

## Peer Review File

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### Reviewer A

The authors report a retrospective series of 63 patients with a diagnosis of Tracheal Stenosis, tracheo-esophageal fistula (TEF) and tracheomalacia (TM) between June 2020 until May 36 2021. All patients had prolonged intubation due to COVID-19 infection.

This is an important report since it highlights the late complications that COVID-19 will have on countries. Indeed, ICUs were overwhelmed with critically ill patients that were much above the capacity of the hospitals. Thus, respiratory care in the ICU setting was probably less than acceptable. Furthermore, at the beginning of the pandemic, as stated by the authors, medical societies recommended that tracheostomies should be performed after 21 days of the initial symptoms. This probably contributed to a higher incidence of laryngo-tracheal complications. As a large country in South America, we are too suffering with the same problems. So, I congratulate your results and the team effort to resolve those cases.

Regarding the manuscript, I will describe my thoughts and comments.

### MAJOR STRENGTHS

The manuscript is generally well-written and easy to read

The series(n) is somewhat large, considering that is not such a common disease  
It approaches a topic that is not yet discussed, which is tracheal complications after the covid-19 pandemic.

### MAJOR ISSUES

The paper is very much focused in surgical results. The series has 63 patients, which is not small, nor large. If we analyze just surgical results after tracheal resection, it's not new information

It is quite long and should be shortened

- Comment 1: Abstract

Concise and adequate

- Reply 1: Thank you for your comment, we are taking into account the format established by the journal and the specific number of words.

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 2: Introduction

It describes the problem that was caused by the COVID-19 pandemic and the justifies the manuscript, and it is well-written. Nonetheless, I believe it could be somewhat shortened.

- Reply 2: Thank you for your comment. In the introduction, the problem has been established which is tracheal stenosis (TS) as a complication of prolonged intubation in patients with COVID-19 infection and its impact in our country, justifying the reason for the investigation. We believe that what is written there reflects clearly the information we want to transmit. Nevertheless, We are eliminating the sentence in the section of Introduction line 62 – 63.

- Changes in the text: We are eliminating the sentence in the section of Introduction line 62 - 63.

Material and Methods

Design, population and sample size

- Comment 3: The study is retrospective. Was it approved by the local ethics committee ? This is an important information

- Reply 3: Thanks for your question. The study protocol followed standard norms of the Declaration of Helsinki and was approved by the Guillermo Almenara Irigoyen National Hospital Specialized Surgery Department (NIT 1141-2021-123). The names and addresses of the people included in the study were not used. Because of the retrospective nature of the work, informed consent was not required, and the authors signed a letter of commitment to the confidentiality of the data.

- Changes in the text: The number of the approval document of the Ethics Committee of the Guillermo Almenara Irigoyen National Hospital is being specified in the section of Methodology.

- Comment 4: Patients were seen at an outpatient facility? Is it dedicated to tracheal diseases exclusively?

- Reply 4: Thank you for your question. Most of the patients were referred from other hospitals with less resolution capacity to our hospital. Specifically to the emergency area or outpatient consultation, and then transferred to our Thoracic Surgery Service, within we have an Airway Surgery unit and another of Pulmonary Transplantation, being currently a national reference center for patients with tracheal pathologies (tracheal stenosis, tracheoesophageal fistula, tracheomalacia)

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 5: It is stated that you included patients that were “previously intubated due to COVID-19 infection from June 2020 until May 2021.” Were they in-hospital during this period? When was the 1st patient submitted to tracheal resection?

- Reply 5: Thank you for your question. The interval data was from June 2020 - May

2021, when the tracheal surgeries were performed. It does not refer to the development of covid 19 infection.

The first tracheal surgery was on June 25, 2020. The patients who were included in the study presented an average endotracheal intubation requirement of  $27.8 \pm 15.8$  days and an average ICU stay of  $35.9 \pm 22.3$  days.

- Changes in the text: We are adding this information in the section of Metodology line 95 – 96.

Data collection and study variables

- Comment 6: Were the variables collected through chart reviews? Does the instutution have electronic charts?

- Reply 6: Thank you for your question. For the collection of variables, an electronic database was used where data such as age, sex, weight, BMI, date of surgery, surgery performed, number of resected rings, percentage of stenosis, etc. were recorded. Our hospital has an electronic medical record system from which information was obtained for the study.

- Changes in the text: There is no changes in the manuscript regarding this comment.

Surgical Technique

- Comment 7:

1) I believe a brief description of the surgical procedure should be included. Nevertheless, the procedures are well-known to the surgical Society. So, the text could be very much shortened.

- Reply 7: Thank you for your comment. Concerning the surgical technique that is already standardized, the reduction will be made in the description of it.

- Changes in the text: We will reduce the text in the Surgery Technique section

- Comment 8:

2) What was the criteria for indicating a tracheal resection? I ask this for 2 reasons. First, because it's importante to understand how your group works and thinks.

- Reply 8: The decision to indicate tracheal resection was made considering multiple factors in the preoperative period; However, the final decision was made intraoperatively according to the findings.

The criteria for performing the tracheal resection and tracheoplasty were: the extent of stenosis (less than 50%), location of the tracheal stenosis (not subglottic location), the elasticity of the trachea, general condition of the patient (WHO functional class I-II)

- Changes in the text: We are adding this paragraph in the Methodology section.

- Comment 9:

3) Second, because most of the patients with tracheal stenosis after COVID that we

receive arrive in very bad general status. Many of them are malnourished (lost >20-30Kg), obese and diabetic. At our institution, patients that are obese and are diabetic are not offered tracheal resection. They are treated w/ silicone stents. So I would like to hear that from you. From your data, Obesity occurred in 39.7%, and diabetes mellitus in 14.3%.

- Reply 9: Our criteria for considering tracheal resection are multiple, if the patient is diabetic/obese and his general condition is good according to functional classification and meets the resection criteria already established in our investigation, proceeds with tracheal resection. On the contrary, a tracheostomy is performed, through steps (first tracheostomy and then tracheal resection as soon as the general condition of the patient improves).

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 10:

4) How the timing for operation was decided. Many of the patients we receive still have an important inflammatory process in the airways. Or, as many say, the stenosis is not mature enough. How do you evaluate that.

- Reply 10:

To define the stenosis as mature or immature we are based on the fiberoptic bronchoscopy findings (immature lesion: erythema, granulomas, friability, ulcer, bleeding, and mature mucosa: pale mucosa, established scar).

Between 2010-2015, our airway surgery team as a general rule in patients with immature tracheal stenosis first underwent placement of a tracheostomy tube to ensure airway and wait a prudent time for the attempt to perform tracheal resection in a second time; however, in the last 5 years in the presence of immature stenosis, our behavior has changed. If the patient meets the other criteria for tracheal resection, already mentioned previously, reconstruction surgery is performed in the first instance, in order to avoid an additional procedure prior to the definitive one and increase the chances of primary reconstruction.

- Changes in the text: We added the specification of this question in the Methodology section. Line 103 - 104

- Comment 11:

5) What was the mean period between hospital discharge and tracheal resection? Do you have this information?

- Reply 11: Thank you for your question. The average time from hospital discharge (hospitalization for COVID 19) to surgery for tracheal reconstruction surgery was 3.4 ± 1.7 months

- Changes in the text: We added these changes in Table 1 section

Results

- Comment 12:

1) What do you mean by functional class I and II? I later found the information in the tables, but you should include that is the WHO classification. I thought it was the NYHA.

- Reply 12: To define functional class we have used the WHO scale "Classification of Functional State of the World Health Organization"

TABLE 2 ] Classification Criteria That Impact Management for Benign Airway Strictures

Criteria	Description
Functional class	Modified World Health Organization functional classification
1	Asymptomatic: ordinary physical activity does not cause symptoms
2	Symptomatic on exertion: there is no discomfort at rest, but normal physical activity causes increased symptoms
3	Symptomatic with daily activity: there is no discomfort at rest, but less than ordinary activity causes increased symptoms
4	Symptomatic at rest: symptoms may be present at rest and are increased by almost any physical activity
Extent	Location and distribution of the stenotic airway segment
Vertical length	(< 1 cm, 1-4 cm, > 4 cm)

- Changes in the text: We added the specification of this question in the Methodology section. Line 107 - 111

- Comment 13:

2) You describe 5 surgical procedures (Primary surgery, Ring resection + T tube , Ring resection + TQT, T tube insertion, TQT canula insertion ) Nevertheless, the decision process for each procedure is not described. I would like to see such description in the methods section. This way we could figure out why each procedure was selected.

- Reply 13: In patients with poor general condition (WHO III-IV), we decided to ensure airway with tracheostomy (as the first step to later perform tracheal resection surgery)

In patients with very extensive and subglottic tracheal stenosis, we decided to place a T-tube.

In patients with fistula tracheoesophageal and tracheal stenosis in poor general condition, the fistula was closed, tracheal rings were removed and tracheostomy cannula was placed.

Tracheal rings were resected, and a T-tube was placed in patients with risk anastomosis, in order to increase the probability of successful T-tube decannulation later.

- Changes in the text: We added the specification of this question in the Methodology section. Line 138 - 144

- Comment 14:

3) Do you perform tracheal resection and insert the T-Tube at the same surgical procedure? In what situations do you do that? And why?

We sometimes judge that there is too Much tension in the anastomosis, and leave a tracheostomy below the suture line. If there is any problem afterwards, we put a T-Tube. But we prefer to do this a couple of weeks after the initial operation.

- Reply 14: The tracheal injuries we observed in post-covid 19 patients were extensive, severe, and associated in many cases with tracheoesophageal fistula, tracheomalacia.

If the patient is not able to perform tracheal resection surgery, the option is to place a T-tube. However, the Montgomery T-tube is not free of complications (obstruction, formation of proximal and distal granulomas, cough, bacterial colonization, etc.)

There is a probability that the patient will keep the T-tube permanently, and the subsequent decannulation will not be possible.

Considering that a factor of failure to remove the T-tube is the extension of the lesion, to increase the chances of decannulation in patients with long and complex stenoses, we resect the maximum number of injured tracheal rings, perform the anastomosis and leave a shorter T-tube for a lower complication rate.

**Montgomery T-tube placement in the treatment of benign tracheal lesions.**

Angelo Carretta, et al. *European Journal of Cardio-Thoracic Surgery*, Volume 36, Issue 2, August 2009, Pages 352–356, <https://doi.org/10.1016/j.ejcts.2009.02.049>.

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 15:

4) What was the proposed treatment for patients with vocal cords paralysis?

- Reply 15: Thank you for the question. In the case of bilateral vocal cord paralysis, it was decided that the treatment would be the placement of a tracheostomy cannula and evaluation by an otorhinolaryngologist.

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 16:

5) How were the complications dealt with? I believe a table w/ the complications would be adequate. And you could discuss them specifically in the text. Example: patients with dehiscence required tracheostomy or just observation? How many patients with infection were treated with antibiotics? Did them require surgical debridement of the wound?

ps: I found out that there is a table of complications, but not refered in the text. Thus,

you are repeating information in the text and in the table. Refer the table in the text and discuss your major complications in the text.

- Reply 16: We had 2 patients with non-severe anterior wall level tracheal anastomosis dehiscence who were managed conservatively with observation and antibiotic therapy, and spontaneous closure was achieved.

Besides, There was two tracheoesophageal fistula closure dehiscence; one was mild that was managed with observation, NPO, antibiotic therapy, and enteral nutrition and spontaneous seal; and the second presented significant fistula dehiscence, a tracheostomy tube was placed and currently is awaiting corrective surgery.

- Changes in the text: We added the specification of this question in the Results section. Line 217 – 223

- Comment 17:

6) One patient died. What was the cause of death? You should describe this case in details.

- Reply 17: The deceased patient was a 61-year-old male, overweight, who had severe COVID-19 infection in March 2020, a patient referred from a less capacity hospital with diagnoses of tracheal stenosis and tracheoesophageal fistula.

He came emergency with stridor and in poor general condition and underwent emergency surgery resection of tracheal rings + closure of tracheoesophageal fistula and tracheostomy, awaiting definitive corrective surgery, after improving his clinical condition, he died of an acute myocardial infarction two months after.

- Changes in the text: We added the specification of this question in the Results section. Line 226 – 233

- Comment 18:

7) How long were patients followed after surgery?

- Reply 18: Thank you for your question. Postoperative follow-up of the patients was performed for a period of 4 to 6 months by outpatient consultation in the cases of patients who underwent tracheal resection. In the case of patients using the Montgomery T-tube, a follow-up is performed every 3 months, where the condition of the T-tube and the possibility of removal or replacement are evaluated.

- Changes in the text: There is no change in the manuscript regarding this comment.

## Discussion

- Comment 19:

Your discussion is quite long, and in my opinion, is lacking a clear focus. The first paragraph should be a summary of your results. The second, a comparison with other publications. And then you should discuss the topic (and your results) in other 3-4 paragraphs. I think it would be important to discuss the difference between patients with TS with and without Covid, and what were your difficulties during the whole

pandemic process. This would be a more interesting discussion in my point of view.

- Reply 19: Thank you for your comment. The discussion will be expanded with the articles mentioned:

**Long-term results of laryngotracheal resection for benign stenosis** [Antonio D'Andrilli](#), et al. *European Journal of Cardio-Thoracic Surgery*, Volume 33, Issue 3, March 2008, Pages 440–443, <https://doi.org/10.1016/j.ejcts.2007.12.014>

HNO. 2007 Jan;55(1):21-8.[**Segmental tracheal resection for the treatment of tracheal stenoses**][Article in German][M Weidenbecher Jr](#)<sup>1</sup>, [M Weidenbecher](#), [H Iro](#). DOI: [10.1007/s00106-006-1392-9](https://doi.org/10.1007/s00106-006-1392-9)

[Tex Heart Inst J](#). 2005; 32(2): 154–158. PMID: PMC1163461

**Tracheal Stenosis after Tracheostomy or Intubation** Review with Special Regard to Cause and Management [Alpay Sarper](#), MD, [Arife Ayten](#), MD, [Irfan Eser](#), MD, [Omer Ozbudak](#), MD, and [Abid Demircan](#), MD

*Eur J Cardiothorac Surg*. 1990;4(5):265-8; discussion 268-9. **Management of non-tumoral tracheal stenosis in 112 patients** [F París](#)<sup>1</sup>, [J M Borro](#), [V Tarrazona](#), [M Casillas](#), [G Galan](#), [J M Caffarena Jr](#), [J Segui](#) DOI: [10.1016/1010-7940\(90\)90250-4](https://doi.org/10.1016/1010-7940(90)90250-4)

*Eur J Cardiothorac Surg*. 2002 Sep;22(3):352-6.**Benign tracheal and laryngotracheal stenosis: surgical treatment and results** [Federico Rea](#)<sup>1</sup>, [Donatella Callegaro](#), [Monica Loy](#), [Andrea Zuin](#), [Surendra Narne](#), [Tobia Gobbi](#), [Melania](#)

Author*	París et al.	Rea et al.	Sarper et al.	Weidenbecher et al.	Andrilli et al.	Palacios et al. (Our study)
<b>Research</b>	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort
<b>Year of Publication</b>	1990	2002	2005	2007	2008	2022
<b>Range of Years</b>	1973 - 1989	1991 – 2001	1985 – 2004	1985 – 2002	1991 – 2006	2020 – 2021
<b>Number of Years</b>	16 years	10 years	19 years	17 years	15 years	1 year
<b>Number of Patients</b>	112	65	45	101	35	63
<b>Male</b>	68	26	34	55	19	47
<b>Female</b>	44	33	11	46	16	16
<b>Ratio M/F</b>	1.50/1	0.78	3.1/1	1.2/1	1.2/1	2.93/1
<b>Age Mean</b>	41	33	38	NR	43	49
<b>Age Range</b>	9 – 81 years	14 – 74 years	2 – 72 years	7 – 77 years	14 – 71 years	30 – 77 years
<b>VMI (Days)</b>	NR	NR	8 – 11 days	NR	NR	25
<b>Tracheal Lesions Associated</b>						
<b>Tracheomalacia</b>	7 (6.3%)	NR	NR	NR	NR	6 (9.5%)
<b>TEF</b>	3 (2.7%)	NR	NR	NR	NR	20 (31.7%)
<b>Vocal Cord Paralysis</b>	NR	NR	NR	12 (11.8%)	NR	7 (11.1%)
<b>Surgery Technique</b>						
<b>Resected Tracheal Length (cm)</b>	2.7 (1.5 – 7)	2.5 (1.5 – 4)	1.5 – 4	2 – 6	1.5 – 6	3.5 (2 – 5)
<b>Previous Treatment</b>						
<b>Tracheal Dilatation</b>	NR	NR	NR	NR	NR	1 (1.6%)
<b>Tracheostomy</b>	28 (25%)	38 (38.5%)	NR	NR	13 (37%)	21 (33.3%)
<b>Tracheal Complications</b>						
<b>Infection</b>	NR	5 (8%)	2 (6%)	NR	NR	3 (8.4%)
<b>Dehiscence</b>	NR	4 (6%)	NR	NR	NR	NR
<b>Granuloma</b>	NR	2 (3%)	3 (9%)	NR	NR	NR
<b>Death</b>	NR	1 (1.5%)	1 (3%)	NR	NR	1 (1.6%)



- Changes in the text: We will add this text in the Discussion section.

Figures

- Comment 20:

1 and 2 are very good and w/ high definition

Figure 5 adds little to the manuscript

- Reply 20: Thank you for your comment. We hope the graphics help a better understanding of what is described in the manuscript.

- Changes in the text: Since we will add a summary table of retrospective studies previously performed in patients with TS, Figure 5 will be removed from the manuscript.

Final comments to the authors

I enjoyed reading this manuscript, and as I said, our home institution is also facing the same issues. We too are a referral center for tracheal diseases.

I believe your manuscript has very important information, but the focus is not the best. The main focus of your manuscript is surgical results. From a literature stand of view, 63 patients with tracheal resection would not add much, and I probably not recommend publication.

Nonetheless, we will face many patients with tracheal stenosis after covid-19, and your publication could help to bring this to light.

But in my point of view, your manuscript should highlight tracheal stenosis AND COVID. What were the challenges, how you managed the patients, how was the decision process, and the differences between covid stenosis and non-covid. For me, it would be a much more interesting read.

Keep up the good work.

### **Reviewer B**

Dear authors,

thank you for the opportunity to review the manuscript "Tracheal stenosis as a complication of prolonged intubation in COVID-19 patients. A peruvian cohort." for Journal of Thoracic Disease.

You spend a lot of effort in preparation of this manuscript and are according to the STROBE Checklist.

Your experiences are very interesting and the presentation is clear. Grammar and syntax are fine and the manuscript is easily readable.

I got few annotations:

- Comment 1: page 3, line 73 “MIV can go” might be replaced by “last up to”
- Reply 1: Thank you for your comment. The correction has already been made in the manuscript.
- Changes in the text: The specification of this suggestion was added to the manuscript
  
- Comment 2: page 5, line 135 “and” instead of “y”?
- Reply 2: Thank you for your comment. The correction has already been made in the manuscript.
- Changes in the text: The specification of this suggestion was added to the manuscript
  
- Comment 3: page 6, line 168f “n=x” for “TS, TS + TEF...” is more informative than the percentage.
- Reply 3: Thank you for your comment. The correction has already been made in the manuscript.
- Changes in the text: Numerical data was added in the variables TS, TS + TEF instead of the percentage data
  
- Comment 4: You present differences between your cohort and several case reports concerning Cotton-Myer classification. First, descriptive comparison of 63 patients with one or two is ineffectual. Second and more important, you describe the differences in the classification, but you do not show up any conclusion. There is no discussion of these findings at al.
- Reply 4: Thanks for your observation. Regarding the comment, the comparison of our results with the case reports was placed in the comparison since in both cases the etiology of ET was associated with COVID-19 infection, however, it is right since it is ineffective to compare 1 - 2 patients out of 63. Also, ET investigations in COVID-19 patients with a number large enough to allow comparison and analysis have not yet been conducted. We will perform the comparison with cohorts of patients with TS post-intubation before the COVID-19 pandemic.

**Long-term results of laryngotracheal resection for benign stenosis** [Antonio D'Andrilli](#), et al. *European Journal of Cardio-Thoracic Surgery*, Volume 33, Issue 3, March 2008, Pages 440–443, <https://doi.org/10.1016/j.ejcts.2007.12.014>

HNO. 2007 Jan;55(1):21-8.[Segmental tracheal resection for the treatment of

tracheal stenoses][Article in German][M Weidenbecher Jr](#)<sup>1</sup>, [M Weidenbecher](#), [H Iro](#).  
DOI: [10.1007/s00106-006-1392-9](https://doi.org/10.1007/s00106-006-1392-9)

[Tex Heart Inst J](#). 2005; 32(2): 154–158. PMID: PMC1163461

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*Eur J Cardiothorac Surg*. 1990;4(5):265-8; discussion 268-9. **Management of non-tumoral tracheal stenosis in 112 patients** [F Paris](#)<sup>1</sup>, [J M Borro](#), [V Tarrazona](#), [M Casillas](#), [G Galan](#), [J M Caffarena Jr](#), [J Segui](#) DOI: [10.1016/1010-7940\(90\)90250-4](https://doi.org/10.1016/1010-7940(90)90250-4)

*Eur J Cardiothorac Surg*. 2002 Sep;22(3):352-6. **Benign tracheal and laryngotracheal stenosis: surgical treatment and results** [Federico Rea](#)<sup>1</sup>, [Donatella Callegaro](#), [Monica Loy](#), [Andrea Zuin](#), [Surendra Narne](#), [Tobia Gobbi](#), [Melania Grapeggia](#), [Francesco Sartori](#) DOI: [10.1016/s1010-7940\(02\)00342-1](https://doi.org/10.1016/s1010-7940(02)00342-1)

- Changes in the text: We will add the comparison of our work with other series of ET cases prior to the COVID-19 pandemic to the discussion.

- Comment 5: Same in the comparison with the study of Zias et al. You show up differences in the management of patients with and without COVID-19 infection, but you just illustrate the facts.

- Reply 5: Thanks for your question.

We reevaluated research by Zias et al. where only a small percentage of his work underwent surgical management so it would not help us for our analysis and discussion. The comparison of our work with other series of ET cases prior to the COVID-19 pandemic is being added to the discussion.

- Changes in the text: It was decided to withdraw this bibliography of the manuscript

- Comment 6: In the comparison of the cohort with the survey of Macchiarini et al. the link to the reference is missing. The “discussion” of the differences is again just a description. You should look for explanations for the differences in the cohorts. Additionally, any references of Macchiarini should be treated with caution.

- Reply 6: Thank you for your comment. In consensus with the research group, the research team decided to withdraw the discussion paragraph that refers to the work of Macchiarini et al.

- Changes in the text: We reduced discussion paragraph that refers to the work of Macchiarini et al. in the Discussion section

- Comment 7: The figures are very well and give a good illustration of surgical management.

- Reply 7: Thank you for your comment. We hope the graphics help a better understanding of what is described in the manuscript.

- Changes in the text: There is no changes in the manuscript regarding this comment.

### Reviewer C

Thank you for the opportunity to review this important manuscript reviewing laryngotracheal complications in COVID-19 patients. I have observed that patients suffer greatly from the laryngeal and tracheal injuries described in this study, and I commend the authors for their efforts to improve the lives of affected individuals and sharing this experience. Perhaps no country has been hit harder per capita than Peru during this Pandemic and too little of this global experience is reflected in the current literature. The article is large series that adds significant new information to the existing literature on this subject.

I have several recommendations to strengthen the article before it is suitable for acceptance.

1. Although the article is well-referenced in terms of corrective techniques for laryngotracheal injuries, it needs better framing of the considerations around care of critically ill patients with Severe COVID-19. I have provided comments and some suggested references to strengthen this aspect of the paper.

- Comment 1: • First, the article should note that the topic of timing to tracheostomy affects duration of trans-laryngeal intubation and has been extensively discussed in the literature on COVID-19. Although early in the pandemic, approximately 90% of protocols recommended >2 weeks of intubation ( <https://pubmed.ncbi.nlm.nih.gov/33138722/> PMID: 33138722 DOI: 10.1177/0194599820961985 ), it later became clear that earlier tracheostomy was appropriate and could be beneficial to patients. A subsequent guidance document moved the standard to assessment at 10 days: (Mcgrath et al <https://pubmed.ncbi.nlm.nih.gov/32422180/> PMID: 32422180 PMCID: PMC7228735 DOI: 10.1016/S2213-2600(20)30230-7 )

- Reply 1: Thanks for your question. As you said, in 2020 Bier-Laning et al. conducted a comparative study of protocols and clinical practice guidelines in 26 countries, including Peru, where recommendations were made regarding the time to perform a tracheostomy in patients with COVID19 infection. Many sources lacked a clear recommendation regarding the interval time.

Some authors recommended never performing a tracheostomy if it could be avoided, while other sources treated mechanical ventilator (MV); dependent patients, similarly to all other critically ill MV patients. When the time for tracheostomy was

established, it ranged from 3-4 days to 21-28 days. Most protocols recommended a minimum of 14 days of MV for consideration of performing a tracheostomy. Likewise, they considered some contraindications to performing a tracheostomy such as cardiac instability or respiratory instability, positive COVID19 test, poor prognosis, absence of clinical improvement.

Subsequently, McGrath et al. conducted a multidisciplinary guideline where they say the tracheostomy could be delayed up to the 10th day of MV and considered only when patients show signs of clinical improvement, also a conservative approach was proposed for extubation attempts where it is limited only to patients who have a high probability of success.

- Changes in the text: The text described above is added to the Discussion section

- Comment 2: • In this series, the patients were referred for TS, TM, or TEF and were intubated for an average of over 25 days. Suggested references supporting evolution toward earlier timing are :

(a) Schultze et al in JAMA <https://pubmed.ncbi.nlm.nih.gov/32880624/> PMID: 32880624 DOI: 10.1001/jamaoto.2020.2630

(b) Mahmood et al <https://pubmed.ncbi.nlm.nih.gov/34029231/> PMID: 34029231 PMCID: PMC8265239 DOI: 10.1097/SLA.0000000000004955

(c) Rosano et al <https://pubmed.ncbi.nlm.nih.gov/33201005/> PMID: 33201005 DOI: 10.1097/CCM.0000000000004752

- Reply 2: In our population, the majority of patients were referred from centers with lower resolution, saturated by the number of patients with COVID-19, with a lack of personnel and equipment, reasons that could explain the prolonged time of endotracheal intubation.

- Changes in the text: We written this paragraph previously described in the Introduction section

- Comment 3: • Some may regard the injuries reported here as inevitable, but there is evidence to the contrary and guidance from the pandemic. Below are articles that have discussed regarding safe practices for managing aerosol generating procedures in the ICU setting from the standpoint of multidisciplinary teams in the nursing, speech language pathology, and intensive care literature. These emphasize how team-based approaches can be used to optimize safety / team-based care and reduce untoward events for patients : Meister et al <https://pubmed.ncbi.nlm.nih.gov/32960148/> PMID: 32960148 PMCID: PMC8198753 DOI: 10.1177/0194599820961990

Pandian et al <https://pubmed.ncbi.nlm.nih.gov/32929453/> ; PMID: 32929453 DOI: 10.4037/ajcc2020561

- Reply 3: Thank you for your comment. We agree multidisciplinary management of an intubated patient in an intensive care unit reduces the probability of airway injuries.

However, our country has one of the lowest rates in Latin America of intensive care physicians and nurses per million inhabitants as well as poor equipment, which we consider to be important factors in the increased incidence of tracheal injuries in patients intubated by COVID -19.

- MONITOREO DE LA RESPUESTA DE PAÍSES SUDAMERICANOS FRENTE A LA PANDEMIA DE COVID 19. Organización Panamericana de la Salud. Programa Subregional para América del Sur OPS/OMS. 2020

- Changes in the text: The above is specified in the Introduction section.

- Comment 4: • There is a nice article on tracheoesophageal fistula and transmural injuries that I do not think was cited: <https://pubmed.ncbi.nlm.nih.gov/33211087/> PMID: 33211087 PMCID: PMC7677875 DOI: 10.1001/jamaoto.2020.4148

- Reply 4: Thanks for the article. We found it very interesting, it is a retrospective study that explains the incidence of TEF in patients with prolonged endotracheal intubation in COVID-19 patients, as well as the possible mechanisms of injury that would explain the large percentage of TEF associated with ET (31.7%) in the cohort. : high dose of systemic corticosteroids, the prothrombotic and antifibrinolytic state, high viral replication that weakens the tracheal mucosa, among others.

- Changes in the text: We will cite this article in the Discussion section

Below are several specific edits to improve English language usage and clarity with corresponding line numbers:

- Comment 5: 1. Please specify that TM stands for tracheomalacia, if not stated elsewhere

94 all the patients referred to our center with a diagnosis of TS, TEF, and  
95 TM who were previously intubated due to COVID-19 infection from June 2020  
until May  
96 2021.

- Reply 5: Thank you for your comment. In the abstract section line 35, the term tracheomalacia is described for the first time and it is specified with the initials TM

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 6: 2. Please change “reference” to referral in the lines below:

92 The Service of Thoracic Surgery of Hospital Nacional Guillermo Almenara Irigoyen is a

93 national reference [referral]

- Reply 6: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

- Comment 7: 3. Please change “ubication” to “location”

102 ubication [location] although technically correct, would best be changed to .

- Reply 7: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

- Comment 8: 4. Please change “ fiber bronchoscopy” to “fiberoptic bronchoscopy”

107 fiber bronchoscopy à fiberoptic bronchoscopy

- Reply 8: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

- Comment 9: 5. Please change Tracheal light to tracheal lumen

111 Tracheal light

- Reply 9: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

- Comment 10: 6. Please change 124 midde line to midline

124 midde line à midline

- Reply 10: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

Several other edits are listed below by line

- Comment 11: 127 Mobilization of the trachea from the anterior tissular part was made with blunt dissection [please remove “tissular...” and change to “from anterior tissues with blunt dissection”

- Reply 11: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript
  
- Comment 12: 135 Damaged tracheal rings are removed y stitches (please change “y” to “and”)
- Reply 12: Thank you for your comment. The correction has already been made in the manuscript
- Changes in the text: The specification of this suggestion was added in the manuscript
  
- Comment 13: 137 3/0 polyglycolic acid that (please change to “3/0 polyglycolic acid suture that”)
- Reply 13: Thank you for your comment. The correction has already been made in the manuscript
- Changes in the text: The specification of this suggestion was added in the manuscript
  
- Comment 14: 140 A nasogastric tube was introduced through the proximal trachea and [we] asked the anesthesiologist (please add the word “we”)
- Reply 14: Thank you for your comment. The correction has already been made in the manuscript
- Changes in the text: The specification of this suggestion was added in the manuscript
  
- Comment 15: 186 the most frequently used. Additionally, plasty of tracheomalacia was made in 3 patients. (please use the word “repair” in place of “plasty”)
- Reply 15: Thank you for your comment. The correction has already been made in the manuscript
- Changes in the text: The specification of this suggestion was added in the manuscript
  
- Comment 16: 197 than 30 mmHg determines a decrease in capillary perfusion on the tracheal mucosa, (please change “determines” to “results in”)
- Reply 16: Thank you for your comment. The correction has already been made in the manuscript
- Changes in the text: The specification of this suggestion was added in the manuscript
  
- Comment 17: 297 For primary repair of the trachea, good prognosis factors are age, sex, size (Please change “good prognosis” to “favorable prognostic “



- Reply 17: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

- Comment 18: 220 age of 49 years old, being more frequently diagnosed in males (74.6%).

- Reply 18: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

If possible, I would encourage review of this work by a native English speaker to ensure the author's intended meaning is faithfully conveyed throughout the manuscript.

Additional minor edits:

- Comment 19: For Figure 1 caption, please indicate that there is both subglottic and tracheal stenosis (not just tracheal stenosis). The narrowing and webbing is clearly in continuity with the larynx and not limited to an isolated tracheal segment.

- Reply 19: Thank you for your comment. The correction has already been made in the manuscript

- Changes in the text: The specification of this suggestion was added in the manuscript

#### **Reviewer D**

I have read the manuscript with pleasure and find it clinically relevant, however there are some points which should be addressed before manuscript publication.

- Comment 1: Introduction: I would suggest to cite studies in which intubation and/or ICU admission rate is lower. Indicated herein numbers suggest falsely that most of hospitalized patients are intubated.

- Reply 1: Thank you for your comment. The data we put in the manuscript are those we found in the study by Wunsch et al. where he describes various studies, and it is stated that the percentage of endotracheal intubation in patients admitted to the ICU ranges between 29.1 - 89.9%, while the endotracheal intubation percentage in patients who are hospitalized, ranges between 2.3 - 33.1%

**Table 1.** Comparison of Rates of Invasive Mechanical Ventilation in a Sample of Epidemiology Studies of Patients with COVID-19

Study	Location	Hospitalized (n)	ICU Admission (n)	n	Invasive Mechanical Ventilation	
					Percent of ICU Patients	Percent of Hospitalized Patients
Richardson (4)	New York City	5,700	1,281	1,151	89.9	20.2
Petrilli (17)	New York City	1,999	534*	445	83.3	22.3
Goyal (13)	New York City	393	NA	130	NA	33.1
ICNARC (14)	UK	NA	3,883	2,291 <sup>†</sup>	59.0	NA
Grasselli (15)	Lombardy, Italy	NA	1,300 <sup>‡</sup>	1,150	88.5	NA
Zhou (18)	Wuhan, China	191	50	32	64.0	16.8
Wang (3)	Wuhan, China	NA	344	100	29.1	NA
Guan (19)	China	1,099	55	25	45.5	2.3

Definition of abbreviations: COVID-19 = coronavirus disease; ICNARC = Intensive Care National Audit & Research Centre; NA = not available.

\*Excludes 116 patients deemed critically ill who were discharged to hospice or died without either intensive care or mechanical ventilation.

<sup>†</sup>Within first 24 hours.

<sup>‡</sup>1,591 admitted to ICU but only 1,300 with respiratory support information.

Wunsch, H. (2020). Mechanical Ventilation in COVID-19: Interpreting the Current Epidemiology. American Journal of Respiratory and Critical Care Medicine. doi:10.1164/rccm.202004-1385ed

- Changes in the text: We cut some sentences from the manuscript regarding this comment in the Introduction section. Line 62 – 63

- Comment 2: Tracheostomy is generalized whereas there are two major approaches: surgical tracheostomy and transcutaneous tracheostomy both approaches with different types and likelihood of complications – this should be indicated in the text.

- Reply 2: Thank you for your comment. In our work, we considered surgical tracheostomy as an option for airway salvage treatment in patients with severe TS. The specific criteria for each type of surgical technique were the following: Tracheostomy: patients admitted in poor general condition or functional class III - IV according to WHO scale con estridor severo

- Changes in the text: We added the comment you suggested to us in the Methodology section.

- Comment 3: Peru is one of the most affected countries due to COVID-19 in all Latin America, with an incidence of 23.57 newly diagnosed cases per 1000 population- this should be cited with time period or date such as up till xxxx date...

- Reply 3: Thank you for your question. The incidence data was during the month of September 2021.

- Changes in the text: We added the data suggested in your comment in the manuscript.

- Comment 4: Study variables: why Asthma was selected whereas COPD omitted. Looking at the patients age, average smoking habits COPD seems to be likely as well. Please indicate the criterion of asthma

- Reply 4: Thank you for your question. We decided to evaluate the percentage of patients with TS after COVID-19 who had a history of asthma because it is a

pathology more prevalent in our population as opposed to COPD.

- Changes in the text: There is no changes in the manuscript regarding this comment.

- Comment 5: The authors state that the observation was retrospective however later on authors state that: “In those patients where after tracheal ring resection, it was noticed inflammatory immature 147 tissue, extensive damage, disease at the level of cricoid or subglottic, extensive damage of more 148 than 50% of the trachea, we opted for the placement of a Montgomery T tube, verifying proper 149 positioning in its proximal end and distal one, with intraoperative flexible fiber bronchoscopy.” Which seems more likely like prospective approach.

- Reply 5: Thanks for your question. As you mention, our study is retrospective because it analyzes patients in whom treatment and evaluation have already been carried out. The text you mention refers to the same operative act where the resection of stenotic tracheal rings is performed in the operative field and immediately afterward, depending on the maturity of the tissue, subglottic involvement, damage to the cricoid cartilage, the placement of a T-tube is considered. However, we will specify that the decision is immediately after, during the same surgical act.

- Changes in the text: The changes will be placed in the Metodology section.

- Comment 6: If the results the authors state that: Six patients (9.5%) had re-stenosis; 7 patients (11.1%) had T 191 tube obstruction.- this should be explain in more detail including the time from surgery after which this complication has occurred. Moreover the complications should be matched with the type of treatment.

- Reply 6: Thank you for your comment. We had six patients who presented restenosis, 2 underwent grade I Cotton-Myer restenosis in whom the management was conservative, 3 patients underwent grade II Cotton-Myer restenosis in which a T-tube was changed in 1 patient and a T-tube was placed in the other 2, 1 patient presented grade III Cotton-Myer restenosis in whom a T-tube was placed.

Of the 7 patients in whom T-tube obstruction was presented, fiberoptic bronchoscopy was performed in 5 patients, T-tube replacement in 1 patient, and placement of a tracheostomy cannula in 1 patient.

- Changes in the text: The changes will be placed in the Results section.

- Comment 7: In result section the authors state that “ The average amount of tracheal rings 184 removed was  $6.9 \pm 1.6$ ” this indicates a large tracheal injury, therefore the type of tracheostomy technique made in observed population should be described in the population description part.

- Reply 7: Thank you for your question. After pre-surgical evaluation, surgical options were tracheoplasty, Montgomery T tube placement (with or without tracheal resection), tracheostomy cannula placement (with or without tracheal resection) and TEF closure

The choice was made considering the extent of injury (number of damaged rings),

involvement of the subglottic region, the elasticity of the trachea, presence of associated lesions (TEF or TM), previous procedures in stenotic areas (dilatation, tracheostomy, laser) and the overall status of the patient.

The criteria for tracheal resection were extension of the stenosis <50% of the tracheal length, that the location of the stenosis does not cover the subglottic region, the elasticity of the trachea and functional class of the patient I - II according to WHO scale, however, the final decision was made intraoperatively.

The specific criteria for each type of surgical technique were the following: Tracheostomy: patients admitted in poor general condition or functional class III - IV according to WHO scale.

- Changes in the text: We will add what is described above in the Methodology section

- Comment 8: Discussion the author cite findings reported by other groups, however the discussion should be more narrative comparing or contrasting other reports with their findings and looking for reasons for this discrepancies.

- Reply 8: Thank you for your comment. We will expand the discussion with the articles mentioned.

**Long-term results of laryngotracheal resection for benign stenosis** [Antonio D'Andrilli](#), et al. *European Journal of Cardio-Thoracic Surgery*, Volume 33, Issue 3, March 2008, Pages 440–443, <https://doi.org/10.1016/j.ejcts.2007.12.014>

HNO. 2007 Jan;55(1):21-8.[**Segmental tracheal resection for the treatment of tracheal stenoses**][Article in German][M Weidenbecher Jr](#)<sup>1</sup>, [M Weidenbecher](#), [H Iro](#). DOI: [10.1007/s00106-006-1392-9](https://doi.org/10.1007/s00106-006-1392-9)

[Tex Heart Inst J](#). 2005; 32(2): 154–158. PMID: PMC1163461

**Tracheal Stenosis after Tracheostomy or Intubation** Review with Special Regard to Cause and Management [Alpay Sarper](#), MD, [Arife Ayten](#), MD, [Irfan Eser](#), MD, [Omer Ozbudak](#), MD, and [Abid Demircan](#), MD

*Eur J Cardiothorac Surg*. 1990;4(5):265-8; discussion 268-9. **Management of non-tumoral tracheal stenosis in 112 patients** [F Paris](#)<sup>1</sup>, [J M Borro](#), [V Tarrazona](#), [M Casillas](#), [G Galan](#), [J M Caffarena Jr](#), [J Segui](#) DOI: [10.1016/1010-7940\(90\)90250-4](https://doi.org/10.1016/1010-7940(90)90250-4)

*Eur J Cardiothorac Surg*. 2002 Sep;22(3):352-6.**Benign tracheal and laryngotracheal stenosis: surgical treatment and results** [Federico Rea](#)<sup>1</sup>, [Donatella Callegaro](#), [Monica Loy](#), [Andrea Zuin](#), [Surendra Narne](#), [Tobia Gobbi](#), [Melania Grapeggia](#), [Francesco Sartori](#) DOI: [10.1016/s1010-7940\(02\)00342-1](https://doi.org/10.1016/s1010-7940(02)00342-1)

- Changes in the text: We will add these comments in the Discussion section.

- Comment 9: The discussion should include “study limitation section”, whereas the

conclusions should be shortened significantly.

- Reply 9: Thank you for your question. Initially, a cohort was proposed where two groups are covered, one with a history of severe COVID-19 infection with endotracheal intubation criteria and the control group where endotracheal intubation is not associated with COVID-19 infection. However, a similar number of 63 patients was not found, so a retrospective descriptive study was carried out. We will place this in the limitations section. However, it is proposed to carry out further studies where a cohort can be achieved by comparing both groups.

- Changes in the text: Se esta agregando la seccion limitaciones del estudio al manuscrito.

- Comment 10: Table 1: Functional class – WHO- at the time of admission, or after treatment ? Smoking satus including pack-years should be reported as well.

- Reply 10: Thanks for your question. The functional class was evaluated during the admission due to the symptoms of ET, FTE, or TM. Unfortunately, we do not have specific data on the number of packs per year for all 63 patients in the study.

- Changes in the text: There is no changes in the manuscript regarding this comment

- Comment 11: In whole manuscript the text should be English edited to avoid grammar and style mistakes.

- Reply 11: Thank you for your comment. We have re-checked the English language of the manuscript to avoid all possible grammatical errors.

- Changes in the text: The corrections suggested by the reviewers were made.

### **Reviewer E**

Comment 1:

This paper has significant useful information including a large number of patients with tracheal complications after covid intubation. I think it would be greatly strengthened if the focus was not on how these patients were treated but on how they compare to a similar cohort pre covid and on which factors within this group separated them similar covid patients who did not have complications. If we could learn that this group of patients had a higher incidence of specific complications compared to a pre covid cohort, and that these patients had a higher rate of complications compared to other covid patients when stratified by factors (length of intubation, ET tube size, open vs perc trach etc) it would be much more impactful.

- Reply 1: Thank you for your comment. The discussion will be expanded with the articles mentioned:

**Long-term results of laryngotracheal resection for benign stenosis** [Antonio D'Andrilli](#), et al. *European Journal of Cardio-Thoracic Surgery*, Volume 33, Issue 3, March 2008, Pages 440–443, <https://doi.org/10.1016/j.ejcts.2007.12.014>

HNO. 2007 Jan;55(1):21-8.[Segmental tracheal resection for the treatment of

tracheal stenoses][Article in German][M Weidenbecher Jr](#)<sup>1</sup>, [M Weidenbecher](#), [H Iro](#).  
DOI: [10.1007/s00106-006-1392-9](https://doi.org/10.1007/s00106-006-1392-9)

[Tex Heart Inst J](#). 2005; 32(2): 154–158. PMID: PMC1163461

**Tracheal Stenosis after Tracheostomy or Intubation** Review with Special Regard to Cause and Management [Alpay Sarper](#), MD, [Arife Ayten](#), MD, [Irfan Eser](#), MD, [Omer Ozbudak](#), MD, and [Abid Demircan](#), MD

*Eur J Cardiothorac Surg*. 1990;4(5):265-8; discussion 268-9. **Management of non-tumoral tracheal stenosis in 112 patients** [F Paris](#)<sup>1</sup>, [J M Borro](#), [V Tarrazona](#), [M Casillas](#), [G Galan](#), [J M Caffarena Jr](#), [J Segui](#) DOI: [10.1016/1010-7940\(90\)90250-4](https://doi.org/10.1016/1010-7940(90)90250-4)

*Eur J Cardiothorac Surg*. 2002 Sep;22(3):352-6. **Benign tracheal and laryngotracheal stenosis: surgical treatment and results** [Federico Rea](#)<sup>1</sup>, [Donatella Callegaro](#), [Monica Loy](#), [Andrea Zuin](#), [Surendra Narne](#), [Tobia Gobbi](#), [Melania Grapeggia](#), [Francesco Sartori](#) DOI: [10.1016/s1010-7940\(02\)00342-1](https://doi.org/10.1016/s1010-7940(02)00342-1)

- Changes in the text: We will add this text in the Discussion section.

Editing for wording and grammar would also be helpful