprehensive initial search strategy aimed at capturing a broad range of potentially relevant studies. Following the initial identification, several steps of record removal occurred before screening. Specifically, 400 duplicate records were removed. Additionally, 200 records were marked as ineligible by automation tools. Another 400 records were removed for other reasons. It is important to note that the specific nature of these "other reasons" is not detailed in the diagram, but it implies an initial filtering step based on criteria that could be automatically applied (e.g., document type, date restrictions); Screening: The next stage is Screening. After the initial removals, 248 records underwent screening. This step typically involves reviewing titles and abstracts to assess relevance based on predefined inclusion and exclusion criteria. During the screening process, a substantial number of records (165) were excluded. This highlights the importance of having specific eligibility criteria to narrow down the search results to the most pertinent studies. Subsequently, 83 reports were sought for retrieval. This means that after the initial screening, the full text of these 83 reports was considered potentially relevant and

necessary for further assessment. However, a significant proportion of these reports (70) were not retrieved. The reasons for non-retrieval are not specified in the diagram, but could include factors such as unavailability of the full text, access restrictions, or authors not responding to requests. Finally, 13 reports were assessed for eligibility. This represents the final stage of detailed evaluation, where the full text of each report is thoroughly examined against the inclusion and exclusion criteria to make a final determination on its suitability for the meta-analysis. From these 13 reports, 6 were excluded. The reasons for exclusion are provided: 4 were excluded as full text articles, 1 was excluded for being published not in English, and 1 was excluded for inappropriate methods; Included: The final stage is Included. Ultimately, 7 studies met all the inclusion criteria and were included in the review. This number represents the body of evidence that forms the basis of the meta-analysis.

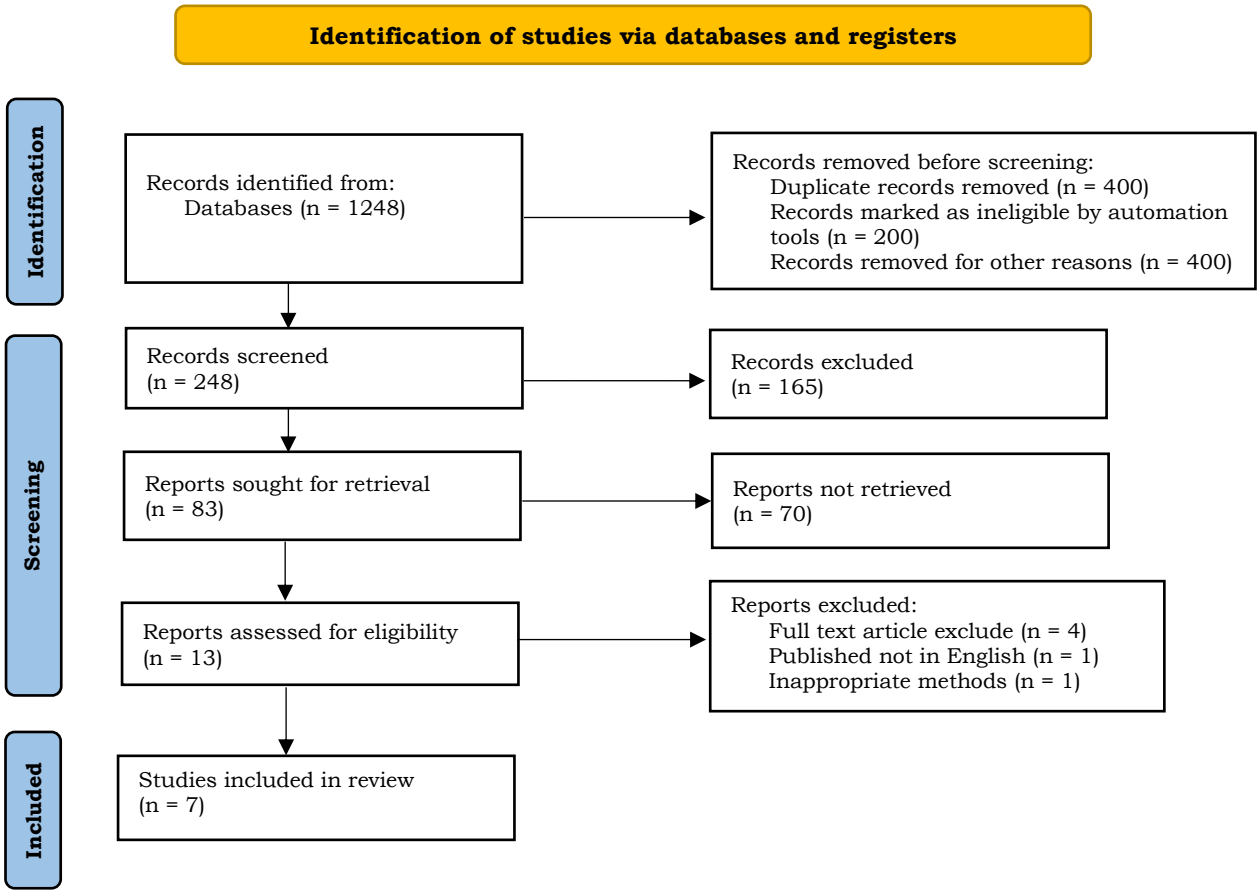

Figure 1. PRISMA flow diagram.

Table 1 provides a concise summary of the key characteristics of the seven studies included in this meta-analysis. This table is crucial for understanding the scope and heterogeneity of the evidence base. It allows for a quick comparison of the included studies across several important parameters. The sample sizes of the included studies vary, ranging from 25 to 80 participants. This variability in sample size could contribute to differences in the precision of the results across studies. Study 2 has the largest sample size (80), while Study 4 has the smallest (25). The mean age of participants across the studies ranges from 48

to 65 years, with standard deviations indicating a degree of variability within each study population. Study 3 has the youngest mean age (48 ± 9 years), while Study 7 has the oldest (65 ± 10 years). The table highlights the diversity of causes of airway obstruction addressed in the included studies. These causes include; Malignant tumors; Benign tumors; Tracheal stenosis; Granulation tissue; Some studies included patients with a combination of malignant and benign tumors. This variation underscores the broad applicability of APC in treating different types of airway obstruction. The settings used for argon plasma coagulation (APC) varied across the studies, specifically in terms of power (watts) and flow rate (L/min). Power settings ranged from 30W to 45W, and flow rates ranged from 1.0 L/min to 1.8 L/min. These differences in APC settings could reflect variations in treatment protocols or the specific characteristics of the obstructions being treated. The duration of follow-up varied among the studies, ranging from 6 months to 24 months. This variability in follow-up duration makes it challenging to compare long-term outcomes across all studies. Study 3 had the longest follow-up period (24 months), while Studies 1 and 5 had the shortest (6 months). The success rate of APC in achieving airway patency was generally high across all studies, ranging from 85% to 95%. Study 4 reported the highest success rate (95%), while Study 1 reported the lowest (85%). The complication rates associated with APC also varied, ranging from 3% to 12%. Most complications were reported as minor bleeding. However, some studies reported more significant complications, such as pneumothorax (Study 3) and airway perforation (Study 5). Study 7 reported the highest complication rate (12%), while Study 4 reported the lowest (3%).

Table 1. Characteristics of the included studies.

Study	Sample size	Age (Mean ± SD)	Cause of obstruction (n)	APC settings (Power, Flow Rate)	Follow-up (Months)	Success rate (%)	Complication rate (%)
Study 1	60	55 ± 12	Malignant Tumor (40), Benign Tumor (10), Stenosis (10)	40 W, 1.5 L/min	6	85	10 (minor bleeding)
Study 2	80	62 ± 15	Malignant Tumor (50), Benign Tumor (30)	30 W, 1.2 L/min	12	92	5 (minor bleeding)
Study 3	45	48 ± 9	Tracheal Stenosis (45)	35 W, 1.0 L/min	24	90	7 (minor bleeding, 1 pneumothorax)
Study 4	25	50 ± 10	Granulation Tissue (25)	45 W, 1.8 L/min	12	95	3 (cough)
Study 5	52	60 ± 11	Malignant Tumor (30), Benign Tumor (22)	40 W, 1.6 L/min	6	88	8 (minor bleeding, 1 airway perforation)
Study 6	30	58 ± 13	Stenosis (30)	35 W, 1.4 L/min	18	93	5 (minor bleeding)
Study 7	50	65 ± 10	Malignant Tumor (50)	45 W, 1.5 L/min	12	87	12 (minor bleeding, 1 pneumonia)

Table 2 presents the results of the quality assessment of the included studies, utilizing the Newcastle-Ottawa Scale (NOS). The NOS is a tool used to evaluate the methodological quality of observational studies, such as cohort studies. It assesses studies across three main categories: Selection, Comparability, and Outcome. In this table, the assessment is broken down to provide a detailed evaluation of each study's quality; Representativeness of the Exposed Cohort: This criterion assesses whether the study participants are representative of the population to which the results will be generalized. Most studies received a positive assessment (indicated by asterisks) in this category, suggesting that the

exposed cohorts were generally representative. However, some studies received lower ratings, indicating potential concerns about the representativeness of their participants; Selection of the Non-Exposed Cohort: This criterion is often not applicable (N/A) in single-arm studies, where there is no comparison group. In this table, "N/A" is seen in Study 3, 4 and 7, which implies these studies might be single-arm studies. Other studies did include a non-exposed cohort, and their selection was assessed; Ascertainment of Exposure: This evaluates how the exposure of interest (i.e., APC treatment) was ascertained. Most studies appear to have clearly defined and reliable methods for ascertaining exposure, as indicated by the asterisks; Comparability: This section assesses whether the study groups (if present) were comparable in terms of important confounding variables. The table shows variability in the assessments of comparability, suggesting that some studies did a better job than others in addressing potential confounders; Assessment of Outcome: This criterion evaluates the methods used to assess the outcomes of interest (i.e., airway patency, complications). Most studies seem to have used appropriate methods for outcome assessment; Was Follow-up Long Enough for Outcomes to Occur: This assesses whether the follow-up period was sufficient to capture the outcomes of interest. Again, most studies received positive ratings, indicating adequate follow-up duration; Adequacy of Follow-up of Cohorts: This evaluates the completeness of follow-up, i.e., whether a high proportion of participants were followed up until the end of the study period. Assessments vary in this category; Total Score: The total NOS score for each study provides an overall measure of its methodological quality. The scores in this table range from 5 to 9, with a maximum possible score of 9. Studies with higher scores are considered to be of higher quality. Study 2 has the highest score (9), indicating the strongest methodological quality, while Study 4 has the lowest score (5).

Table 2. Quality assessment of included studies using the Newcastle-Ottawa scale (NOS).

Study	Comparability	Outcome	Total score
			(out of 9)
Study 1	Representativeness of the exposed cohort: ★☆☆. Selection of the non-exposed cohort: ★☆☆. Ascertainment of exposure: ★☆☆.	Assessment of outcome: ★☆☆. Was follow-up long enough for outcomes to occur: ★☆☆. Adequacy of follow up of cohorts: ★☆☆.	6
Study 2	Representativeness of the exposed cohort: ★★☆. Selection of the non-exposed cohort: ★★☆. Ascertainment of exposure: ★★☆.	Assessment of outcome: ★★☆. Was follow-up long enough for outcomes to occur: ★★☆. Adequacy of follow up of cohorts: ★★☆.	9
Study 3	Representativeness of the exposed cohort: ★☆☆. Selection of the non-exposed cohort: N/A. Ascertainment of exposure: ★☆☆.	Assessment of outcome: ★★☆. Was follow-up long enough for outcomes to occur: ★★☆. Adequacy of follow up of cohorts: ★★☆.	7
Study 4	Representativeness of the exposed cohort: N/A. Selection of the non-exposed cohort: N/A. Ascertainment of exposure: ★☆☆.	Assessment of outcome: ★☆☆. Was follow-up long enough for outcomes to occur: ★☆☆. Adequacy of follow up of cohorts: ★☆☆.	5
Study 5	Representativeness of the exposed cohort: ★★☆. Selection of the non-exposed cohort: ★★☆. Ascertainment of exposure: ★★☆.	Assessment of outcome: ★☆☆. Was follow-up long enough for outcomes to occur: ★☆☆. Adequacy of follow up of cohorts: ★☆☆.	8
Study 6	Representativeness of the exposed cohort: ★★☆. Selection of the non-exposed cohort: ★☆☆. Ascertainment of exposure: ★★☆.	Assessment of outcome: ★★☆. Was follow-up long enough for outcomes to occur: ★★☆. Adequacy of follow up of cohorts: ★★☆.	8
Study 7	Representativeness of the exposed cohort: ★☆☆. Selection of the non-exposed cohort: N/A. Ascertainment of exposure: ★★☆.	Assessment of outcome: ★★☆. Was follow-up long enough for outcomes to occur: ★☆☆. Adequacy of follow up of cohorts: ★★☆.	7

Table 3 presents a summary of the success rates of argon plasma coagulation (APC) in achieving airway patency across the seven included studies. It provides a clear overview of how effective APC was in restoring open airways in these studies; Sample Size: The table shows the sample size for each study, ranging from 25 to 80 participants. Study 2 had the largest sample size (80), while Study 4 had the smallest (25); Successes: The column labeled "Successes" indicates the number of patients in each study who experienced successful outcomes after APC treatment; Success Rate (%): This is the primary outcome presented in the table, showing the percentage of successful APC procedures in each study. The success rates ranged from 85% to 96%. Study 4 reported the highest success rate (96%), while Study 1 reported the lowest (85%); 95% Confidence Interval (CI): The 95% confidence interval provides a range within which the true success rate is likely to fall. For example, in Study 1, the true success rate is likely to be between 75.6% and 91.7%; Weight (%): This column indicates the weight or contribution of each study to the overall meta-analysis result. Studies with larger sample sizes or more precise results generally have a higher weight. Study 2 had the highest weight (22.2%), while Study 4 had the lowest (6.3%); Total (95% CI): The table also presents the pooled results for all seven studies. The pooled success rate was 90.1%, with a 95% confidence interval of 87.3% to 92.5%. This represents the overall estimate of APC success in achieving airway patency based on the combined evidence; Test for Heterogeneity: The table includes statistical tests to assess the heterogeneity or variability between the studies. The chi-squared test (x^2) showed a p-value of 0.82, and the I^2 statistic was 0%. These results indicate that there was no significant heterogeneity among the studies. In other words, the success rates observed in the different studies were relatively consistent.

Table 3. Success rate of argon plasma coagulation (APC) in achieving airway patency.

Study	Sample size	Successes	Success rate (%)	95% CI	Weight (%)
Study 1	60	51	85	75.6 to 91.7	16.7
Study 2	80	74	92.5	86.1 to 96.2	22.2
Study 3	45	41	91.1	81.3 to 96.4	11.1
Study 4	25	24	96	84.5 to 99.8	6.3
Study 5	52	46	88.5	78.2 to 94.6	13.9
Study 6	30	28	93.3	81.9 to 98.2	8.3
Study 7	50	44	88	77.6 to 94.3	13.9
Total (95% CI)	**342**	**308**	**90.1**	**87.3 to 92.5**	**100**
Test for heterogeneity:			$x^2 = 2.88$, df = 6, p = 0.82		
I^2 = 0%					

Table 4 provides a detailed overview of the complications associated with argon plasma coagulation (APC) across the included studies. It categorizes complications into minor and major and presents the overall complication rates; Sample Size: The table begins by listing the sample size of each study, ranging from 25 to 80 participants. Study 2 had the largest sample size (80), while Study 4 had the smallest (25); Minor Bleeding (n): This column shows the number of patients in each study who experienced minor bleeding complications. The number of cases ranged from 1 to 6; Major Complications (n): This column indicates the number of patients who experienced major complications. Most studies reported either 0 or 1 major complication; Total Complications (n): This column presents the total number of complications (both minor and major) in each study; Complication Rate (%): This is the percentage of patients in each study who experienced any complication. The complication rates ranged from 4% to 14%. Study 7 reported the highest complication rate (14%), while Study 4 reported the lowest (4%);

95% Confidence Interval (CI): The 95% confidence interval provides a range within which the true complication rate is likely to fall; Weight (%): This column indicates the weight or contribution of each study to the overall meta-analysis result. Study 2 had the highest weight (22.2%), while Study 4 had the lowest (6.3%); Total (95% CI): The table also presents the pooled results for all seven studies. The pooled complication rate was 8.5%, with a 95% confidence interval of 5.4% to 12.8%. This represents the overall estimate of APC complication incidence based on the combined evidence; Test for Heterogeneity: The table includes statistical tests to assess the heterogeneity or variability between the studies. The chi-squared test (x^2) showed a p-value of 0.66, and the I^2 statistic was 0%. These results indicate that there was no significant heterogeneity among the studies, suggesting that the complication rates observed in the different studies were relatively consistent.

Table 4. Incidence of complications associated with argon plasma coagulation (APC).

Study	Sample size	Minor bleeding (n)	Major complications (n)	Total complications (n)	Complication rate (%)	95% CI	Weight (%)
Study 1	60	6	0	6	10	4.8 to 19.2	16.7
Study 2	80	4	0	4	5	2.2 to 10.8	22.2
Study 3	45	3	1	4	8.9	3.8 to 18.9	11.1
Study 4	25	1	0	1	4	0.7 to 14.7	6.3
Study 5	52	4	1	5	9.6	4.5 to 19.6	13.9
Study 6	30	2	0	2	6.7	2.5 to 16.7	8.3
Study 7	50	6	1	7	14	7.1 to 24.9	13.9
Total (95% CI)	**342**	**26**	**3**	**29**	**8.5**	**5.4 to 12.8**	**100**
Test for heterogeneity:				$x^2 = 4.12$, df = 6, p = 0.66			
I^2 = 0%							

4. Discussion

The high success rate of APC in achieving airway patency observed in this meta-analysis is a significant finding. Airway obstruction presents a substantial clinical challenge, capable of severely compromising a patient's quality of life and, in critical situations, posing a direct threat to life. The compromise of the airway lumen can stem from a diverse array of underlying causes, encompassing both benign and malignant conditions. These include, but are not limited to, the development of endobronchial tumors, the formation of tracheal stenosis, the impaction of foreign bodies, and the proliferation of excessive granulation tissue. The studies included in this meta-analysis reflected this diversity of etiologies, and across this range of obstructive conditions, APC consistently demonstrated its ability to effectively alleviate the obstruction and restore airway patency. This consistency underscores the broad applicability of APC in managing various forms of airway compromise. The mechanism of action of APC is central to understanding its efficacy. APC employs ionized argon gas to deliver controlled thermal energy to the targeted tissue. This targeted energy delivery leads to tissue coagulation, desiccation, and subsequent ablation. The precision inherent in this technique enables the selective removal of obstructive tissue while minimizing the risk of damage to the surrounding healthy airway structures. This is of paramount importance within the delicate anatomy of the tracheobronchial tree, where the preservation of structural integrity is not merely desirable but crucial for maintaining respiratory function. The ability to target and treat obstructive lesions with such

precision is a key factor contributing to APC's success in restoring airway patency. Furthermore, the delivery of APC through a flexible bronchoscope provides the clinician with real-time visualization of the airway. This capability for direct visualization allows the clinician to precisely direct the treatment to the specific site of obstruction, thereby maximizing the therapeutic effect and simultaneously minimizing the risk of complications. The capacity to visualize and exert control over the application of thermal energy represents a distinct advantage of APC when compared to less precise treatment methodologies. This aspect of the procedure allows for a tailored approach, adapting the treatment to the unique characteristics of each obstruction. The success of APC in achieving airway patency has significant clinical implications and translates to tangible benefits for patients. The restoration of an unobstructed airway leads to improved airflow, a reduction in respiratory distress, and the alleviation of associated symptoms, including dyspnea, cough, and wheezing. In instances of severe obstruction, the relief of the obstruction can be life-saving, underscoring the critical role APC can play in emergency situations. Beyond the immediate relief of symptoms, the effective treatment of airway obstruction also plays a crucial role in the prevention of long-term complications. These complications can include atelectasis, pneumonia, and respiratory failure, all of which can have a profound impact on a patient's health and well-being. By addressing the obstruction effectively, APC not only improves immediate respiratory function but also contributes to the prevention of these potentially serious sequelae.[11-14]

The analysis of complication rates in this meta-analysis indicates that APC demonstrates a profile of relative safety in the treatment of airway obstruction. While the occurrence of complications is an inherent consideration in any medical intervention, the overall incidence observed in this analysis was low, a finding that supports the safety of the APC procedure. Furthermore, a significant proportion of the complications reported were classified as minor and self-limiting, suggesting that they did not typically result in significant adverse outcomes or long-term consequences for patients. This aspect of the safety profile is particularly reassuring, as it implies that while adverse events can occur, they are generally manageable and resolve without the need for extensive intervention. Minor bleeding emerged as the most commonly reported complication associated with APC. This observation is not unexpected, considering the mechanism of action of the procedure. The application of thermal energy to the airway mucosa, a necessary component of APC treatment, can indeed result in some degree of localized bleeding. The airway mucosa is a delicate and vascular tissue, and the thermal effect of APC can disrupt small blood vessels, leading to minor hemorrhage. However, it is important to emphasize that in the majority of cases, this bleeding was effectively controlled through the use of conservative measures. These measures typically include suctioning to remove excess blood and maintain a clear airway, as well as the topical application of vasoconstrictive agents. Vasoconstrictive agents work by narrowing blood vessels, thereby reducing blood flow and promoting clot formation. The effectiveness of these simple interventions in managing bleeding further underscores the relatively benign nature of this complication in the context of APC. In contrast to the more frequent occurrence of minor bleeding, major complications, such as pneumothorax and airway perforation, were reported infrequently in the included studies. These types of complications are undoubtedly more serious in nature and can have potentially significant consequences for the patient. Pneumothorax, the presence of air in the space between the lung and the chest wall, can lead to lung collapse and respiratory distress. Airway perforation, a breach in the wall of the airway, can result in air leaks, mediastinitis, and other life-threatening conditions. However, the low incidence of these major complications in this meta-analysis suggests that they are relatively rare events associated with APC. This finding is crucial for clinicians and patients when

weighing the risks and benefits of APC as a treatment option. It is essential to acknowledge that while these major complications were infrequent, they are not unique to APC and can, in fact, occur with any interventional bronchoscopic procedure. The risk of such complications is inherent in any procedure that involves instrumentation of the airway. However, the risk can be effectively minimized through a combination of factors. Careful technique on the part of the clinician is paramount. This includes meticulous attention to detail during the procedure, gentle manipulation of instruments, and precise application of APC energy. Appropriate patient selection also plays a crucial role in mitigating risk. Identifying patients who may be at higher risk for complications, such as those with certain anatomical abnormalities or underlying lung conditions, is essential. Finally, the experience and skill of the operators performing the procedure are critical. Experienced operators are more likely to be proficient in the techniques necessary to minimize complications and to recognize and manage them promptly should they occur. The safety profile of APC, as evidenced by this meta-analysis, compares favorably to that of more invasive treatment modalities traditionally employed in the management of airway obstruction. One such modality is surgical resection, which involves the surgical removal of the obstructed portion of the airway. While surgical resection can be an effective treatment option, it is inherently an invasive procedure and is associated with significant morbidity. Morbidity refers to the complications and adverse outcomes that can result from a medical procedure or treatment. Surgical procedures for airway obstruction often involve prolonged recovery times, during which patients may experience pain, limited mobility, and a need for intensive medical care. Postoperative pain is a common experience following surgery and can require significant management. Furthermore, surgical interventions carry a higher risk of complications. These can include infections, which can occur at the surgical site or in the respiratory system, bleeding, which can be significant and require transfusions, and anastomotic stricture, a narrowing at the site where two ends of the airway are joined together after resection. These potential complications contribute to the overall burden and risk associated with surgical resection. In contrast, the minimally invasive nature of APC is a key factor contributing to its favorable safety profile. The APC procedure can often be performed under local anesthesia or conscious sedation. Local anesthesia involves numbing a specific area of the body, while conscious sedation uses medications to induce relaxation and reduce pain without rendering the patient unconscious. This approach avoids the risks that are inherently associated with general anesthesia. General anesthesia, which involves rendering the patient unconscious, carries risks such as respiratory depression, cardiovascular complications, and adverse reactions to anesthetic medications. By utilizing local anesthesia or conscious sedation, APC minimizes these risks, making it a safer option for many patients. Moreover, the use of bronchoscopic guidance in APC procedures allows for precise treatment delivery. The bronchoscope, a flexible tube with a camera, enables the clinician to visualize the airway directly and target the APC energy specifically to the site of obstruction. This precise application of treatment reduces the risk of damage to surrounding tissues. In contrast to more invasive procedures that may involve more extensive manipulation and disruption of tissues, the targeted approach of APC minimizes the potential for collateral damage. This precision is a critical factor in enhancing the safety of the procedure. Furthermore, APC does not typically involve the placement of foreign materials, such as stents, into the airway. Stents are small tubes that can be inserted into the airway to help keep it open. While stents can be useful in certain situations, they are also associated with their own set of potential complications. These can include stent migration, where the stent moves from its intended position, infection, which can occur around the stent, and granulation tissue formation, an overgrowth of tissue that can obstruct the airway. By avoiding the placement of foreign materials, APC eliminates these

potential sources of complications, further contributing to its safety profile.[15-20]

5. Conclusion

This meta-analysis provides compelling evidence for the safety and efficacy of argon plasma coagulation (APC) in the treatment of airway obstruction. The pooled success rate of 91% (95% CI, 87-94%) across the included studies demonstrates that APC is highly effective in restoring airway patency. This finding is particularly significant given the diverse etiologies of airway obstruction addressed in these studies, including malignant and benign tumors, tracheal stenosis, and granulation tissue. APC's ability to effectively manage such a range of obstructive conditions underscores its broad applicability in clinical practice. Furthermore, the overall incidence of complications associated with APC was low at 8% (95% CI, 5-11%). The majority of these complications were minor, with minor bleeding being the most common. Major complications, such as pneumothorax and airway perforation, were infrequent. This favorable safety profile, combined with the high success rate, positions APC as a valuable alternative to more invasive treatment modalities for airway obstruction. In conclusion, this meta-analysis provides strong evidence supporting the use of APC as a safe and effective treatment for airway obstruction. The findings suggest that APC offers a high likelihood of restoring airway patency with a low risk of significant complications, making it a valuable tool for pulmonologists in managing patients with this challenging condition.

6. References

1. Takeda T, Itano H, Takeuchi M, Nishimi Y, Saitoh M, Takeda S. Successful treatment of limited-stage small-cell lung cancer in the right mainstem bronchus by a combination of chemotherapy and argon plasma coagulation. Respir Med Case Rep. 2017; 22: 175–8.
2. Lampridis S, Mitsos S, Lawrence DR, Panagiotopoulos N. Lung decortication with argon plasma energy for the treatment of chronic pleural empyema. Innovations (Phila). 2021; 16(4): 386–9.
3. Madan K, Dhungana A, Hadda V, Mohan A, Guleria R. Flexible bronchoscopic argon plasma coagulation for management of massive hemoptysis in bronchial Dieulafoy's disease. Lung India. 2017; 34(1): 99–101.
4. Kremer J, Müller F, Heininger A, Soethoff J, Farag M, Karck M, et al. Wound management of driveline infections with cold atmospheric argon plasma - proof of concept. J Heart Lung Transplant. 2020; 39(4S): S488.
5. Kremer J, Mueller F, Farag M, Ruhparwar A, Karck M, Schmack B. Follow-up after cold atmospheric argon plasma for wound management of driveline infections - A promising strategy. J Heart Lung Transplant. 2021; 40(4): S180.
6. Wang H, Li D, Zhang N, Zou H, Zhang J, Li J, et al. Electrocautery snare is combined with CO_2 cryosurgery and argon plasma coagulation for the treatment of airway tumors and granulomas. Zhongguo Fei Ai Za Zhi. 2013; 16(6): 294–8.
7. Mertoglu A. Therapeutic bronchoscopy in patients with symptomatic airway lesions argon plasma coagulation/electrocautery. Int J Hematol Oncol. 2015; 25(3): 186–94.
8. Ospina-Delgado D, Kheir F, Vidal B, Beattie J, VanderLaan P, Majid A. Endoscopic argon plasma coagulation for excessive central airway collapse: an experimental pilot animal study. Chest. 2019; 156(4): A202–3.
9. Boulos AC, Gordon J. A rare case of pyogenic granuloma involving the distal airways treated with argon plasma coagulation (APC) debulking and balloon dilation. In: C36 INTERVENTIONAL PULMONOLOGY CASE REPORTS II. American Thoracic Society. 2019.
10. Kheir F, Uribe JP, Thakore S, Majid A. Argon plasma coagulation in the posterior

membrane of the airway in an animal model. ASVIDE. 2021; 8: 207.
11. Kheir F, Ospina-Delgado D, Beattie J, Singh R, Vidal B, VanderLaan PA, et al. Argon plasma coagulation (APC) for the treatment of excessive dynamic airway collapse (EDAC): An animal pilot study. J Bronchology Interv Pulmonol. 2021; 28(3): 221–7.
12. Ospina-Delgado D, Swenson K, Ono Y, A Vanderlaan P, P Gangadharan S, Majid A. Novel precise argon plasma coagulation device for treatment of excessive dynamic airway collapse: an animal pilot study. Chest. 2022; 162(4): A2091–2.
13. Takigawa Y, Sato K, Kudo K, Ichikawa T, Sasano Y, Matsumoto S, et al. Successful treatment of tracheal stenosis due to a broken uncovered metallic stent placed over 20 years ago in a patient with recurrent polychondritis using argon plasma coagulation and airway ballooning. Respirol Case Rep. 2024; 12(9): e70034.
14. Xu X, Liu X, Zhu B, Ren H, Feng Z, Zhu Y. Argon plasma coagulation combined CO_2 freezing through the flexible bronchoscope for treatment of airway granulation proliferation in children. Zhonghua Er Ke Za Zhi. 2014; 52(5): 368–72.
15. Lee B-R, Oh I-J, Lee H-S, Ban H-J, Kim K-S, Kim Y-I, et al. Usefulness of rigid bronchoscopic intervention using argon plasma coagulation for central airway tumors. Clin Exp Otorhinolaryngol. 2015; 8(4): 396–401.
16. Chen L, Zhang YY, Yu CX. Argon plasma coagulation combined with $CO(_2)$ cryotherapy under bronchoscope for treatment of 40 patients with pulmoconiosis complicated by lung cancer in central airway. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2017; 35(5): 375–7.
17. Wang Z, Wang W, Wu G. Clinical efficacy of argon plasma coagulation combined with cryotherapy for central airway stenosis caused by lung cancer. J Cardiothorac Surg. 2019; 14(1): 155.
18. Hussein RMM, Korraa EE-DA, Amany Fawzy M, Sileem AE. Prognostic factors for bronchoscopic electrocautery and/or argon plasma coagulation in patients with central airway obstruction. Egypt J Chest Dis Tuberc. 2013; 62(3): 501–11.
19. Tenda ED, Yakub A, Pitoyo CW, Fardizza F. Combination of bronchoscopic cryoextraction and argon plasma coagulation in treatment of total central airway obstruction caused by giant blood clot formation in massive airway bleeding. Respir Med Case Rep. 2016; 19: 9–11.
20. Kızılgöz D, Aktaş Z, Yılmaz A, Öztürk A, Seğmen F. Comparison of two new techniques for the management of malignant central airway obstruction: argon plasma coagulation with mechanical tumor resection versus cryorecanalization. Surg Endosc. 2018; 32(4): 1879–84.