Turkish Journal of Thoracic and Cardiovascular Surgery 2025;33(2):217-225

ORIGINAL ARTICLE / ÖZGÜN MAKALE

# The efficacy of topical mitomycin-C in the treatment of benign tracheal stenosis: A comparative study

*Benign trakeal stenozların tedavisinde topikal mitomisin-C'nin etkinliği: Karşılaştırmalı bir çalışma*

**Efsun Gonca Uğur Chousein[1], Demet Turan[1], Elif Tanrıverdi[1], Binnaz Zeynep Yıldırım[1], Mustafa Vedat Doğru[2], Halit Çınarka[1], Mehmet Akif Özgül[1], Erdoğan Çetinkaya[1]**

[1]Department of Chest Diseases, University of Health Sciences, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Türkiye
[2]Department of Thoracic Surgery, University of Health Sciences, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Türkiye

## ABSTRACT

***Background:*** This study aims to examine the efficacy of mitomycin-C (MMC) in patients with benign tracheal stenosis who have re-stenosis requiring repeated interventional bronchoscopy.

***Methods:*** Between January 2009 and December 2019, a total of 25 patients who underwent repeated procedures for re-stenosis were retrospectively analyzed. The study group consisted of 11 patients (7 males, 4 females; median age: 37 years; range, 16 to 63 years) who underwent MMC following routine dilation and the control group consisted of 14 patients (8 males, 6 females; median age: 52 years; range, 19 to 73 years) who underwent dilation alone and did not receive MMC. Demographic data of the patients, the etiology of stenosis, comorbidities, medications used, imaging studies, location, degree and length of re-stenosis, details of interventional bronchoscopy, pre- and post-procedural time intervals between mechanical dilation, and cost were reviewed.

***Results:*** The percentage changes of re-stenosis and mean re-stenotic segment length significantly decreased (p=0.013 and p=0.029, respectively), and the medical cost (p=0.021), and number of repeated dilations (p=0.020) were lower in the MMC-treated group, compared to the control group. However, the improvement rate was not significantly different (p=0.070) between the MMC-treated group and control group.

***Conclusion:*** Mitomycin-C is helpful to decrease the tracheal re-stenosis percentage changes and the number of repeated dilations in patients with benign tracheal stenosis. It also decreases the median re-stenotic segment lengths which may be crucial for limited reserve surgery in tracheal resections. Taken together, MMC is a cost-effective, time-saving and tracheal-sparing treatment in patients with benign tracheal stenosis.

***Keywords:*** Bronchoscopy, efficacy, mitomycin-C, tracheal stenosis.

## ÖZ

***Amaç:*** Bu çalışmada tekrarlayan girişimsel bronkoskopi gerektiren restenozu olan benign trakeal stenozlu hastalarda mitomisin-C'nin (MMC) etkinliği incelendi.

***Çalışma planı:*** Ocak 2009 - Aralık 2019 tarihleri arasında restenoz nedeniyle tekrarlayan işlem yapılan toplam 25 hasta retrospektif olarak incelendi. Çalışma grubu rutin dilatasyon sonrası MMC verilen 11 hastadan (7 erkek, 4 kadın; medyan yaş: 37 yıl; dağılım, 16-63 yıl) ve kontrol grubu yalnızca dilatasyon yapılan ve MMC verilmeyen toplam 14 hastadan (8 erkek, 6 kadın; medyan yaş: 52 yıl; dağılım, 19-73 yıl) oluşuyordu. Hastaların demografik verileri, stenoz nedeni, eşlik eden hastalıklar, kullanılan ilaçlar, görüntüleme çalışmaları, restenozun yeri, derecesi ve uzunluğu, girişimsel bronkoskopinin detayları, mekanik dilatasyon arasında işlem öncesi ve sonrası zaman aralıkları ve maliyet değerlendirildi.

***Bulgular:*** Kontrol grubuna kıyasla, MMC ile tedavi edilen grupta restenoz yüzde değişim oranı ve ortalama restenoz segment uzunluğu anlamlı düzeyde azaldı (sırasıyla, p=0.013 ve p=0.029) ve tıbbi maliyet (p=0.021) ve tekrarlayan dilatasyon sayısı (p=0.020) daha düşük bulundu. Ancak, iyileşme oranı MMC ile tedavi edilen grup ve kontrol grubu arasında istatistiksel olarak anlamlı değildi (p=0.070).

***Sonuç:*** Mitomisin-C, benign trakeal stenozlu hastalarda restenoz yüzdesindeki değişiklikleri ve tekrarlayan bronkoskopik dilatasyon sayısını azaltmada yardımcıdır. Ayrıca, trakeal rezeksiyonlarda sınırlı rezerv cerrahisi için önemli olabilecek medyan restenoz segment uzunluklarını azaltır. Sonuç olarak, benign trakeal stenozlu hastalarda MMC maliyet-etkin, zaman kazandıran ve trakeayı koruyucu bir tedavidir.

***Anahtar sözcükler:*** Bronkoskopi, etkinlik, mitomisin-C, trakeal stenoz.

**Corresponding author:** Efsun Gonca Uğur Chousein.
E-mail: efsungoncachousein@yahoo.com

Doi: 10.5606/tgkdc.dergisi.2025.27157

**Received:** November 15, 2024
**Accepted:** January 16, 2025
**Published online:** April 30, 2025

***Cite this article as:*** Uğur Chousein EG, Turan D, Tanrıverdi E, Yıldırım BZ, Doğru MV, Çınarka H, et al. The efficacy of topical mitomycin-C in the treatment of benign tracheal stenosis: A comparative study. Turk Gogus Kalp Dama 2025;33(2):217-225. doi: 10.5606/tgkdc.dergisi.2025.27157.

Tracheal stenosis is defined as ≥50% obliteration of the tracheal lumen secondary to malignant or benign diseases which can lead to potentially fatal results.[1,2] Compared to patients with malignant tracheal stenosis who have comparatively short survival times, patients with benign tracheal stenosis (BTS) require longer lasting treatments and pose a greater challenge to physicians working in this field.[2,3]

The most frequent cause of BTS is post-intubation tracheal stenosis which is increasingly recognized due to widespread utilization of intensive care. Its prevalence increases despite prevention efforts and confers high medical costs.[4,5]

Patients with web-like/simple stenosis (no destruction of cartilage) can be treated with interventional bronchoscopy (IB), while those with the complex-type stenosis (cartilage destruction) are treated primarily with surgery.[1,6] Suggested treatment methods for BTS, not suitable for surgery, include IB methods, such as mechanical dilation/resection, thermal ablation, airway stenting and a multimodal approach with topical agents including mitomycin-C (MMC).[2]

Airway stenoses are the result of an abnormal wound healing with various chemical mediators. Mitomycin-C is an anti-metabolite with anti-proliferative and anti-fibrotic effects. Its topical use reduces fibrosis by prolonging the process of tissue healing via apoptosis of fibroblasts, which play an important role in wound healing. There are conflicting data on the efficacy of topical MMC in patients with BTS.[2,7-9] Several studies conducted with this agent are usually small-scale studies and lack of control groups.[3,8-11]

In the present study, we aimed to examine the efficacy of MMC in patients with BTS who had re-stenosis requiring repeated IB.

## PATIENTS AND METHODS

This single-center, retrospective study was conducted at University of Health Sciences, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Department of Pulmonology, Interventional Pulmonology Clinic between January 2009 and December 2019. A total of 111 BTS patients who underwent IB were screened. Cases with novel coronavirus disease 2019 (COVID-19)-related BTS were excluded. Of them, 29 who underwent repeated procedures for re-stenosis were identified. Of these, 15 had topical MMC application following dilation. Four of these 15 patients were excluded from the study, as an airway stent was placed concurrently. Finally, 11 patients (7 males, 4 females; median age: 37 years; range, 16 to 63 years) who underwent MMC following routine dilation were recruited as the study group. The control group consisted of 14 patients (8 males, 6 females; median age: 52 years; range, 19 to 73 years) who underwent dilation alone and did not receive MMC (Figure 1). A written informed consent was obtained from each patient. The study protocol was approved by the Hamidiye Health Sciences University, Scientific Research Ethics Committee (date: 24/04/2020, no: 20/125-46418926-050.03.04). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients' demographic data, the etiology of stenosis, comorbidities, medications used, imaging

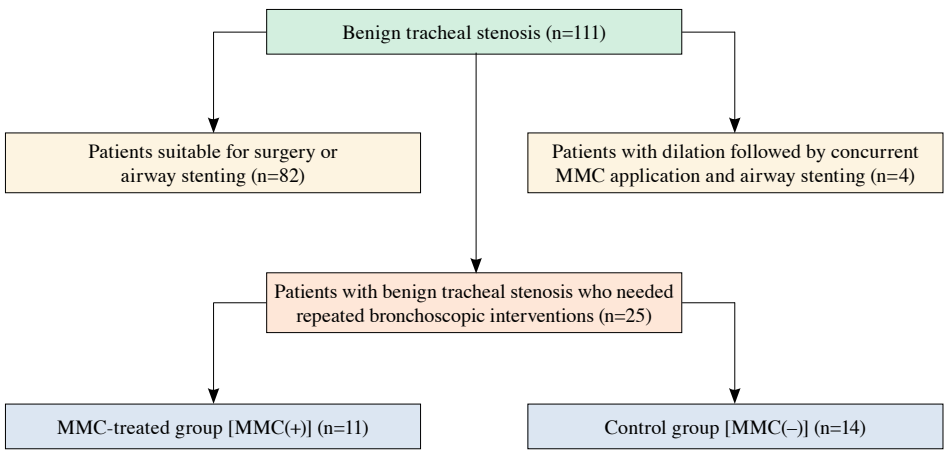


**Figure 1.** Study flowchart.
MMC: Mitomycin-C.

studies, location, degree and length of re-stenosis, details of IB, pre- and post-procedural time intervals between mechanical dilation, and cost were reviewed.

The degree of tracheal stenosis was assessed by bronchoscopy using the supposed Cotton-Myer classification system which is widely accepted in the field of interventional pulmonology. The length of the stenotic segment was determined by marking the measured points on a rigid tube or flexible bronchoscope, starting from the level of the vocal cords, and then measuring these markings with a ruler (Figure 2a).

Since the measurements may be closely related to the treatment time and the treatment modalities used, the tracheal wall thickness measurements were taken from non-contrast thoracic computed tomography (CT) scans performed one to seven days before the first procedures and 15 to 30 days after the patients' final procedures during the study period. The anterior and lateral tracheal wall thicknesses were measured based on the wall thickness at the point where the tracheal lumen was the narrowest on thoracic CT (Figure 3a, b).

Medical expenses included only the costs directly related to the management of tracheal stenosis, such as radiological and laboratory examinations, hospitalization, and treatment, and were limited to procedures performed exclusively at our center. All


**Figure 2.** The processing stages of a postintubation tracheal stenosis (after ICU stay due to gastrointestinal hemorrhage treated with MMC. **(a)** Rigid bronchoscopy revealed a 2-cm stenotic segment of complex type, starting 3 cm below the vocal cords and obstructing 75% of the tracheal lumen. **(b)** Mechanical dilation and MMC treatment. **(c)** Permanent patency of tracheal lumen after six months.
ICU: Intensive care unit; MMC: Mitomycin-C.

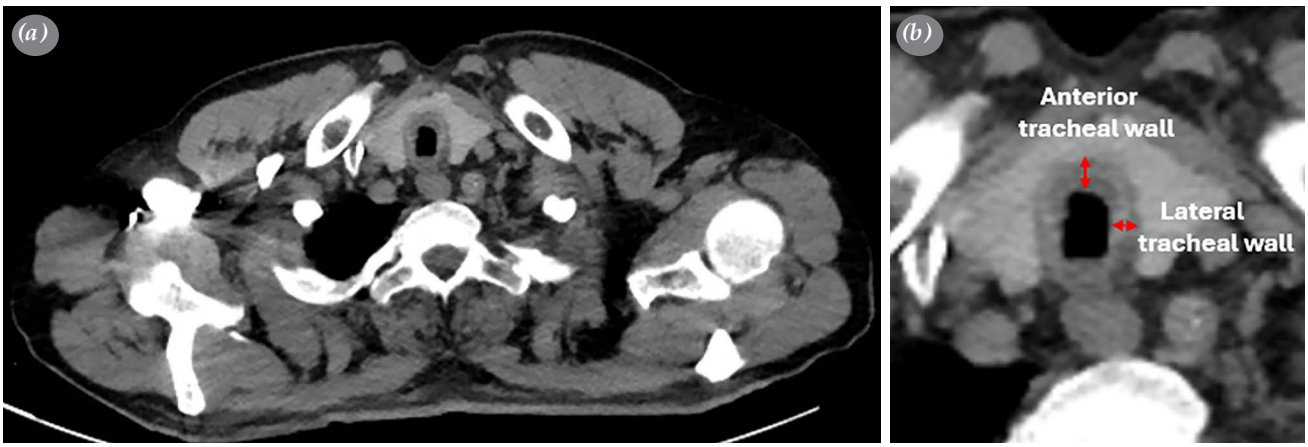


**Figure 3.** The measurement technique of the anterior and lateral wall thickness shown at the thoracic CT section where the tracheal lumen was the narrowest. **(a)** Chosen thoracic CT section including the narrowest tracheal lumen. **(b)** Closer view of the measurement technique of the anterior and the lateral tracheal wall with red arrows.
CT: Computed tomography.

patients in both groups had national insurance system coverage. However, during the study period, patients in the MMC-treated group were responsible for covering the cost of the MMC agent, which ranged from $14 to $20, which was included in the total cost calculation.

All patients were monitored with electrocardiography and oxygen saturation ($SpO_2$) under general anesthesia. Induction was achieved with midazolam (0.05 to 0.10 mg/kg), propofol (maximum dose: 1,000 mg), remifentanil (maximum dose: 2 mg), and rocuronium (maximum dose: 50 mg). The equipment included the Dumon® Series II rigid bronchoscopes (Efer Endoscopy, La Ciotat, France) with optical system. The argon plasma coagulation (APC) (40 W, blended mode/continuous flow) was applied using an instrument by ERBE Elektromedizin GmbH (Tubigen, Germany). Cryotherapy was performed with the ERBOKRYO system (Elektromedizin GmbH, Tubingen, Germany).

Mechanical dilation involves expanding stenotic airway segments using rigid tubes with progressively increasing diameters. A total of 10 to 20 mg of MMC is diluted in isotonic saline to a concentration of 1.0 mg/mL for topical use of MMC in the airways. Gauze patches are soaked in this bluish-lilac solution and applied to the dilated area for a total of 4 min.

The patients' final outcomes were evaluated based on "improvement", "suitability/referral for surgery", and "follow-up status" with/without airway stenting. "Improvement" was defined as a condition where airway patency was permanently maintained at >50% and the patient had no additional respiratory symptoms (Figure 2b, c).

### Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 25.0 software (IBM Corp., Armonk, NY, USA). Continuous data were presented in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and frequency. The Independent sample t-test was used for numerical variables fitting normal distribution. Otherwise, the Mann-Whitney U test was used. The chi-square test was used for comparing categorical variables. A $p$ value of <0.05 was considered statistically significant.

## RESULTS

A total of 25 patients included 11 MMC-treated cases and 14 control cases were enrolled. The median follow-up was 20 (range, 14 to 109) months for the MMC-treated group and 18 (range, 6 to 101) months for the control group (Tables 1 and 2).

Intubation indications were respiratory disorders in 10 (40%), central nervous system (CNS) disorders in six (24%), cardiovascular system diseases in four (16%), traffic accident in three (12%), and gastrointestinal bleeding and carbon monoxide intoxication in two (8%) patients (Table 1). A total of 21 patients had post-intubation tracheal stenosis. Four patients had re-stenosis following tracheal resection. According to the Death Registration System data, 88% of the patients were still alive.

Except for one patient with simple stenosis in each group, all patients had complex type tracheal stenosis. In MMC-treated group, the pre-treatment

**Table 1. Demographic and clinical characteristics of patients**

| | n | % |
|---|---|---|
| MMC | | |
| MMC (+) | 11 | 44.0 |
| MMC (-) | 14 | 56.0 |
| Sex | | |
| Male | 15 | 60.0 |
| Female | 10 | 40.0 |
| Reason for ICU admission | | |
| Respiratory disorders | 10 | 40.0 |
| CNS disorders | 6 | 24.0 |
| CVS disorders | 4 | 16.0 |
| Road traffic accident | 3 | 12.0 |
| Others | 2 | 8.0 |
| Diagnosis | | |
| Postintubation/tracheostomy TS | 21 | 84.0 |
| Post surgery TS | 4 | 16.0 |
| Comorbidity | | |
| Present | 16 | 64.0 |
| Absent | 9 | 36.0 |
| Status | | |
| Alive | 22 | 88.0 |
| Dead | 3 | 12.0 |
| Final outcome | | |
| Improved | 7 | 28.0 |
| Referred for surgery | 12 | 48.0 |
| Airway stenting | 4 | 16.0 |
| Follow-up care | 2 | 8.0 |

MMC: Mitomycin-C; ICU: Intensive care unit; CNS: Central nervous system; CVS: Cardiovascular system; TS: Tracheal stenosis.

**Table 2. Comparison of MMC-treated study group and control group**

| | MMC (+) | | | | | MMC (–) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | Mean±SD | Median | Min-Max | n | % | Mean±SD | Median | Min-Max | t | *p* |
| Age (year) | | | | 37 | 16-63 | | | | 52 | 19-73 | 44.5 | 0.075 |
| Follow-up duration (month) | | | | 20 | 14-109 | | | | 18 | 6-101 | 60.5 | 0.373 |
| Percentage of tracheal stenosis (%) | | | | | | | | | | | | |
| Initial | | | 79.82±12.93 | | | | | 80.29±14,90 | | | 0.082 | 0.935 |
| Final | | | 54.09±20.59 | | | | | 70.93±23.33 | | | 1.884 | 0.072 |
| Length of stenotic segment | | | | | | | | | | | | |
| Initial | | | | 2 | 0.5-8 | | | | 2 | 0.5-6 | 59.5 | 0.344 |
| Final | | | | 1 | 0-6 | | | | 2 | 1-10 | 37 | 0.029 |
| CT measurements (cm) | | | | | | | | | | | | |
| Anterior wall thickness | | | 0.65±0.11 | | | | | 0.66±0.25 | | | 0.121 | 0.905 |
| Lateral wall thickness | | | 0.47±0.16 | | | | | 0.37±0.17 | | | 23 | 0.028 |
| Repeated dilation intervals (day) | | | | 80 | 7-194 | | | | 29 | 8-109 | 25.5 | 0.053 |
| Number of repeated dilations | | | | | | | | | | | 7.652 | 0.020 |
| 2 | 8 | 72.7 | | | | 8 | 57.1 | | | | | |
| 3 | 0 | 0 | | | | 4 | 28.6 | | | | | |
| 4 | 0 | 0 | | | | 2 | 14.3 | | | | | |
| Medical cost* | | | | 295 | 143-611 | | | | 739 | 282-442 | 35 | 0.021 |
| Final outcome | | | | | | | | | | | 6.369 | 0.070 |
| Improved | 5 | 45.5 | | | | 2 | 14.3 | | | | | |
| Referred for surgery | 3 | 27.3 | | | | 9 | 64.3 | | | | | |
| Airway stenting | 1 | 9.1 | | | | 3 | 21.4 | | | | | |
| Follow-up care | 2 | 18.2 | | | | 0 | 0 | | | | | |

MMC: Mitomycin-C; SD: Standard derivation; CT: Computed tomography; * Medical cost expressed in United States Dollars.

percentage of tracheal stenosis ranged from 60 to 99% (mean: 79.82±12.93%), and the median stenotic segment length was 2 (range, 0.5 to 8) cm. The mean post-treatment percentage of tracheal stenosis and the mean stenotic segment length were 54.09±20.59% and 1 (range, 0 to 6) cm. The pre-treatment percentage of tracheal stenosis in the control group ranged from 50 to 99% (mean: 80.29±14.90%), and the median stenotic segment length was 2 (range, 0.5 to 6) cm.

The mean percentage of tracheal re-stenosis in the control group was 70.93±23.33% and the median re-stenotic segment length was 2 (range, 1 to 10) cm. There was a statistically significant difference between the study and control group in terms of tracheal re-stenosis percentage changes and median re-stenotic segment lengths (p=0.013 and p=0,029, respectively) (Table 2). Regarding the re-stenosis situation, changes in stenosis percentages and stenotic segment lengths, airway obstruction progressed in two patients in the MMC-treated group and in five patients in the control group after the IB procedures. In the MMC-treated group, one patient achieved stable CNS during the study period and successfully underwent surgery, while the other remains under follow-up. In the control group, a progression was observed in five patients. Of these, stents were placed in three patients, while the other two proceeded to surgery. Considering patients who were initially unsuitable for surgery in both groups, IB played a crucial time-saving role in enabling surgery for 12 patients.

The mean anterior tracheal wall thickness measured based on the wall thickness at the point where the tracheal lumen was the narrowest was 0.65±0.11 cm in the MMC-treated group and 0.66±0.25 in the control group, indicating no statistically significant difference (p=0.905). The mean lateral tracheal wall thickness was 0.47 (range, 0.41 to 0.89) cm in the study group and 0.37 (range, 0.26 to 0.8) cm in the control group, indicating a statistically significant difference (p=0.028).

The median repeated dilation interval was 80 (range, 7 to 194) days in MMC-treated group and 29 (range, 8 to 109) days in the control group. Despite the 2.7-fold prolongation of intervals, there was no statistically significant difference between the groups (p=0.053). Three MMC-treated patients did not require any additional dilations. There were 14 patients in the control group and eight patients in the study group who needed ≥2 dilations (Table 2).

The medical costs (expressed in US Dollars) were lower in the MMC-treated group ($295 [143-3,611] vs. $739 [282-7,442]) with a statistical significance (p=0.021).

In the MMC-treated group, five (45%) patients improved (<50% of re-stenosis), one (9%) needed stent placement, three (27%) were referred for surgery, and two (18.2%) were still under follow-up. In the control group, improvement was observed in only two (14.3%) patients. Three (21.4%) patients needed stent placement and nine (64.3%) were referred for surgery. There was no statistically significant difference between the groups in terms of improvement (p=0.070) (Table 2). Additional MMC treatment in three patients did not result in a significant improvement (p>0.05).

In the MMC-treated group, one patient had a tracheostomy at the time of admission. Following IB, the patient's condition improved, and he regained the ability to speak. In the control group, two patients presented with tracheostomies and one with T-tube upon admission. Among them, one patient showed improvement after IB, while two required stenting. However, all patients in the control group ultimately regained the ability to speak.

## DISCUSSION

The management of BTS is determined based on the location, length, and percentage of the stenosis, the severity of symptoms, existing comorbidities, the patient's and physician’s preference. Methods of IB such as mechanical dilation/resection, thermal ablation and airway stenting and a multimodal approach with topical agents such as MMC are primarily recommended for simple types of stenosis. Surgery is considered in case of re-stenosis following repeated dilations. For BTS involving a segment longer than 1 cm, where malacia or a damaged cartilage structure may be present, surgery is often the preferred method. For both types of stenosis, an initial IB and a multidisciplinary approach with surgery reserved for recurrent stenosis may sometimes be reasonable.[2,12,13] Due to their relatively long-life expectancy and the likelihood of re-stenosis despite surgery and IB, patients with BTS are the most challenging group for interventional pulmonologists.

In the present study, we found that the percentage changes of re-stenosis and mean re-stenotic segment length and the number of repeated dilations were lower in the MMC-treated tracheal stenosis group. Also, the medical cost was lower, but the improvement rate

was not significantly different in the MMC-treated group than the controls.

Recurrent stenosis following IB is a common condition. While the majority of patients achieve prompt symptomatic relief following dilation, long-term re-stenosis remains a significant concern. In certain cases, the degree of stenosis may exceed the severity of the initial presentation. In our study, an increase in the percentage of stenosis or the length of the stenotic segment was observed in two patients within the MMC-treated group and in five patients in the control group. These patients were subsequently managed either through stent placement or gained time for their surgical intervention.[10]

Most studies have focused on re-stenosis and need for repeated dilations following MMC.[10-12] In the study by Cataneo et al.,[14] a decrease in the percentage of re-stenosis and its length in patients with re-stenosis was reported. In our study, similarly, the percentage of stenosis of cases with BTS and the length of the stenotic segment decreased significantly after MMC. This reduction in the re-stenotic segment length also enables surgical resection. Previous studies have shown that MMC significantly decreases the number of post-procedural repeated dilations and increases dilation intervals in patients with tracheal stenoses/re-stenosis compared to the control group.[3,10] Similarly, our study demonstrated that topical MMC treatment following dilation of the stenotic area is effective in decreasing number of repeated procedures.

Studies on the submucosal application technique rather than topical application are mostly case-based studies. Reviewing a case series study by Tiran et al.,[3] consisting of 10 cases, submucosal application could also yield slightly more promising results consisting mostly of mild residual stenosis after a five-year follow-up. The differences in complication rates between the two techniques should also be considered. In our clinical practice, only topical MMC application is used; however, current findings formed an idea that submucosal injection or a combination of both techniques might increase the success rate in providing a permanent airway.

As in the Chinese and Brazilian studies, MMC treatment was cost-effective in patients with BTS. The cost was 2.5 times lower in patients with BTS treated with MMC, the result was statistically significant.[12,14,15]

Furthermore, it has been shown that MMC increases symptom-free periods of the patients by extending the intervals between the repeated procedures.[10,16] In the present study, despite the 2.7-fold prolongation of intervals, no statistically significant result was reached due to the small number of participants.

The study by Cataneo et al.[14] which did not include a control group reported an improvement rate of 53%. Although our study found a similar improvement rate of 45% following MMC treatment, this did not reach a statistical significance compared to the control group. These improvement rates are remarkable, considering that the patients in the MMC-treated group have no other treatment options. The MMC-treated group included patients not suitable for surgery, such as those left with a short remnant tracheal length following surgical resection and/or disorders with widespread involvement of the trachea up to 8 cm length. Of these, three patients were in the MMC-treated group, and nine were in the control group. In the light of these findings, MMC can be considered as the last resort, when no other options are available.[14]

Patients with respiratory symptoms suggesting an airway obstruction are evaluated with chest X-ray and thoracic CT. Thoracic CT can be valuable for guiding treatment. The measurement of wall thickness at the narrowest point of the stenosis by CT helped us compare and evaluate the treatment result. Prince et al.[17] showed that tracheal wall thickness as determined by CT imaging assisted physicians in tailoring the IB. Tracheal stenosis can be anywhere and of any length from the subglottic region to the tip of the endotracheal tube.[17,21] After examining the entire stenosis area on the CT, the anterior and lateral wall thickness were measured at the section where the stenosis was the most critical (narrowest). We consider that thickening on the lateral wall of the trachea in addition to anterior wall does not always indicate an extensive lesion, but it may show the tracheal segment where the cartilage tissue is most damaged. In our study, patients chosen for MMC treatment had thicker lateral tracheal walls, suggesting that tracheal lumen is narrowed circumferentially and involves more severely.

Some studies reported conflicting data on the onset of action and duration and effect of topical MMC. It has been proposed that repeated topical

applications are more efficient.[3,10,16] In the present study, three patients were treated twice with MMC, and none improved.

Nonetheless, the study has some limitations. First, patients could have been evaluated before and after the procedure by symptom scales, such as a Modified Medical Research Council or respiratory assessment tests, to better indicate the efficacy of MMC. Second, it is a retrospective study with a relatively small sample size yielding the results of topical MMC application alone. Nevertheless, studies involving larger numbers of patients are lacking. Unlike studies conducted with an average of 10 to 50 patients, often without a control group and involving heterogeneous groups, the novelty and strength of our study is its' homogeneous structure, focusing exclusively on BTS caused by post-intubation tracheal stenosis and including a control group.

In conclusion, mitomycin-C is helpful in decreasing the re-stenosis percentage changes and median re-stenotic segment lengths, and reducing the number of repeated dilations and treatment-costs in patients with benign tracheal stenosis. It is also trachea-sparing, which can be a critical point for the decision of tracheal resection in benign tracheal stenosis. However, further studies are required to better elucidate the efficacy and the application technique of mitomycin-C.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Idea/concept, design: E.G.U.C., E.C.; Control/ supervision: E.C., M.A.O., H.C.; Data collection and/or processing: D.T., E.T., B.Z.Y.; Analysis and/or interpretation: E.G.U.C., M.V.D.; Epidemiological and statistical decision making, materials: E.G.U.C., D.T.; Literature review, references: E.T., B.Z. Y., M.V.D.; Writing the article, critical review: E.G.U.C., E.C., M.A.O., H.C.

**Conflict of Interest:** The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

**Funding:** The authors received no financial support for the research and/or authorship of this article.

## REFERENCES

1. Murgu SD, Egressy K, Laxmanan B, Doblare G, Ortiz-Comino R, Hogarth DK. Central Airway Obstruction: Benign strictures, tracheobronchomalacia, and malignancy-related obstruction. Chest 2016;150:426-41. doi: 10.1016/j.chest.2016.02.001.
2. Oberg CL, Holden VK, Channick CL. Benign Central Airway Obstruction. Semin Respir Crit Care Med 2018;39:731-46. doi: 10.1055/s-0038-1676574.
3. Tiran B, Perluk T, Kleinhendler E, Man A, Fomin I, Schwarz Y. Fiberoptic bronchoscopic submucosal injection of mitomycin C for recurrent bening tracheal stenosis: A case series. Isr Med Assoc J 2020;22:757-60.
4. Farzanegan R, Feizabadi M, Ghorbani F, Movassaghi M, Vaziri E, Zangi M, et al. An overview of tracheal stenosis research trends and hot topics. Arch Iran Med 2017;20:598-607.
5. Kocyildirim E, Kanani M, Roebuck D, Wallis C, McLaren C, Noctor C, et al. Long-segment tracheal stenosis: Slide tracheoplasty and a multidisciplinary approach improve outcomes and reduce costs. J Thorac Cardiovasc Surg 2004;128:876-82. doi: 10.1016/j.jtcvs.2004.07.008.
6. Grillo HC, Mathisen DJ, Ashiku SK, Wright CD, Wain JC. Successful treatment of idiopathic laryngotracheal stenosis by resection and primary anastomosis. Ann Otol Rhinol Laryngol 2003;112:798-800. doi: 10.1177/000348940311200909.
7. Hirshoren N, Eliashar R. Wound-healing modulation in upper airway stenosis-myths and facts. Head Neck 2009;31:111-26. doi: 10.1002/hed.20925.
8. Rojas-Solano J, Becker HD. Bronchoscopic application of mitomycin-C as adjuvant treatment for benign airway stenosis. J Bronchology Interv Pulmonol 2011;18:53-5. doi: 10.1097/LBR.0b013e318205be75.
9. Yung KC, Chang J, Courey MS. A randomized controlled trial of adjuvant mitomycin-C in endoscopic surgery for laryngotracheal stenosis. Laryngoscope 2020;130:706-11. doi: 10.1002/lary.28025.
10. Smith ME, Elstad M. Mitomycin C and the endoscopic treatment of laryngotracheal stenosis: Are two applications better than one? Laryngoscope 2009;119:272-83. doi: 10.1002/lary.20056.
11. Viveiros F, Gomes J, Oliveira A, Neves S, Almeida J, Moura e Sá J. Topical application of mitomycin-C as an adjuvant treatment to bronchoscopic procedures in post-intubation tracheal stenosis. Rev Port Pneumol 2013;19:276-80. English, Portuguese. doi: 10.1016/j.rppneu.2013.06.006.
12. Díaz-Jiménez JP, López RL. Benign airways stenosis. In: Díaz-Jiménez JP, Rodríguez AN, editors. Interventions in pulmonary medicine. Cham: Springer; 2023.
13. Faisal M, Harun H, Hassan TM, Ban AY, Chotirmall SH, Abdul Rahaman JA. Treatment of multiple-level tracheobronchial stenosis secondary to endobronchial tuberculosis using bronchoscopic balloon dilatation with topical mitomycin-C. BMC Pulm Med 2016;16:53. doi: 10.1186/s12890-016-0209-1.
14. Cataneo DC, Ximenes AMG, Cataneo AJM. Mitomycin C in the endoscopic treatment of tracheal stenosis: A prospective cohort study. J Bras Pneumol 2018;44:486-90. doi: 10.1590/S1806-37562017000000423.
15. Ubell ML, Ettema SL, Toohill RJ, Simpson CB, Merati AL. Mitomycin-c application in airway stenosis surgery: Analysis of safety and costs. Otolaryngol Head Neck Surg 2006;134:403-6. doi: 10.1016/j.otohns.2005.10.057.

16. Al-Awady MK, El-Morsy MA, Tawfik MH. Effect of topical application of mitomycin-C as an adjuvant treatment of laryngotracheal stenosis. Sci J Al-Azhar Med Fac Girls 2020;4:262-68.
17. Prince JS, Duhamel DR, Levin DL, Harrell JH, Friedman PJ. Nonneoplastic lesions of the tracheobronchial wall: Radiologic findings with bronchoscopic correlation. Radiographics 2002;22:S215-30. doi: 10.1148/radiographics.22.suppl_1.g02oc02s215.
18. Barnes D, Gutiérrez Chacoff J, Benegas M, Perea RJ, de Caralt TM, Ramirez J, et al. Central airway pathology: Clinic features, CT findings with pathologic and virtual endoscopy correlation. Insights Imaging 2017;8:255-70. doi: 10.1007/s13244-017-0545-6.
19. Allen CT, Lee CJ, Meyer TK, Hillel AD, Merati AL. Risk stratification in endoscopic airway surgery: Is inpatient observation necessary? Am J Otolaryngol 2014;35:747-52. doi: 10.1016/j.amjoto.2014.06.014.
20. Fiz I, Koelmel JC, Piazza C, Fiz F, Di Dio D, Bittar Z, et al. Predictors of recurrence after surgical treatment of idiopathic progressive subglottic stenosis. Acta Otorhinolaryngol Ital 2018;38:417-23. doi: 10.14639/0392-100X-1872.
21. Zias N, Chroneou A, Tabba MK, Gonzalez AV, Gray AW, Lamb CR, et al. Post tracheostomy and post intubation tracheal stenosis: Report of 31 cases and review of the literature. BMC Pulm Med 2008;8:18. doi: 10.1186/1471-2466-8-18.