This submission includes:

1. Original protocol

Estimation of the Non-Inferiority of the Laringocel® Videolaryngoscope Compared With the C-MAC D-BLADE (Karl Storz®) for First-Attempt Intubation in Adult Patients Undergoing Elective Surgery at *Hospital Alma Máter de Antioquia* (2025–2026). Randomized Non-Inferiority Clinical Trial Protocol. LARINGOCOL

Gabriel Ricardo Muñoz Miranda

Thesis protocol submitted in partial fulfillment of the requirements for the degree of Master in Clinical Epidemiology

Advisor

Mario Andrés Zamudio Burbano: Physician and Surgeon, Specialist in Anesthesiology and Resuscitation, and Master in Clinical Epidemiology.

Universidad de Antioquia
Faculty of Medicine

Master in clinical Epidemiology

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2025

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I. Administrative Information

1. Title and Structured Summary

a. Title: Estimation of the Non-Inferiority of the Laringocel® Videolaryngoscope Compared to the C-MAC D-BLADE (Karl Storz®) in First-Attempt Intubation in Adult Patients Scheduled for Elective Surgery at *Hospital Alma Máter de Antioquia* (2025–2026). Investigator-Initiated Randomized Parallel-Group Non-Inferiority Clinical Trial Protocol.

Short Title: LARINGOCOL

b. Summary: Dataset from the World Health Organization Trial Registry

Primary Registry / Trial Identifying Number	x
Date of Registration in Primary Registry	x
Secondary Identifying Numbers	IN29-2025
Sources of Monetary or Material Support	Universidad de Antioquia, Hospital Alma Máter de Antioquia
Primary Sponsor	Universidad de Antioquia
Secondary Sponsors	Hospital Alma Máter de Antioquia
Contact for Public Queries	Gabriel R. Muñoz Miranda. gabrielr.munozm@udea.edu.co
Contact for Scientific Queries	Gabriel R. Muñoz Miranda. gabrielr.munozm@udea.edu.co
Public Title	**LARINGOCOL**
Scientific Title	Estimation of the Non-Inferiority of the Laringocel® Videolaryngoscope Compared to the C-MAC D-BLADE (Karl Storz®) in First-Attempt Intubation in Adult Patients Scheduled for Elective Surgery at Hospital Alma Máter de Antioquia.
Countries of Recruitment	Colombia
Health Condition(s) or Problem(s) Studied	First-attempt intubation success rate using videolaryngoscopy
Interventions	**Group 1:** Orotracheal intubation via videolaryngoscopy with the Laringocel device.
	Group 2: Orotracheal intubation via videolaryngoscopy with the C-MAC D-BLADE (Karl Storz®) device

Key Inclusion/Exclusion Criteria	**Inclusion Criteria:** • Patients over 18 years of age • Patients scheduled for elective surgery under general anesthesia • Patients requiring orotracheal intubation with a single-lumen tube
	Exclusion Criteria: • Patients with an anticipated difficult airway • Patients who decline participation in the study
Study Type	Non-inferiority efficacy **Allocation:** Randomized, parallel-group, 1:1, permuted block design **Masking:** Participants and data analyst
Date of First Enrollment	Estimated 11/2025
Target and Final Sample Size	Planned sample: 126 patients per group
Recruitment Status	Not yet recruiting
Primary Outcome	Proportion of successful first-attempt orotracheal intubation
Key Secondary Outcomes	i. Estimate whether differences exist between the intervention and control in: 1. Overall intubation success (up to 3 attempts) 2. Percentage of glottic opening (POGO) 3. Fremantle score 4. Intubation time 5. Operator satisfaction 6. Situational awareness ii. Adverse events in both groups: 1. Postoperative sore throat (1 hour post-extubation) 2. Dental loss 3. Pharyngeal or oral mucosal injuries
Ethics Review	Approved on September 11, 2025
Trial Completion Date	Pending
Summary Results	Pending
Individual Participant Data (IPD) Sharing Statement:	Database access will be allowed upon prior request to the principal investigator.

Estimated Study Duration:	12 months

2. Versión del protocolo:

The development of this protocol has been based on the SPIRIT 2025 Statement (Standard Protocol Items: Recommendations for Interventional Trials) and CONSORT 2010 (Consolidated Standards of Reporting Trials), including the extension for "Non-Inferiority and Equivalence Trials." (1,2).

Protocol Version	Date	Modifications	Page	Responsible
V 1.0	11/2025	Initial version	All	Principal Investigator

3. Roles and Responsibilities:

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GRM and MZ conceived the study. GRM leads the project, including protocol writing, methodological, statistical, and ethical design, overall coordination, and dissemination of the proposal. MZ participates as co-investigator and study advisor, contributing his expertise in anesthesiology and methodological aspects. He also critically reviewed the document and provided corrections and suggestions.

b. Sponsor

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c. Sponsorship role

Neither the sponsorship by the University of Antioquia nor that of the authors has any influence on the study design; data collection, management, analysis, or interpretation; report writing; or the decision to submit the manuscript for publication.

d. Coordination:

This trial will not have a clinical trial coordinating committee. Coordination will be the responsibility of the principal author.

II. Open Science

4. Study Identifier and Trial Registry Name

This clinical trial will be registered on the ClinicalTrials.gov platform once the protocol is approved.

5. Access to Protocol and Analysis Plan

The full protocol will be made available in repositories once approved.

6. Data Sharing

Individual participant data will be anonymized and securely stored in Redcap. Upon study completion and after publication of the main results, the following will be available for a period of 5 years after trial completion: a dataset, the data dictionary, and the statistical code used for analyses. These may be shared with other researchers upon formal request. External investigators must agree to use the data exclusively for research purposes.

7. Funding and Conflicts of Interest

a. Funding Sources

The University of Antioquia financially supports the research director's time. This support includes time dedicated to planning, methodological development, protocol writing, and statistical analysis.

Hospital Alma Máter de Antioquia provides institutional and logistical support, granting access to facilities, medical devices, and personnel required for study implementation.

No direct or indirect funding has been received from industry.

b. Funding and Provision of Equipment:

- Provision of the Laringocel device and accessories is funded by the authors, without contracts or outcome-related clauses with the company TRONICAL S.A.S.
- Provision of the C-MAC D-BLADE and accessories is funded by Hospital Alma Máter de Antioquia, which holds the device in its inventory.
- Gifts and travel support from the manufacturer are prohibited during the study.

c. Conflicts of Interest:

The research team declares no economic, contractual, or intellectual property ties with the manufacturer or distributor of the Laringocel videolaryngoscope (TRONICAL). None of the investigators receive fees, financial incentives, in-kind support, or benefits derived from commercialization of the device.

To date, no financial or personal relationships exist with manufacturers or distributors of the devices under evaluation (employment, consultancies, honoraria, travel, patents, stock ownership, royalties, or others).

The study's design, conduct, analysis, and publication are independent from the equipment supplier; the supplier does NOT participate in recruitment, has no access to real-time data, and holds no veto rights over results or manuscripts. The protocol and analysis plan are pre-specified and will be publicly registered (ClinicalTrials.gov) prior to the first enrollment.

The participation of TRONICAL S.A.S is limited to providing, at the request of the ethics committee, the regulatory and technical documentation required by INVIMA and safety evidence for approval, without involvement in protocol design, trial conduct, or result analysis.

This study is developed as part of a master's thesis to obtain the degree of Master in Clinical Epidemiology at the University of Antioquia.

8. Dissemination Policy

a. Results Communication Plan

The authors commit to disclosing the study results regardless of the nature of the findings, whether favorable, neutral, or unfavorable.

Initially, results will be presented as a requirement to obtain the Master in Clinical Epidemiology degree at the University of Antioquia. They will also be shared with the Academic Group of Clinical Epidemiology (GRAEPIC) of the same university, with the anesthesiology group at Hospital Alma Máter de Antioquia, and with the institution's Research and Innovation department.

In a second stage, the findings will be presented at national and international academic events in anesthesiology. Finally, the study results will be submitted for peer review and potential publication in a scientific journal indexed or recognized by Colciencias.

b. Authorship Plan:

Authorship assignment for publications derived from the study will follow the recommendations of the International Committee of Medical Journal Editors (ICMJE).

For this trial, authorship requires meeting all four criteria:

1. Substantial contribution to the conception or design of the work, or acquisition, analysis, or interpretation of project data.
2. Drafting the work or critically reviewing it for important intellectual content.
3. Final approval of the version to be published.
4. Agreement to be accountable for all aspects of the work, ensuring that questions related to accuracy or integrity of any part are appropriately investigated and resolved.

No external professional writers will be engaged in manuscript preparation. Document preparation will be the direct responsibility of the research team.

c. Public Access to the Protocol:

To ensure public access, the protocol will be registered in ClinicalTrials.gov and its complete version will be published in a protocol repository such as protocols.io. If necessary, it will be made publicly available through publication in an indexed journal or as supplementary material in the scientific article.
Regarding the participant dataset and statistical code used for analysis, these will be made available upon request to the principal investigator, ensuring protection of participant confidentiality.

III. Introduction

9. Background and Rationale

a. Problem Statement, Rationale, and Research Question

In anesthetic practice, orotracheal intubation is generally considered a safe and effective procedure (3). However, the Fourth National Audit Project (NAP4) of the

Royal College of Anaesthetists identified that 42% of adverse events in airway management are related to failures in the orotracheal intubation process, making it a major cause of morbidity and mortality as well as a frequent reason for medicolegal claims against anesthesiologists (4,5).

These failures are closely linked to difficult airway (DA) scenarios (6), in which most adverse events occur during difficult laryngoscopy or tracheal intubation, with a combined incidence ranging between 1.8% and 8% (7–9). In this context, videolaryngoscopy has emerged as a promising tool due to improved visualization and higher success rates (10), although its high cost limits implementation in many settings (11). This situation has encouraged the search for more affordable devices, such as the Laringocel®, whose performance and safety have not yet been studied, highlighting the need for new investigations.

Difficult laryngoscopy is characterized by the inability to visualize the vocal cords, which complicates passage of the endotracheal tube and often requires multiple intubation attempts (6). This is significantly associated with increased risk of adverse outcomes, such as esophageal intubation (RR 6; 95% CI: 3.7–8.7), severe hypoxemia (RR 14; 95% CI: 7.3–24.3), regurgitation (RR 7; 95% CI: 2.8–10), bradycardia (RR 4; 95% CI: 1.7–6.7), and cardiac arrest (RR 7; 95% CI: 2.3–9.8). Moreover, this situation may culminate in difficult or even failed tracheal intubation (7,12).

These outcomes not only carry significant clinical impact but also increase medicolegal claims, often linked to inadequate prediction and poor management of difficult airway. Analyses in the United States (2019) and Canada (2020) reported that in 59% of cases preoperative evaluation was inadequate, and 65% of errors occurred during decision-making (6,13). One major cause of such errors is cognitive perseveration bias, manifested in the repetition of the same technique despite failed attempts (7,14). For example, Joffe's study found that, in the face of difficult intubation, 67% of physicians persisted in using direct laryngoscopy (15), even though subsequent attempts show a failure rate close to 80%. Adopting strategies such as changing the operator or using a videolaryngoscope in the second attempt can avoid this scenario and raise the success rate to 92% (16).

he risks associated with DA underscore the importance of accurate prediction; however, current clinical tests lack sufficient discriminatory power to anticipate DA, representing a major challenge (17,18). Prospective studies indicate that between 75% and 93% of difficult intubations are unanticipated, increasing the risk of critical complications such as the "can't ventilate, can't oxygenate" (CVCO) scenario, with an incidence of up to 15% (19–21). Therefore, preparation for unexpected situations is essential to achieve first-attempt intubation success, ensuring patient safety through the use of the best available tools (7).

For over a century, direct laryngoscopy has been the standard method for tracheal intubation, allowing a direct line of sight between the operator and the glottis (22,23). Nevertheless, it fails in up to 8% of cases after three attempts and in 30% on the first attempt (7). Given this risk, since 2001 videolaryngoscopy has emerged as a promising alternative, as it provides better visualization even in unfavorable anatomy and higher first-attempt success rates (4,10). Furthermore, it facilitates teaching and enhances situational awareness, supporting real-time shared decision-making (24–26).

A recent Cochrane systematic review demonstrated that videolaryngoscopes with hyperangulated blades, compared with direct laryngoscopy, reduce the rate of failed intubation (RR 0.51; 95% CI: 0.34–0.76) and, in difficult airway cases, further decrease this outcome (RR 0.29; 95% CI: 0.17–0.48). They also reduce the rate of esophageal intubation (RR 0.39; 95% CI: 0.18–0.81), improve glottic visualization in grade 3/4 Cormack-Lehane views (RR 0.15; 95% CI: 0.10–0.24), increase first-attempt intubation success (RR 1.03; 95% CI: 1.00–1.05), and reduce hypoxemia when a Macintosh-type blade is used (RR 0.72; 95% CI: 0.52–0.99). The authors concluded that these devices reduce failed intubations, hypoxemia, and improve glottic visualization and overall procedural safety (10).

This positive impact has led to their inclusion in international guidelines such as those from the Difficult Airway Society (DAS), the Canadian Airway Focus Group (CAFG), and the Project for Universal Management of Airways (PUMA), which recommend their routine use as first-line devices (7,27), training all anesthesiologists, and ensuring immediate access to this tool (28). These guidelines emphasize maximizing success on the first intubation attempt, rather than the second, which is inherently more complicated (29).

Nevertheless, despite the robust evidence supporting videolaryngoscopy and its wider availability following the COVID-19 pandemic (30), implementation remains limited by economic factors (31). In countries like the United Kingdom, the cost of a videolaryngoscope can reach USD 9,273.20, compared with approximately USD 100 for a Macintosh laryngoscope (32). Moreover, many lower-cost models are disposable or use disposable blades, significantly increasing maintenance expenses (up to USD 10 per intubation) and raising environmental concerns (33). In high-volume hospitals, such costs accumulate quickly, hindering widespread adoption (11).

In middle-income countries such as Colombia, adoption of videolaryngoscopes faces barriers related to high costs, the need for importation, and lack of accessibility. As noted by Arteaga IM —"*videolaryngoscopes are unfortunately limited in our setting due to cost and maintenance"* (34)—, this situation not only deprives patients of the

benefits of improved intubation effectiveness but also hinders the training of students, residents, and physicians by reducing opportunities to practice in difficult airway scenarios (35).

In response to this need, and following international recommendations, Colombian prototypes such as the Laringocel® have been developed—a hyperangulated, reusable, non-channeled videolaryngoscope, designed in 2022. Its low cost (~USD 384) is explained by the use of a borescope transmitting images via Wi-Fi to mobile devices (35), eliminating the need for an integrated screen, while offering the possibility to store visual material for academic or legal purposes (36); However, no studies are currently available comparing its efficacy and safety with established devices such as the C-MAC D-BLADE (Karl Storz®), nor assessing the extent to which factors such as camera location or dependence on an external device influence image quality and usability in surgical settings, as described by other investigations (22).

To address these uncertainties, this project is based on the hypothesis that the Laringocel® is non-inferior to the C-MAC D-BLADE (Karl Storz®) in first-attempt intubation.

The results obtained could support the use of the Laringocel® in future cost-effectiveness studies and facilitate its adoption in clinical settings, offering a more economical alternative for videolaryngoscopy. Accordingly, this project poses the following research question:

In patients over 18 years undergoing elective surgery, is the Laringocel® videolaryngoscope non-inferior to the C-MAC D-BLADE videolaryngoscope for first-attempt intubation?

b. Choice of Comparator

There are various types of videolaryngoscopes, classified according to blade angulation (hyperangulated or Macintosh-type) and the presence of a channel (with or without stylet). Compared with direct laryngoscopy and other videolaryngoscopes, these features facilitate intubation in difficult airway (DA) scenarios (10) and the guidance of the endotracheal tube (37,38). These devices show a rapid learning curve (39), for both inexperienced physicians (26) and those experienced in conventional laryngoscopy (21,40) or other videolaryngoscopes (41). Nonetheless, despite their shared principle of indirect visualization, they differ in camera placement, illumination, connectivity, and materials, which influence costs, lifespan, and the magnitude of benefits (37,42).

A systematic review and network meta-analysis comparing channeled (Airtraq, Airwayscope, and King Vision) and non-channeled (GlideScope, C-MAC, C-MAC D-

Blade, and McGrath) videolaryngoscopes found significant differences in effect sizes for intubation success depending on device and clinical context; in particular, the C-MAC D-Blade videolaryngoscope stood out for its high success and safety in both normal and difficult airways, while other devices showed strengths in aspects such as speed, image quality, or intubation time (43).

These performance discrepancies can largely be attributed to the design of the blades and video screens of each device: channeled videolaryngoscopes (Airtraq, Airwayscope, King Vision) often have disposable, angulated blades with direct screens, facilitating a wide view of the glottis and minimizing maneuvers during intubation. In contrast, non-channeled models (GlideScope, C-MAC, C-MAC D-Blade) require a stylet and have less angulated blades, although they compensate with a pronounced distal curvature that reduces cervical movement (22). Given that the Storz® C-MAC D-Blade has demonstrated a particularly favorable balance between efficacy and safety across different clinical scenarios, and adequately represents the design characteristics of non-channeled videolaryngoscopes, it was selected as the comparator for the present study.

c. Evidence for C-MAC D-Blade

The accumulated clinical evidence consistently supports the performance and safety of the C-MAC D-Blade (Karl Storz®) videolaryngoscope. In the general population, overall success (up to three attempts) ranges from 81% to 100%, with first-attempt success close to 92.7% in patients with difficult airways (22). In practical terms, ~7 out of every 100 patients are not intubated on the first attempt with this videolaryngoscope; this does not equate to intubation failure, as it is usually resolved with subsequent attempts or adjunct maneuvers. Moreover, rates of esophageal intubation are very low with videolaryngoscopy; in some series, no events were reported, suggesting a favorable safety profile.

In a randomized trial by Tosh et al., the C-MAC D-Blade showed additional advantages over direct laryngoscopy, reducing the incidence of sore throat at 2 hours (15.4% vs. 78.5%), eliminating its persistence at 24 hours (0% vs. 67.7%), and decreasing hoarseness (0% vs. 13.8%) and cough (4.6% vs. 23.1%) (44).

Regarding timing, the average time to achieve intubation with this device ranges from 25 to 32 seconds (43). Although there is heterogeneity by operator, anatomy, and stylet strategy, this range positions it as an efficient tool in critical scenarios. Likewise, in a randomized non-inferiority trial against GlideScope, the C-MAC D-Blade achieved first-attempt success of 507/541 (93.7%; 90.35% CI: 0.917–0.952) (45).

Finally, a network meta-analysis comparing the C-MAC D-Blade with the Macintosh laryngoscope showed in its supplementary material league table that the C-MAC D-

Blade reduces the odds of failed intubation by 63.5% (OR: 0.365; 95% CI: 0.152–0.874), decreases the likelihood of difficult intubation by 80.8% (OR: 0.192; 95% CI: 0.071–0.520), and reduces the chance of difficult laryngoscopy (Cormack–Lehane grade ≥3) by 83% (OR: 0.170; 95% CI: 0.074–0.392), with no significant differences in mean intubation time (43). Taken together, these effects favor clinical safety and efficacy

Key technical aspects.

The hyperangulated design facilitates glottic visualization without aligning the oropharyngeal–laryngeal–tracheal axes, which is especially useful in difficult airway. Since ETTs are optimized for DL, use of a hockey-stick–shaped stylet and a progressive stylet withdrawal technique is recommended, in accordance with the manufacturer and German airway guidelines (20,36).

d. Evidence for Laringocel

Post-marketing observational clinical information on the Laringocel® (TRONICAL®) videolaryngoscope was provided by the developing company to the principal investigator (supplementary material 3).
In an institutional registry of 534 intubations in the general population, performed by both anesthesiologists and non-anesthesiologist physicians, the following outcomes were documented:

- First-attempt success rate: 525/534 (98.3%)
- Overall success rate: 532/534 (99.8%)
- Failure rate: 1/534 (0.2%), resolved with fiberoptic bronchoscopy

With these data, overall success with Laringocel—at two attempts—was 533/534 procedures (99.8%). Although this is observational evidence, without a control group and with possible risk of underreporting, the documented performance suggests a high probability of first-attempt success and a very low need for rescue techniques. These findings reflect outstanding clinical performance under real-world practice conditions, with success proportions comparable to or even exceeding those reported for reference videolaryngoscopes, and a minimal frequency of complications. Overall, the available evidence supports the potential safety and feasibility of Laringocel use in anesthetic practice.

e. Device comparison

The Laringocel® and the C-MAC D-Blade (Karl Storz®) are rigid videolaryngoscopes that share a pronounced angulation (approximately 45° and 40°, respectively), a similar intended use—orotracheal intubation, including difficult airway—and the absence of a channel. These shared characteristics allow for a direct comparison between both devices in terms of clinical performance and ease of use (36,46).

Within the international regulatory framework, the FDA classifies laryngoscopes as Class I or II medical devices, subject to technical controls for performance, electrical and optical safety, labeling, and validation, without requiring prior clinical studies when substantial equivalence with a predicate device exists under the 510(k) mechanism (47). Under this framework, a Class II device such as Laringocel® can be evaluated in a randomized controlled clinical trial to measure its performance without requiring prior FDA authorization (48).

In Colombia, Laringocel® holds a valid sanitary registration issued by the National Institute for Food and Drug Surveillance (INVIMA) through Resolution No. 2024036011 dated August 1, 2024, with registration number 2024DM-0029237 and a 10-year validity. It was classified as a Class IIa medical device (moderate risk) under the Andean Technical Regulation, authorized for manufacture and sale by TRONICAL S.A.S. Its intended use in orotracheal intubation, including difficult airway, with real-time video transmission to different receiving devices is recognized (see supplementary material 2).

During the evaluation process, INVIMA requested and reviewed the complete technical dossier in accordance with current regulations (form ASS-RSA-FM007). This included, where applicable, design specifications; electrical, optical, and mechanical safety tests; biocompatibility; quality management; labeling and instructions for use; as well as software and performance validations. Compliance with specific regulatory safety requirements was also mandated: “scientific information supporting its safety and performance” (Art. 18, item j, point 15) and the “risk analysis issued by the manufacturer” (Art. 18, item j, point 16). Additionally, the agency certified the accessory borescope as part of the system, whose medical-grade components (polycarbonate, aluminum, ceramic, PVC, and encapsulated LED) reinforce the device’s technical safety (see supplementary materials 4 and 5).

f. Expected adverse events

In adults undergoing orotracheal intubation with a non-channeled videolaryngoscope, the most relevant adverse events and their expected ranges—based on literature comparable to the study context—for both devices are:

a. **Esophageal intubation:** (≈2.1% with videolaryngoscopy vs 6.6% with direct laryngoscopy in the ICU) (49); therefore, we expect ≤1–2% in our trial with trained operators in elective surgery. Moreover, several meta-analyses in critically ill patients confirm lower esophageal intubation with videolaryngoscopy compared with direct laryngoscopy (10,50). Additionally, confirmation by capnography will alert to esophageal intubation and will be managed by the attending anesthesiologist.

b. **Pharyngolaryngeal symptoms:** These include postoperative sore throat (POST) and cough, most of which are self-limited. A clinical trial with the C-MAC D-Blade showed less sore throat at 2 h (15.4% vs 78.5%) and absence at 24 h (0% vs 67.7%); it also showed less hoarseness at 24 h (0% vs 13.8%) and less cough at 24 h (4.6% vs 23.1%). Based on these data, we expect in both groups sore throat ≤15% at 2 h and ≈0–5% at 24 h, hoarseness ≈0% at 24 h, and cough ≈3–5% at 24 h with videolaryngoscopy (44).
c. **Dental trauma**: In the Cochrane systematic review and meta-analysis by Hansel et al. (2022), comparing hyperangulated videolaryngoscopy (such as C-MAC D-Blade) with direct laryngoscopy, the relative risk of dental trauma was 0.51 (95% CI: 0.16–1.59; I^2=0%), with no statistically significant differences but with a trend favoring videolaryngoscopy and very infrequent events (hyperangulated videolaryngoscopes: 2/1876 vs 7/1621 with direct laryngoscopy; aggregated data from the included trials), so we expect a frequency <1% with both devices (50).

Consequently, the selection of a non-inferiority design is supported by the potential benefit of Laringocel®, which may offer a combination of safety and efficacy at an affordable cost for the Colombian health system. Thus, the objective is to generate evidence supporting the adoption of a more economical device without compromising safety or effectiveness in airway management.

10. Specific Objectives or Hypotheses

a. Research Hypothesis

The Laringocel® videolaryngoscope is non-inferior to the C-MAC D-BLADE (Karl Storz®) for first-attempt intubation success in patients over 18 years scheduled for elective surgery at Hospital Alma Máter de Antioquia.

b. Primary Objective

To determine whether, in patients over 18 years scheduled for elective surgery, the Laringocel® videolaryngoscope is non-inferior to the C-MAC D-Blade videolaryngoscope for first-attempt intubation.

c. Secondary Objectives

i. To estimate whether differences exist between the intervention and control in:
   1. Overall intubation success (3 attempts)
   2. Percentage of Glottic Opening (POGO)
   3. Fremantle score
   4. Intubation time
   5. Operator satisfaction
   6. Situational awareness (SAGAT)

ii. To describe adverse events in both groups:
    1. Postoperative sore throat
    2. Dental loss
    3. Oral mucosal injuries

d. Trial Estimand

Attribute	Definition
Population	Adult patients scheduled for elective surgery at Hospital Alma Máter de Antioquia who are randomized.
Intervention	Experimental group: Laringocel® videolaryngoscope. Control group: C-MAC D-BLADE (Karl Storz®).
Endpoint	First-attempt intubation success, defined as correct placement of the endotracheal tube on the first attempt, confirmed by a capnography waveform.
Summary measure	Difference in proportions of first-attempt intubation success between the experimental group and the control group.
Handling of intercurrent events	**Device switches:** Patients who switch from the assigned device (Laringocel or C-MAC) will be excluded from the analysis (per-protocol analysis). However, an intention-to-treat sensitivity analysis will be performed.

IV. Methods: Patient and Public Involvement, Trial Design

11. Patient and Public Involvement

No direct involvement of patients or the public in the trial design has been planned.

12. Trial Design Description

This clinical trial is conceived as a non-inferiority study with a parallel-group design and 1:1 random allocation using permuted blocks.

Clinical trials commonly aim to demonstrate superiority. However, when an intervention is already well established—as is the case with videolaryngoscopy, which achieves first-attempt intubation success rates above 90%—demonstrating a significant advantage with a new device is challenging. This is because any difference between groups is expected to be small, which would require very large sample sizes to detect a statistically significant difference.

Conversely, a new intervention may demonstrate efficacy and safety similar to the current standard, or even a slight decrease in performance, but with substantial advantages such as lower cost, greater affordability, and improved availability. In such cases, non-inferiority trials allow assessment of whether the new intervention is not clinically worse than the accepted standard within a predefined margin, while leveraging its additional benefits (51,52).

Therefore, Laringocel® was compared with the C-MAC D-BLADE (Karl Storz®) under a non-inferiority design, with the objective of evaluating its performance in first-attempt intubation without compromising safety or clinical efficacy, while offering the benefits of lower cost, greater affordability, and availability.

V. Methods: Participants, Interventions, and Outcomes

13. Study Setting

clinical trial will be conducted in Colombia, at Hospital Alma Máter, a high-complexity university institution in the city of Medellín, Antioquia.

The institution primarily receives patients from urban areas but also from neighboring rural regions and has one hospital-based site and one ambulatory site, both included as data collection locations.

Available infrastructure includes fourteen [14] operating rooms at the main site and four [4] at the ambulatory site, equipped with vital signs monitors, capnography, videolaryngoscopes [C-MAC D-BLADE, Laringocel], and senior personnel specialized in anesthesiology.

Site selection was based on the availability of candidates for surgery under general anesthesia, the presence of operational operating rooms, and the commitment of the research team.

The list of operational sites and operating rooms involved in the study can be consulted in Appendix C.

14. Eligibility

a. Participants

Inclusion criteria

- Patients over 18 years of age
- Patients scheduled for elective surgery under general anesthesia
- Patients requiring single-lumen orotracheal intubation
- Compliance with indication and preoperative fasting

Exclusion criteria

- Patients with an anticipated difficult airway (more than 2 anatomical risk factors for difficult airway)
- Patient refusal to participate in the study via informed consent

b. Intervention Operators

Participating physicians must be specialists in Anesthesiology with learning-curve experience in both interventions.

15. Intervention and Comparator

a. SPIRIT items 15a to 15d (53) **are described according to the TIDieR checklist** (54)**.**

i. **Intervention (Laringocel):** (See images in Appendix D)

TIDIeR	Item
1.	**BRIEF NAME** Intubation with LARINGOCEL
	WHY
2.	Videolaryngoscopy has been shown to be superior to direct laryngoscopy for first-attempt intubation and overall intubation success, with lower rates of hypoxemia, esophageal intubation, and improved glottic view (10). Laringocel is chosen as a relatively affordable, easily accessible videolaryngoscope that can provide the benefits of hyperangulated videolaryngoscopes in airway management at lower cost.
	WHAT WILL BE USED
3.	**Materials:** Patients will be intubated using the Laringocel videolaryngoscope, a reusable, hyperangulated, non-channeled device whose blade is made of polycarbonate. This videolaryngoscope has an integrated borescope (camera), illumination guide, the capability to transmit real-time images to mobile devices via Wi-Fi up to 10 meters, and a 450 mA internal rechargeable battery with 90 minutes of autonomy. Images generated by Laringocel will be transmitted through the “Laringocel” mobile application to a Huawei MatePad 11 tablet, which will be placed at the patient’s head using an adjustable stand. (A photograph of the materials is included in Appendix D.)
	WHAT (PROCEDURES)
4.	**Procedures:** Patients will be under general anesthesia with neuromuscular relaxation, with anesthetic induction determined at the discretion of the professional performing the intervention. Neuromuscular relaxation will be achieved using depolarizing or non-depolarizing muscle relaxants, according to the

administrator's clinical judgment, ensuring at least a dose equivalent to ED95 (effective dose in 95% of cases). If succinylcholine is used, the intervention will be performed 45 seconds after drug administration. For cisatracurium, a 4-minute wait will be observed, and for vecuronium and rocuronium, 2 minutes before proceeding. These intervals are established to ensure adequate muscle relaxation.

WHO PROVIDES

5. The intervention will be performed by anesthesiology specialists who have completed their learning curve, assessed by CUSUM (Cumulative Sum). Non-anesthesiologist administrators such as students, interns, or anesthesiology residents will be excluded from performing the intervention.

HOW

6. Videolaryngoscopy with Laringocel will be performed in person in the operating room on an individual basis.

WHERE

7. Operating rooms at Hospital Alma Máter, hospital or ambulatory site, Medellín, Antioquia, Colombia.

WHEN AND HOW MUCH

8. The intervention will be carried out once adequate neuromuscular relaxation conditions have been achieved. For measurement of the primary outcome, intubation will be performed in a single attempt. If necessary, up to three attempts may be performed to assess the overall intubation outcome.

ADAPTATIONS

9. The intervention is not designed as a planned or adaptive procedure and does not contemplate a titration approach during its execution.

MODIFICATIONS

10. If the third intubation attempt fails, the intervention may be modified by using C-MAC or direct laryngoscopy, at the discretion of the professional in charge of the intervention. If technical failures occur with Laringocel (such as connection issues, equipment damage, camera or battery failure), an alternative may be used according to the clinical judgment of the intervention administrator.

ADHERENCE

11. To ensure procedural fidelity, the following strategies will be implemented:

1. All participating anesthesiology specialists will receive a training session on the use of Laringocel, the intubation criteria defined in the protocol, and the standardization of the following key concepts: intubation attempt, failed intubation, confirmation of intubation. (See definitions in Appendix D.)
2. Procedure oversight will include subsequent review of the Laringocel intubation recording.

For more information on Laringocel®, see the official page: https://www.laringocel.com/

ii. **Comparator** (C-MAC D-Blade):

TIDIeR	Item
	BRIEF NAME
1.	Intubation with C-MAC D-BLADE
	WHY
2.	Videolaryngoscopy with C-MAC D-BLADE has demonstrated, compared with direct laryngoscopy, a higher proportion of first-attempt intubation success, reduced probability of failed intubation, reduced likelihood of difficult intubation, and reduced risk of difficult laryngoscopy (10,43). C-MAC D-BLADE is chosen as the comparator videolaryngoscope due to its documented efficacy and safety and the availability of the device.
	WHAT WILL BE USED
3.	**Materials:** Patients will be intubated using the C-MAC D-BLADE videolaryngoscope, a reusable, hyperangulated, non-channeled device made of titanium. It is equipped with a high-resolution CMOS camera that provides HD-quality images with a resolution of 1280 × 800 pixels. Illumination is provided by two 1 W white LEDs. The device is compatible with the universal C-MAC® system, allowing Plug & Play connection via a 200 cm C-MAC connection cable. Captured images will be transmitted to an integrated screen on a C-MAC monitor 8403 ZX Storz® or C-MAC 8104 ZX, which will be positioned at the patient's head using an adjustable stand. The C-MAC® D-BLADE has a working length of 109 mm, a handle width of 28 mm, and a distal tip width of 19 mm. (A photograph of the materials is included in Appendix D) (55).
	WHAT (PROCEDURES)
4.	**Procedures:** Patients will be under general anesthesia with neuromuscular relaxation, with anesthetic induction determined at the discretion of the professional performing the intervention. Neuromuscular relaxation will be achieved using depolarizing or non-depolarizing muscle relaxants, according to the administrator's clinical judgment, ensuring at least a dose equivalent to ED95 (effective dose in 95% of cases). If succinylcholine is used, the intervention will be performed 45 seconds after drug administration. For cisatracurium, a 4-minute wait will be observed, and for vecuronium and rocuronium, 2 minutes before proceeding. These intervals are established to ensure adequate muscle relaxation.

WHO PROVIDES

5. The intervention will be performed by anesthesiology specialists who have completed their learning curve, assessed by CUSUM (Cumulative Sum). Non-anesthesiologist administrators such as students, interns, or anesthesiology residents will be excluded from performing the intervention.

HOW

6. Videolaryngoscopy with C-MAC® D-BLADE will be performed in person in the operating room on an individual basis.

WHERE

7. Operating rooms at Hospital Alma Máter, hospital or ambulatory site, Medellín, Antioquia, Colombia.

WHEN AND HOW MUCH

8. The intervention will be carried out once adequate neuromuscular relaxation conditions have been achieved. For measurement of the primary outcome, intubation will be performed in a single attempt. If necessary, up to three attempts may be performed to assess the overall intubation outcome.

ADAPTATIONS

9. The intervention with C-MAC® D-BLADE is not designed as a planned or adaptive procedure and does not contemplate a titration approach during its execution.

MODIFICATIONS

10. If the third attempt fails, the intervention may be modified by using Laringocel or direct laryngoscopy, at the discretion of the professional in charge of the intervention. If technical failures occur with C-MAC® D-BLADE (such as connection issues, equipment damage, camera or battery failure), an alternative may be used according to the clinical judgment of the intervention administrator.

ADHERENCE

11. To ensure procedural fidelity, the following strategies will be implemented:

1. All participating anesthesiology specialists will receive a training session on the use of Laringocel, the intubation criteria defined in the protocol, and the standardization of the following key concepts: intubation attempt, failed intubation, confirmation of intubation. (See definitions in Appendix D.)
2. Procedure oversight will include subsequent review of the C-MAC® D-BLADE intubation recording.

For more information on C-MAC D-BLADE (Karl Storz®), see the official page: https://www.karlstorz.com/us/en/product-detail-page.htm?productID=1000111723&cat=1000071971

16. Outcomes

a. Primary

Between the Laringocel and C-MAC groups, the difference in proportions of first-attempt intubation success during orotracheal intubation in operating rooms will be determined.

Relevance: First-attempt intubation success is crucial to reduce the risk of complications such as hypoxemia, aspiration, and other adverse events associated with multiple attempts. A device that enables successful first-attempt intubation would improve safety and effectiveness in clinical practice.

b. Secondary:

i. **Overall intubation success proportion:** In the Laringocel and C-MAC groups, the proportion of intubation success within the first three attempts during orotracheal intubation will be measured (each attempt is defined as insertion of the videolaryngoscope into the oral cavity). If success occurs on the first attempt, no further attempts will be made.
Relevance: To assess intubation effectiveness with the videolaryngoscopes.

ii. **Percentage of Glottic Opening (POGO):** In the Laringocel and C-MAC D-Blade groups, POGO will be measured during intubation and the mean for each group will be calculated; subsequently, the difference in means between groups will be analyzed.
Relevance: Allows quantification of the quality of the laryngeal view obtained during intubation. A higher POGO indicates better visualization of the vocal cords.

iii. **Fremantle score:** In the Laringocel and C-MAC D-Blade groups, the Fremantle score—assessing both laryngeal view and ease of intubation—will be recorded. Subsequently, the frequencies of these scores will be compared between groups.
Relevance: Lower values on the ease component indicate a less complicated intubation, and the scale allows relating the glottic view to intubation ease.

iv. **Intubation time:** In the Laringocel and C-MAC groups, the time elapsed from the start of the intubation procedure (insertion of the videolaryngoscope into the oral cavity) until successful tube placement (confirmation by capnography) will be

measured. The mean intubation time in seconds will be measured using the video material, and the mean intubation time in each group will be analyzed.
Relevance: A shorter intubation time can reduce the risk of hypoxia and other adverse events, improving patient safety.

v. **Operator satisfaction:** In the Laringocel and C-MAC groups, the operator's satisfaction with the device used will be evaluated by four questions addressing physical and technical ease of use, overall satisfaction, and willingness to reuse, rated on a 1–5 Likert scale. This will be measured after the surgical procedure, and the average scores for each group will be analyzed.
Relevance: For new devices, operator satisfaction is a key factor for adoption and sustained use. A videolaryngoscope that meets satisfaction expectations can facilitate adherence in daily practice.

vi. ***Situation Awareness Global Assessment Technique*** **(SAGAT):**
In the Laringocel and C-MAC D-Blade groups, situational awareness will be evaluated based on SAGAT.
An external observer who will view only the videolaryngoscope screen, without participating in the intubation, will be queried. The assessment will be performed after the procedure using a binary-response form with three questions reflecting the three levels of situational awareness (perception, comprehension, projection).
The frequency of responses between the two groups will be compared at each level of situational awareness, defining loss of situational awareness as failure in at least one level. In addition, the probability of failure will be estimated as a function of the device used.
Relevancia: The fundamental role of non-technical skills and their impact on the incidence of adverse events—especially those related to decreased situational awareness—is well established (56,57). Real-time visualization of the intubation procedure by all members of the surgical team may improve situational awareness regarding first-attempt intubation success, even among those not directly performing the procedure. This facilitates both timely identification of adverse situations and ongoing clinical teaching.

vii. Adverse events
In the Laringocel and C-MAC D-Blade groups, the proportion of adverse events will be described, including postoperative sore throat, dental loss, and evident injuries to the pharyngeal or oral mucosa. These events will be assessed by the investigator responsible within one hour after extubation, whether in the post-anesthesia recovery room, intensive care unit, or inpatient wards, as applicable.

Relevance: Documenting injuries in both groups allows determination of adverse event incidence and device safety.

17. Harms

In accordance with good clinical research practices for clinical trials, all adverse events occurring during the study will be collected, assessed, and reported. The evaluated intervention (orotracheal intubation via videolaryngoscope) is a routine and safe procedure in anesthetic practice; therefore, a significant incidence of serious adverse events attributable to the study is not expected.

Adverse events will be assessed by the responsible investigator immediately after patient extubation in the operating room, or as soon as the patient is transferred to the post-anesthesia recovery room, intensive care unit, or inpatient ward. This assessment will be documented using a structured form and stored on the REDCap platform.

Adverse events will be considered those occurring after the participant's intervention, regardless of their causal relationship with the procedure. However, only those adverse events with a direct temporal and clinical relationship to the intubation procedure will be considered secondary outcomes of the study—for example, postoperative sore throat, dental loss, or injury to the oral or pharyngeal mucosa. If an adverse event occurs before the intubation procedure, it will be recorded but not as a secondary outcome.

Any serious and unexpected adverse event occurring during intubation—such as the urgent need for a surgical airway or hemodynamic instability—will be documented immediately on the corresponding form and reported to the Institutional Ethics Committee within the first 24 hours, following Good Clinical Practice recommendations.

18. Participant Timeline: Enrollment, Interventions, and Assessments

Patients will be recruited in the inpatient ward or preoperative area, either the day before or the same day as surgery. There, inclusion and exclusion criteria will be verified to determine eligibility for study participation. Subsequently, the informed consent process and signature will take place.

Once recruited, demographic data collection and baseline assessment will proceed, including inspection of the oral cavity to detect preexisting lesions. Intervention assignment will be randomized and recorded in opaque envelopes. Allocation will remain concealed until the investigator opens the sealed envelope and informs the anesthesiologist responsible for intubation. The estimated time between baseline assessment and intervention allocation is approximately one hour.

Approximately 5 minutes will be available for the intervention administrator to prepare the necessary elements for videolaryngoscopy (assigned videolaryngoscope, its

correct functioning and connectivity, a stylet standardized to the device's shape, and the orotracheal tube).

Patients will be under general anesthesia with neuromuscular relaxation, with induction determined at the discretion of the professional in charge. Neuromuscular relaxation will be achieved using depolarizing or non-depolarizing muscle relaxants, ensuring at least a dose equivalent to ED95. If succinylcholine is used, the intervention will be performed 45 seconds after its administration; with cisatracurium, a 4-minute wait; and with rocuronium, 2 minutes before proceeding with intubation. Induction and neuromuscular relaxation are estimated to take between 2 and 6 minutes. The intubation procedure will be carried out with the assigned videolaryngoscope, either Laringocel or C-MAC D-Blade, recording the video material for subsequent evaluation of primary and secondary outcomes.

The primary outcome will be first-attempt intubation success. Tube placement will be confirmed by end-tidal capnography and will be recorded with a mobile device. Surgery will then proceed, with duration varying according to the surgical schedule. At the end of the intervention, patients will be transferred to the recovery room. One hour after extubation, possible adverse events—such as sore throat, oral mucosal injuries, and dental loss—will be assessed. In cases where patients are not extubated at the end of surgery, evaluation of these outcomes will be performed at a later stage, either in the ICU or at a scheduled assessment.

The evaluation of intubation videos and outcome adjudication will be carried out by another investigator, who will record the Fremantle score, POGO, intubation time, and first-attempt intubation success. This analysis will not necessarily be immediate, allowing it to be performed within the first 24–48 hours after the intervention, at which point the intervention will be closed.

Table 2. Participant schedule: enrollment, interventions, and assessments; POGO (Percentage of Glottic Opening)

19. Sample Size

The sample size calculation was based on the non-inferiority hypothesis for the Laringocel videolaryngoscope, considering first-attempt intubation success as the primary outcome.

Study Period											
Moment	Recruitment	Allocation	Post-allocation								Close
	$-t_1$	t_0	t_1	t_2	t_3	t_4	t_5	t_6	t_7	t_8	t_x
Recruitment											
Eligibility screening	χ										
Baseline assessment	χ										
Informed consent	χ										
Allocation		χ									
Interventions											
Laringocel			◆	—	—	◆					
C-MAC D-BLADE			◆	—	—	◆					
Assessments											
First-attempt success						χ					
Overall success						χ					
Fremantle score – POGO					χ					χ	
Intubation time										χ	
Operator satisfaction								χ			
Adverse events								χ			
Delayed adverse events									χ		

It is estimated that the first-attempt intubation success rate with the C-MAC D-Blade will be 93%, taking as reference the randomized clinical trial by Aziz et al., in which a first-attempt success rate of 93.7% was reported (90.35% CI: 91.7%–95.7%) (45).

To preserve assay sensitivity, a non-inferiority margin (Δ) of 8 percentage points was established, corresponding to the absolute difference between the first-attempt success rate with the C-MAC D-Blade (93.7%) (45) and the success rate identified for direct laryngoscopy in the Cochrane systematic review (85.4%) (0.083; 90.35% CI: 0.056–0.107) (10).

The sample size was estimated using the formula for non-inferiority trials with dichotomous outcomes (52,58).

$$2N = \frac{4p(1-p)(Z_\alpha + Z_\beta)}{\delta^2} \quad (1)$$

Where:

- $p = 0.93$: Expected success proportion
- $\delta = 0.08$: Non-inferiority margin.
- $Z\alpha = 1.645$: One-sided 5% significance level.
- $Z\beta = 0.84$: 80% power.

The calculation was implemented in the R statistical software (v4.4.3, R Core Team 2025) and validated using the Sealed Envelope Ltd. 2012 Power calculator for binary outcome non-inferiority trial. A sample size of 126 patients per group was obtained, for a total of 252 patients overall.
No multiplicity correction was applied to the sample size calculation because there will be only one confirmatory outcome; furthermore, due to the brief duration of the intervention and data collection, losses are not expected; therefore, no correction for drop-out was applied.

20. Recruitment Strategy

Participant recruitment will be carried out at the two sites of Hospital Alma Máter (hospital-based and ambulatory), selected based on the availability of patients, operating rooms, and anesthesiologists.
The study investigators (trained to identify predictors of difficult airway) will evaluate patients in the surgical preparation area or earlier, according to the same-day or next-day surgical schedules, as appropriate. Patients scheduled for surgery under general anesthesia will be identified. Once selected, the medical record will be reviewed and the preoperative physical examination performed to confirm eligibility criteria.
The recruitment period is estimated at eight to twelve months, subject to the flow of scheduled patients and the availability of the research team. Currently, approximately thirty surgical procedures are performed per day, Monday through Saturday, at the hospital-based sites, of which an estimated 20% require orotracheal intubation, representing a potentially eligible group for the study and an opportunity to maintain steady recruitment.
To minimize losses to follow-up for postoperative secondary outcomes, a detailed record of participants will be maintained. In cases where patients are not extubated immediately, the evaluation will be performed in the intensive care unit (ICU) or inpatient ward once extubation has taken place.

Participation in the study will not entail additional costs for patients nor modifications to their usual anesthetic management. In addition, no financial incentives for participants are contemplated.

Recruitment month	1	2	3	4	5	6	7	8	9	10	11	12
Current enrollments (current)												
Enrollments to date												
Target enrollments to date												
Actual minus projected												
Success proportion												
Final projected enrollment												
Final deficit or surplus												

Table 3. Monthly evaluation of recruitment status

VI. Methods: Allocation of Interventions

Randomization

21. Method of Generating the Allocation Sequence

a. Who generates the sequence and method

The randomization sequence will be generated by an independent investigator not involved in recruitment, patient intervention, or data collection. The sequence will be generated using the R statistical software (v4.4.3, R Core Team 2025) and its graphical interface RStudio.

b. Type of randomization

Participants will be randomly assigned to the Laringocel and C-MAC D-Blade groups in a 1:1 ratio. Permuted blocks (random sizes of 4, 6, or 8 patients) will be used with a computer-based random number generator.

22. Allocation Concealment Mechanism

Allocation concealment will be ensured through the use of opaque, sealed, sequentially numbered envelopes. These envelopes will be kept locked in a safe,

with access restricted to authorized investigators only. The same investigator who generates the allocation sequence will be responsible for coding and recording the allocation list in opaque, sequentially numbered envelopes (e.g., Pac001, Pac002, etc.) and will safeguard this information under strict confidentiality.

23. Implementation

Participants will be assessed for inclusion by the investigator in charge of recruitment the day before or the same day as surgery, according to the preoperative schedule. Once inclusion and exclusion criteria have been verified and informed consent obtained, the patient's data, date, time, and the investigator's signature will be documented on the outside of the corresponding envelope. Only at that moment will the assigned envelope be opened, the anesthesiologist responsible will be informed of the assigned intervention, and the assigned device will be provided for preparation. This procedure ensures that neither recruiting personnel nor patients know the allocation before enrollment, preventing selection bias.

24. Blinding (Masking)

a. Who will be blinded

Dado el diseño del estudio, se implementarán distintas estrategias de cegamiento para minimizar sesgos de desempeño, medición y análisis:

1. **Participants**
2. **Data analyst**

Outcome assessors for primary and secondary endpoints will be trained adjudicators; however, because the capnography waveform video is needed for the primary endpoint, blinding the assessors to the intervention is not possible. Operators of the intervention (anesthesiologists in this trial) performing the intubation cannot be blinded, as the devices have evident physical differences (see images in Appendix D). However, performance bias will be mitigated by keeping them blinded to the study's purpose (i.e., whether it is superiority, equivalence, or non-inferiority).

b. How masking will be achieved:

Patients will be blinded to the assigned intervention because orotracheal intubation is performed under general anesthesia. However, knowledge of the device is not anticipated to impact on the effect size.

The investigator responsible for statistical analysis will be blinded to the intervention groups. This will be implemented by blinded coding in the study database within the REDCap® platform, which allows concealing group names and working with neutral labels (Group A and Group B).

c. Emergency unblinding:

Because the study compares two widely known medical devices, approved by INVIMA and used in routine patient care (C-MAC and Laringocel), and because the intervention is performed under general anesthesia, no clinical circumstances are anticipated in which knowledge of group assignment is essential for patient management. Additionally, operators are not blinded and know the assigned device from the outset. For these reasons, a formal emergency unblinding procedure is not contemplated in the protocol. Any adverse situation will be managed according to institutional clinical guidelines, regardless of the assigned group.

VII. Methods: Data Collection, Management, and Analysis

25. Data Collection Methods

a. Plans for assessment and data collection

i. Baseline characteristics

Through physical examination and review of the medical record conducted by the recruiting investigator, the following demographic and clinical variables will be recorded: age, body mass index (BMI), sex, place of origin, educational level, Mallampati classification, dentition status, mouth opening and ability for mandibular protrusion, type of surgical procedure, number of previous surgeries, patient status, surgical risk, type of surgery, surgery time, and anesthesia time.

ii. Primary outcome Assessment

The study's primary endpoint will be first-attempt intubation success, defined as successful placement of the orotracheal tube in the trachea without the need for a second attempt. For this study, an intubation attempt will be considered complete when the videolaryngoscope is inserted into the oral cavity and withdrawn after attempting placement of the endotracheal tube. Intubation will be considered successful when, after the attempt, correct placement is confirmed by continuous capnography tracing, a method with sensitivity and specificity close to 100% for verification of endotracheal intubation (59).

Intubation will be considered successful by capnography if a sustained exhaled CO_2 tracing is detected, meeting the following criteria:

1. The CO_2 level increases during expiration and decreases during inspiration.
2. The capnographic tracing shows consistent or increasing amplitude for at least 7 breaths.
3. The peak CO_2 amplitude is at least 7.5 mmHg above baseline.

4. The capnogram pattern is clinically appropriate, avoiding false readings in contexts incompatible with alveolar ventilation.

An attempt will be considered failed if there is a device switch, manipulation by a third party, withdrawal of the videolaryngoscope from the mouth, or absence of effective capnography.
Assessment of the primary endpoint will be performed using the video material obtained during intubation by an investigator.
Data will be stored in the institutional database (REDCap) and will be subject to internal audits to minimize data capture errors.

iii. **Secondary outcome assessment**

1. **Overall intubation percentage**

In this trial, overall intubation success is defined as successful placement of the orotracheal tube in the trachea in a maximum of three attempts using the same technique, in accordance with usual clinical practice. The same criteria used for first-attempt success will be maintained, including confirmation of correct tube placement by continuous capnography tracing.
The outcome will be assessed by the outcome-adjudicating investigator using video material, recording the total number of attempts required, the device, and any maneuvers used.
Intubation will be considered failed if there is protocol deviation.

2. **POGO**

After reviewing the intubation video material, the investigator will record in the electronic form a number between 0 and 100%, corresponding to the maximum Percentage of Glottic Opening. It is defined as the visual estimate of the proportion of the vocal cords or glottic opening seen during videolaryngoscopy; 0% indicates that no vocal cord structures are visualized, and 100% indicates complete visualization from the anterior to the posterior commissure of the vocal cords (60,61). Intermediate values correspond to the approximate estimate of the visible portion of the vocal cords.
POGO has shown inter-rater reliability of 0.614 (95% CI, 0.461–0.740) and accuracy (75.5%) significantly greater than Cormack–Lehane ($p < 0.001$) (62).

3. **Fremantle score**

After reviewing the intubation video material, the investigator will record the Fremantle score (63), which integrates:

- The best laryngeal view obtained (F = full view of the laryngeal inlet, P = partial view of the glottis, N = no laryngeal structures visible).

- Ease of intubation (1 = easy, tube passes on the first attempt; 2 = modified, requires additional attempts or non-predefined maneuvers; 3 = unattainable or technique abandoned).
- The device used for intubation—in this case, C-MAC D or Laringocel.

The Fremantle score allows relating the glottic view to intubation ease and the device used; it shows accuracy of 73.7% and inter-rater reliability of 0.618 (95% CI, 0.616–0.622), both superior to Cormack–Lehane ($p < 0.001$)
POGO and the Fremantle score are more reliable than the Cormack–Lehane classification for documenting the glottic view in videolaryngoscopy (62).

4. **Intubation time**

Intubation time with videolaryngoscope is defined as the interval between insertion of the blade into the oral cavity and the first positive capnography recording. The investigator will time the intubation by viewing the procedure's video material and will record it in the data collection form.

5. **Satisfaction**

After the intervention, the anesthesiologist in charge of the videolaryngoscopy will rate the device according to the following criteria (64) using a Likert scale:

- **Technical ease of use:**
  How easy was it to visualize the glottis?
  (1 = easy to 5 = difficult)
- **Physical ease of use**
  How comfortable was it to handle the device?
  (1 = easy to 5 = difficult)
- **Overall satisfaction**
  How satisfied were you with the device's performance? (1 = very satisfied to 5 = not at all satisfied)
- **Willingness to reuse**
  Would you use this device again for future intubations?
  (1 = I would like to use it to 5 = I would never use it again)

6. **SAGAT:**

Situational awareness of the external observer will be evaluated using an adaptation of SAGAT, focusing on three levels: perception, comprehension, and projection (56,65).
The external observer (medical students, nursing staff, or an anesthesiology resident), without taking part in the intubation, will evaluate the situation exclusively from the videolaryngoscope screen/monitor.

SAGAT assessment will be performed immediately after the procedure and recorded on a structured form using dichotomous responses defined for each level:

- **Perception**
  The observer's ability to recognize key anatomical structures on the screen will be evaluated. The observer will be asked: *Do you see the vocal cords?* YES/NO
- **Comprehension**
  The observer's ability to understand first-attempt intubation success/failure will be evaluated. The observer will be asked: *Was the patient intubated on the first attempt?* YES/NO.
- **Projection**
  The observer's ability to anticipate decision-making based on comprehension will be evaluated. The observer will be asked: *Is any additional maneuver needed regarding the previous point?* YES/NO. If YES, *which one?*

Data will be stored in the institutional database (REDCap) and will be subject to internal audits to minimize data capture errors.

7. **Adverse events**

Adverse events (dental loss, sore throat, and mucosal injuries) are events that may occur in the usual context of orotracheal intubation, whether with direct laryngoscopy or videolaryngoscopy, and will be reported in accordance with good clinical trial practices.

Upon arrival in the recovery room, the designated investigator will inspect the oral and pharyngeal cavity to identify evident mucosal injuries, dental loss, or other alterations. In addition, the patient will be asked about the presence or absence of sore throat.

In cases where patients are not extubated immediately, follow-up and evaluation by the investigator will be ensured once extubation occurs. All findings will be recorded on the data collection form.

b. Plans to promote patient retention and complete follow-up

For this trial, all randomized patients will complete their participation once extubation and the evaluation of safety outcomes have been performed. Loss to follow-up is not expected due to the short duration of the intervention.

Investigators will make reasonable efforts to ensure follow-up of each patient through extubation and evaluation of safety outcomes.

To minimize participant loss, various follow-up strategies will be implemented. A detailed record will be maintained with contact information and key clinical data that allow locating participants within the hospital in those patients who are not extubated immediately in the operating room.

Participants have the right to withdraw from the study at any time and for any reason.

26. Data Management

Study data will be collected through electronic forms and subsequently stored in the institutional database (REDCap).

Data entry will be local and carried out by the investigators responsible for capture. Variables will be coded and categorized according to their nature, level of measurement, form of relationship, and unit of measurement (see Table 4). To ensure security and access control, the cloud database will be accessible only to authorized investigators, who must have specific permissions associated with their institutional email.

To promote data quality and accuracy, an internal audit process will be implemented, whereby an investigator different from the one who performed the initial capture will review the database to identify possible inconsistencies. In addition, backups of the cloud database will be created every 72 hours to prevent data loss.

27. Statistical Methods

a. Between-group comparisons

i. Baseline characteristics

Clinical and demographic characteristics of participants will be described in Table 5. Quantitative variables will be summarized with mean and standard deviation (SD) when they follow a normal distribution (assessed using the Shapiro–Wilk test and graphical methods), and with median and interquartile range (IQR) when normality is not met. Qualitative variables will be reported as absolute frequencies (n) and percentages (%).

No statistical comparisons between groups will be performed for baseline variables, in accordance with good reporting practices in randomized clinical trials, since random allocation aims to balance characteristics between groups and any observed differences are assumed to be due to chance.

Baseline demographic and clinical characteristics of patients		
Characteristics	**Laringocel (n=)**	**C-MAC D-Blade (n=)**

Age, years		
Sex — n (%) Female Male	 x x	 x x
Weight, kg		
Height, cm		
BMI, kg/m²		
Place of residence, n (%) Urban Rural	 x x	 x x
Mallampati classification — n (%) I II III IV	 x x x x	 x x x x
Number of previous surgeries	x	x
Dentition status — n (%) Good Poor Edentulous	 x x x	 x x x
ASA classification — n (%) ASA I ASA II ASA III	 x x x	 x x x
Patient status — n (%) Outpatient Inpatient	 x x	 x x
Surgical risk — n (%) Low risk Moderate risk High risk	 x x x	 x x x
Surgical specialty/model, n (%) General surgery Orthopedic Urologic Gynecologic Neurosurgical Plastic surgery Otorhinolaryngology Ophthalmology Vascular Other	 x x x x x x x x x x	 x x x x x x x x x x
General anesthesia technique, n (%) Balanced — halogenated agents Total intravenous anesthesia	 x	 x
Surgery time, min	x	x
Anesthesia time, min	x	x

Thyromental distance, cm	x	x
Sternomental distance, cm	x	x
Thyromental height, mm	x	x
Neck circumference, cm	x	x
Inter-incisor distance, cm	x	x
Cervical spine mobility n (%) Normal, Reduced Fixed	x	x
Upper-lip bite test, n (%) I II III	x	x

Table 5. Baseline characteristics of participants. μ: mean; SD: standard deviation; kg: kilograms; cm: centimeters; BMI: body mass index; ASA: American Society of Anesthesiology; Me: median; IQR: interquartile range.

ii. **Primary endpoint**

Difference in proportions at first intubation attempt.

a. **Null hypothesis**

$$\pi Laringocel - \pi CMD \leq -\delta$$

b. **Alternative hypothesis**

$$\pi Laringocel - \pi CMD > -\delta$$

To evaluate non-inferiority in the difference in proportions of successful first-attempt intubation between Laringocel and C-MAC, the Farrington and Manning test will be applied, as it is considered a robust method for non-inferiority trials with binary outcomes. The non-inferiority delta is defined ($\delta - 0.08$), reflecting the maximum acceptable difference for Laringocel to be considered non-inferior to C-MAC D-BLADE

This approach explicitly incorporates the non-inferiority hypothesis (the tolerance that Laringocel may be up to a certain margin Δ non-inferior to the standard) into the variance estimation. In this way, equations are solved that adjust the proportions assuming the difference stipulated by the non-inferiority margin, and then the test statistic and confidence interval are calculated based on that “restricted” variance. This procedure reduces the risk of underestimating uncertainty when success proportions are very high and provides a more robust framework for concluding whether Laringocel is non-inferior to C-MAC (66–68).

$$ZFM = \frac{(\widehat{p_1} - \widehat{p_2}) - (-\Delta)}{\sqrt{\frac{\widetilde{p_1}(1-\widetilde{p_1})}{n1} + \frac{\widetilde{p_2}(1-\widetilde{p_2})}{n2}}} \quad (2)$$

Where:

- $\widehat{p_1}\ and\ \widehat{p_2}$ are the observed success proportions in the Laringocel and C-MAC groups, respectively.
- $-\Delta$ is the non-inferiority margin.
- $\widetilde{p_1}\ and\ \widetilde{p_2}$ are the "restricted" proportions estimated under the null hypothesis that $p1 - p2 = -\Delta$. These are obtained by solving maximum likelihood equations that impose this restriction.
- $n1\ and\ n2$ are the sample sizes of each group.
- The numerator compares the observed difference with the maximum tolerable difference $(-\Delta)$
- The denominator represents the variance adjusted to the non-inferiority hypothesis.

If the lower limit of the 90% CI is < 0.08, Laringocel will be considered non-inferior (see Figure 1).

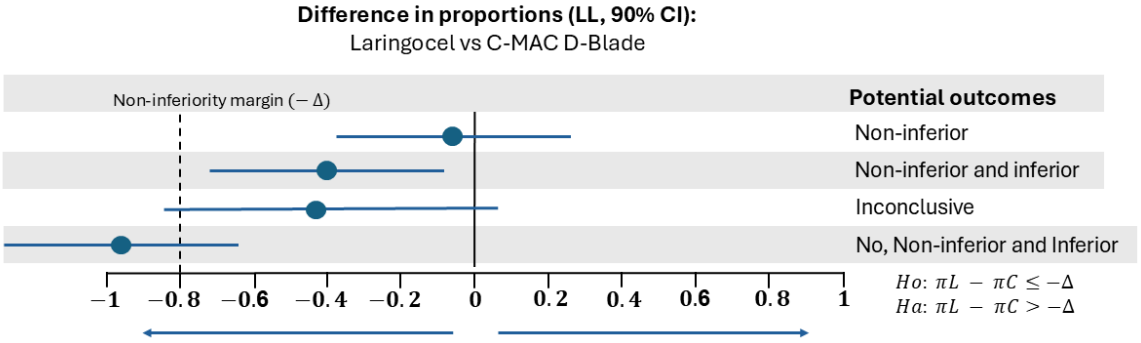

Figure 1. Potential outcomes for the difference in proportions between Laringocel and C-MAC D-Blade. LL: lower limit of the 90% CI.

Secondary outcomes will be considered exploratory. For these analyses, p-values and 95% confidence intervals will be reported without adjustment for multiplicity, since they do not constitute confirmatory hypotheses.

For comparison of quantitative variables between the Laringocel and C-MAC D-Blade groups, the Student's t test for independent samples will be used, provided the assumptions of normality of the distribution (assessed by the Shapiro–Wilk test) and homogeneity of variances (assessed by Levene's test) are met. If these assumptions

are not met, the nonparametric Mann–Whitney U test will be employed to compare medians between groups. Comparison of qualitative variables between groups will be conducted using Pearson's chi-square test, considering its use valid when at least 80% of expected cells have a frequency ≥5. If this criterion is not fulfilled, Fisher's exact test will be used.
Additionally, for the "projection" outcome of the SAGAT instrument, recognizing its logical dependence on the "comprehension" dimension, a logistic regression analysis will be applied, adjusting for the response at the comprehension level.

Multiplicity
Primary non-inferiority hypothesis will be evaluated with a one-sided significance level of α = 0.10.
Additionally, a serial gatekeeping procedure will be applied for three confirmatory secondary endpoints. Conditional on demonstrating non-inferiority, they will be assessed hierarchically with a two-sided significance level of α = 0.05 at each step, ensuring Type I error control via closed testing:

- **Intubation time:** if H_0 is rejected, then →
- **POGO:** if H_0 is rejected, then →
- **Operator satisfaction.**

If at any level H_0 cannot be rejected, the sequence stops and subsequent endpoints will not be analyzed confirmatorily.
Given the anticipated low incidence of adverse events, safety endpoints will be considered hypothesis-generating only and will not be subject to confirmatory testing. All other secondary endpoints will be classified as exploratory: only effect estimates will be reported, without p-values or confidence intervals, with no multiplicity adjustment and no confirmatory interpretation. Consequently, no inferential conclusions will be drawn from them.

iii. Secondary endpoints

Outcome	*Statistic*	*Hypothesis*	*Measure*	*Objective*
Overall success proportion	Proportion of success up to 3 attempts	$Ho: \pi L - \pi C \leq -0.05$ $Ha: \pi L - \pi C > -0.05$	Difference in proportions, RR, NNT (two-sided 95% CI)	Exploratory
POGO	Mean Percentage of Glottic Opening	$Ho: \mu L = \mu C$ $Ha: \mu L \neq \mu C$	Difference in means (95% CI)	Confirmatory

Fremantle score	Proportion in each ordinal category of the Fremantle score	$Ho: \pi LF = \pi CF;\ Ho: \pi LP = \pi CP;\ Ho: \pi LN = \pi CN;\ Ho: \pi L1 = \pi C2;\ Ho: \pi L3 = \pi C3. Ho: \pi LF = \pi CF$ $Ha: Al\ menos\ una\ \pi\ es\ \neq 0$	Absolute and relative frequencies of proportions (95% CI)	Exploratory
Intubation time	Mean in seconds	$Ho: \mu L = \mu C$ $Ha:\ \mu L \neq\ \mu C$	Mean by group (SD), difference in means (95% CI)	Confirmatory
Operator satisfaction	Average scores per item on the Likert scale (1 to 5)	$Ho: \mu L = \mu C$ $Ha:\ \mu L \neq\ \mu C$	Mean score by group, difference in means (95% CI)	Confirmatory
SAGAT	Proportion of overall loss of situational awareness	$Ho: \pi L = \pi C$ $Ha:\ \pi L \neq\ \pi C$	Proportion of participants with loss of situational awareness by group, difference in proportions (95%)	Exploratory
	Multinomial logistic regression for SAGAT failure and assigned group	Ho: No interaction exists between assigned group and SAGAT responses Ha: Interaction exists	OR of belonging to each SAGAT response category by assigned group, 95% CI	
Adverse events (harms)	Proportion of adverse events	$Ho: \pi L = \pi C$ $Ha:\ \pi L \neq\ \pi C$	RR, RAR, NND, difference in proportions (95% CI)	Hypothesis-generating

Table 6. Statistical analysis plan for secondary outcomes

b. Definition of who will be included in the analysis

The primary endpoint will be adjudicated under a per-protocol (PP) analysis, defined as all randomized participants who: (i) met all eligibility criteria; (ii) received the assigned device on the first attempt; (iii) had no prespecified major deviations as listed below; and (iv) have a valid measurement of the primary endpoint within the defined window.

Major deviations (trigger PP exclusion): (a) device change before outcome measurement; (b) non-permitted third-party intervention; (c) violation of eligibility criteria post-randomization; (d) use of co-interventions that impact the outcome; (e) absence of primary outcome measurement; (f) crossovers due to execution error; (g) exceeding the predefined maximum number of attempts.

Non-inferiority rule: Non-inferiority will be declared under the per-protocol analysis.

High adherence is anticipated; nevertheless, it could be compromised by major deviations such as crossover. To strengthen inference, a sensitivity per-protocol analysis will be performed using stabilized inverse probability weighting (IPW) among adherent participants $(A = 1)$ within the PP-eligible cohort. Stabilized weights will be applied as:

$$\boldsymbol{w_i} = \frac{\boldsymbol{Pr(A = 1|G_i)}}{\boldsymbol{P(A = 1)|\ G_i, X_i)}},$$

Where $\boldsymbol{G}$ is the assigned group and $\boldsymbol{X}$ are baseline pre-procedure covariates related to both adherence and the outcome based on clinical relevance and prior literature: Mallampati (49), intubator experience (21,69), body mass index (70), thyromental and sternomental distances, thyromental height, limited cervical motion (71), ASA classification, and other predictors of difficult airway.

The denominator $\boldsymbol{P(A = 1)|\ G_i, X_i)}$ will be modeled with multivariable logistic regression:

$$logit\{Pr\big(A = 1|G, X)\} = a_0 + a_g G + a_X X, \big)$$

and the numerator $\boldsymbol{Pr(A = 1|G_i)}$ will be the observed proportion of adherent participants within each arm.

Covariate balance after weighting will be evaluated using standardized mean differences (SMD), targeting $\boldsymbol{SMD < 0.10}$ for all covariates.

The weighted proportions of first-attempt intubation success will be:

$$\widehat{\boldsymbol{Pa}} = \frac{\sum_{\boldsymbol{i:}} \boldsymbol{G_{i=a,Ai=1} w_i Y_i)}}{\sum_{\boldsymbol{i:}} \boldsymbol{G_{i=a,Ai=1} w_i}}$$

And the difference in proportions will be $\hat{\Delta} = \ \widehat{P}_1 - \ \widehat{P}_0$ Confidence intervals will be obtained by bootstrap.

Complementarily, an intention-to-treat (ITT) analysis will be conducted, including all randomized patients and analyzing them in their originally assigned group, regardless of the device ultimately used or any protocol deviations.

c. Handling of missing data

The expected loss of data is low due to the intraoperative nature of outcome assessment; however, two types of missing data are anticipated in this trial: (1) missing data for the primary outcome (first-attempt intubation success), mainly related to participants who do not complete the assigned procedure (switch of assigned device or no intubation), and (2) missing data for secondary outcomes (POGO, Fremantle, intubation time, operator satisfaction), which may be due to errors in video recording or loss to follow-up when extubation is postponed.
To prevent data loss, data will be collected continuously and systematically, using the REDCap system to ensure record quality and security.

For the primary outcome, a per-protocol analysis will be performed; that is, participants who are intubated with a device different from the one assigned or who withdraw from the trial before the intervention will be excluded from the main analysis so that the analysis reflects each device's performance.

Given that missing data in secondary outcomes (POGO, Fremantle, etc.) may be related to observed variables (device, operator experience), they will be assumed **MAR (Missing At Random)** and handled via multiple imputation (MICE) in R statistical software (v4.4.3, R Core Team 2025).

Variables included in the imputation procedure will be age, sex, device, intubation success, intubation time, operator satisfaction, SAGAT, and adverse events. Continuous variables that do not meet normality assumptions will be transformed, and categorical variables will be treated as factors.

Multiple imputation will be performed separately for each treatment group, generating 20 imputed datasets, and results will be combined using Rubin's Rules. Sensitivity analyses will include: (1) complete-case analysis, (2) MAR analysis with imputation, and (3) MNAR analysis, assuming that missingness represents negative outcomes.

d. Additional analysis methods

The performance of the Laringocel and C-MAC D-Blade videolaryngoscopes will be evaluated in two prespecified subgroups, following ICEMAN recommendations (72).
The subgroup analysis will be applied only to the primary outcome (first-attempt intubation success), and effect-modifying interaction will be sought.
A multivariable logistic regression model will be used that includes:

- Device (Laringocel or C-MAC D-Blade)

- Subgroup variable (type of muscle relaxant or obesity)
- Interaction term between the device and the subgroup variable

The measure of association will be the odds ratio with its 95% confidence interval (95% CI), as well as the absolute success proportion (with 95% CI) for each device within each subgroup.
An interaction will be considered clinically relevant if it is consistent with the a priori hypothesis and the p-value of the interaction term is < 0.05.
This trial is designed to detect an overall difference in the primary outcome between videolaryngoscopes. By nature, subgroup analyses are underpowered to detect anything but large interaction effects. While we recognize the increased risk of Type I error with multiple comparisons, we will not apply a formal multiplicity adjustment, given the exploratory nature of these analyses. This limitation will be explicitly addressed in the interpretation of results.

The following subgroup analyses are planned:

(1) **Obesity:** The performance of the devices will be compared in obese patients (BMI ≥ 30 kg/m²) and non-obese patients (BMI < 30 kg/m (73).
Increased tissue mass in the airways and altered anatomy may hinder laryngoscopy. Our hypothesis is that videolaryngoscopes may show differential efficacy in obese patients compared with non-obese patients. The difference in the success proportion between videolaryngoscopes is expected to be more pronounced in obese patients. We recognize that the BMI cutoff of 30 kg/m² for obesity is arbitrary. We will perform a sensitivity analysis using BMI as a continuous variable to assess the robustness of the findings related to obesity.

(2) **Type of muscle relaxant:** Device performance will be evaluated according to the type of muscle relaxant used: depolarizing (succinylcholine) and non-depolarizing (rocuronium, vecuronium, cisatracurium). This subgroup analysis is based on pharmacological differences among muscle relaxants and their influence on intubation conditions (74,75).
Succinylcholine is expected to provide faster and more complete neuromuscular relaxation compared with non-depolarizing agents. Our hypothesis is that videolaryngoscope performance may differ when non-depolarizing drugs are used, potentially due to variations in the speed and quality of airway exposure. Rocuronium is expected to have better results than cisatracurium and vecuronium.
    a. Rocuronium: Rapid onset, intermediate duration.
    b. Vecuronium: Slower onset, intermediate duration.
    c. Cisatracurium: Slow onset, intermediate duration, elimination independent of renal/hepatic function.

d. Succinylcholine: Ultra-rapid onset, ultra-short duration.

VIII. Methods: Monitoring

28. Data Monitoring Committee

a. Data monitoring

Due to the nature of this trial —a single, short-duration procedure performed by specialists in Anesthesiology as part of routine practice and usual care, which does not involve prolonged treatment administration or long-term follow-up— the establishment of a Data Monitoring Committee is not considered necessary.

b. Interim analysis

No interim analyses or interim assessments are planned for this clinical trial. This decision is based on the relatively rapid recruitment and the collection of immediate intraoperative outcomes.

29. Trial Monitoring

Because this study is short in duration, with a single intervention and immediate outcome collection, independent external audits are not contemplated. Nevertheless, internal quality control mechanisms will be implemented, led by the research team, to verify protocol compliance. These actions will include:

- Cross-review every 15 days of the data collection forms.
- Random verification of records through review of the recorded intubation videos.

All study information will be stored in a database with restricted access control and will be available for evaluation by the institutional ethics committee if required. Given that there is no external sponsor or institutional/commercial funding, oversight and compliance functions will be carried out exclusively by the research team, following Good Clinical Practice principles and local ethical guidelines.

IX. Ethics

30. Ethics Committee Approval

This clinical trial will be conducted in accordance with the principles of the Belmont Report—respect for persons, beneficence, and justice (76), the Declaration of Helsinki (77) and the 2016 CIOMS Guidelines (78). It will also adhere to harmonized Good Clinical Practice ICH E6(R3). In the Colombian context, current regulations will be

followed, in particular Resolution 8430 of 1993 of the Ministry of Health and the personal data protection regime (Law 1581 of 2012 and Decree 1377 of 2013) (79,80).
The study design and conduct will be evaluated against the seven ethical requirements proposed by Emanuel et al.—social value, scientific validity, fair subject selection, favorable risk–benefit ratio, independent review, informed consent, and respect for participants — (81).
The protocol will be reviewed and approved by the Research Ethics Committee of Hospital Alma Máter de Antioquia, within the framework of the master's thesis of the Master's Program in Clinical Epidemiology at the University of Antioquia.

In accordance with the Belmont principles, respect for persons and autonomy will be ensured through free and informed consent that is clear and understandable, explaining the research nature of the project, voluntary participation, random assignment of the device, and the patient's right to withdraw at any time without affecting their usual medical care.

In terms of benefits for participants, videolaryngoscopes will be used in both arms. The anesthesiology literature recognizes them as a first-line strategy for orotracheal intubation, being associated with higher first-attempt success rates and a lower probability of failed intubation compared with direct laryngoscopy, which would be a device likely chosen in the absence of the trial. Videolaryngoscopes are routine practice, have INVIMA registration, and do not entail procedures beyond what the patient would receive as part of standard care. Additionally, patients will be closely followed by the research team from their initial assessment through the post-extubation evaluation, which will allow timely detection of difficult airway and oral cavity injuries. If any of the above are detected, timely referral to the appropriate services will be ensured.

With respect to the technological niche in Medellín and Colombia, the trial will generate local comparative clinical evidence on the performance of a videolaryngoscope developed and assembled in the country. This information will be valuable for acquisition decision-making, for the formulation of institutional policies, and for recommendations in clinical practice guidelines. Likewise, access to new technologies may extend to the training of medical students, general practitioners, and residents in anesthesiology, critical care, and emergency medicine. Regarding scientific output, the study contemplates public data registration, publication of a scientific article, and the availability of an anonymized dataset for secondary research, subject to ethics approval and data use agreements.

The principle of nonmaleficence is preserved because, in the event of failure of the assigned device or if the anesthesiologist considers that patient safety could be compromised, the protocol allows an immediate switch to an alternative intubation strategy without the need to withdraw the participant. Standardized monitoring of adverse

events is also maintained during the intraoperative period and in the immediate postoperative period. Standardized adverse event surveillance will be implemented (mandatory capnography and clinical evaluation after extubation), always ensuring patient safety.

The study contributes to the principle of justice because it seeks to answer a research question that may have a direct impact on populations with limited resources by evaluating a domestically produced device (Laringocel) that is potentially more accessible and economical compared with higher-cost international alternatives. Additionally, Colombian clinical practice guidelines recommend the use of this device and acknowledge its economic limitations.

Risk classification and risk/benefit analysis

With regard to risk classification, in accordance with Resolution 8430 of 1993, this trial is considered to involve greater-than-minimal risk, given that an intervention is performed on patients. However, participation in the study does not expose patients to risks beyond those inherent to orotracheal intubation—a procedure that is part of standard clinical practice in anesthesia. The potential risks related to videolaryngoscopy have been identified and limited.

Risks of the intubation procedure (common to both arms): Transient hypoxemia, esophageal intubation, transient pharyngolaryngeal symptoms such as sore throat, hoarseness, or cough, and dental trauma. All of these events are described as infrequent (see section on expected adverse events), self-limited in most cases, and manageable by the clinical team (10,44,50). Low and comparable frequencies between arms are expected, as both are hyperangulated videolaryngoscopes operated by trained clinicians. No serious adverse events or significant harm attributable to the intervention are anticipated.

The potential benefits (common to both arms) outweigh these risks, as participants will have access to first-line airway devices, with a higher probability of first-attempt success, a lower proportion of esophageal intubation, and reductions in failed intubation and postoperative pharyngolaryngeal symptoms compared with direct laryngoscopy. In addition, there is the indirect benefit of close monitoring by the research team, systematic verification of placement (continuous capnography), active AE recording, and timely management; and at the societal level, the trial will generate local evidence on the effectiveness and safety of a device developed in Colombia, potentially more accessible to the health system, with an impact on equity and availability.

Risk control:

Risk	Source	Expected probability	Mitigations	Residual risk
Transient hypoxemia	Intubation time, desaturation	Low	Preoxygenation, limit of three attempts, capnography, rescue plan	Low
Esophageal intubation	Trajectory error	Low	Glottic visualization, stylet, mandatory $ETCO_2$	Very low
Oropharyngeal/dental trauma	Levering, contact with teeth/tissues	Very low	VL technique without levering, anesthesiologist with CUSUM	Very low
Device failure	Optics/condensation	Very low	Pre-procedure functional check, backup device	Very low

The assessment of this information and its therapeutic impact will be at the sole discretion of the treating clinical team. In line with the bioethical principles established in the Declaration of Helsinki, the research team reaffirms its commitment to seeking the greatest possible benefit for patients. Any information generated during the procedure that has immediate clinical relevance will be communicated in real time to the care team, without waiting for the final analysis of the study. The interpretation and potential therapeutic implementation of such information will be the exclusive responsibility of the treating clinical team.

Regarding participant selection, the inclusion and exclusion criteria do not entail targeted selection of vulnerable populations. The intubation procedure under evaluation constitutes a routine component of anesthetic management, performed by trained professionals under controlled conditions. Individuals such as general physicians, residents, and medical students are excluded as intervention administrators. Participation in the study does not modify the usual course of care nor alter the clinical indications for orotracheal intubation.

The research group undertakes to adhere strictly to a rigorous methodological design, ensuring the quality of the data collected and of the inferences derived from them. Likewise, the protocol will remain under the continuous oversight and scrutiny of the technical and ethics committees for research. We consider the participation of external evaluators indispensable, as from an independent perspective they can identify opportunities for improvement and ensure that the principles guiding this study are upheld throughout its execution.

Transparent dissemination of the results and their public registration on ClinicalTrials.gov are anticipated once the corresponding approvals are obtained.

In summary, the risk–benefit balance is favorable: foreseeable risks are infrequent and mitigable, while the potential benefits—both for participants and for the medical community and the health system—are pertinent and socially valuable.

31. Protocol Amendments

Any modification to the protocol that could impact study conduct, participant safety, potential benefit, or ethical integrity (including changes to objectives, eligibility criteria, sample size, procedures, outcomes, or statistical analyses) will be considered a protocol amendment.
These modifications will require review and approval by the Research Ethics Committee of Hospital Alma Máter de Antioquia.
Amendments will be communicated to all stakeholders prior to implementation, including the research team, ethics committees, and public registries on ClinicalTrials.gov. All protocol versions will be uniquely identified by a version number and update date.

32. Informed Consent

a. Who will obtain informed consent and how

The investigator responsible for recruitment will disclose and obtain informed consent. Prior to enrollment in the trial, all candidates will receive a clear and comprehensive explanation of the research nature, detailing the study objectives, expected social and participant benefits, procedures, possible risks (mucosal injury, dental loss, or pharyngeal pain), and the possibility of withdrawing at any time without repercussions on their medical care.
The process will be complemented by provision of a written informed consent document, which will be read together with the participant. Consent will be signed by the participant before any study-related procedure and will be filed in the trial documentation.

b. Biological samples

No biological samples will be collected from participants. However, data gathered during the study—including clinical, video, and outcome information—may be used in future research that meets ethical requirements.
Participants will be informed that their data may be used for additional research purposes. The consent form will include a specific option for participants to grant or decline consent for future use of their data. Those who grant consent may withdraw it at any time by contacting the principal investigator directly.
Data will be anonymized and stored on the REDCap platform. These data will be retained for a minimum of five years after study completion, ensuring their integrity and availability for future research.

Only the principal investigator (GRM) and authorized personnel will have access to identifiable data, whereas investigators participating in future studies will only be able to access anonymized data.

Access to data for future research will be subject to approval by the Research Ethics Committee. Investigators wishing to use these data must submit a formal request describing the study objective and ensuring compliance with ethical requirements.

33. Confidentiality

Access to data will require a personal, non-transferable password granted following approval by the ethics and technical committees of Hospital Alma Máter de Antioquia for the REDCap database.

Electronic data will be managed through the institutional REDCap platform, which has encryption systems and password-controlled access.

Only the authorized research team will have access to the information, which will be handled confidentially.

Study results will be reported without including information that would allow participant identification

34. Ancillary and Post-Trial Care

This trial evaluates videolaryngoscopy devices that are part of the usual armamentarium available to anesthesiologists, without introducing experimental interventions beyond standard clinical practice. Therefore, no additional ancillary care needs are anticipated as a result of participation in the trial.

If any adverse event occurs during the procedure, it will be managed by the responsible medical team as part of standard care.

X. Appendices

35. Appendix B. PRECIS

a. **Step 1: What design approach are you adopting?**

   The stance regarding the trial focuses on answering whether the Laringocel videolaryngoscope is non-inferior under usual clinical practice conditions, compared with C-MAC® D-BLADE. The design aims for a pragmatic approach.

b. **Step 2: Consider your trial design options for each PRECIS-2 domain**

c. Step 3: Score the options chosen in Step 2 from 1 to 5 and plot on the PRECIS-2 wheel

a. 1. Very explanatory
b. 2. Rather explanatory
c. 3. Equally pragmatic and explanatory
d. 4. Rather pragmatic
e. 5. Very pragmatic

Item	Rating	Justification
Eligibility	4	The trial will include patients who reflect usual care conditions in the context of orotracheal intubation, specifically those scheduled for elective surgery under general anesthesia. However, patients with an anticipated difficult airway will be excluded, since this scenario shifts the context from intubation under general anesthesia to awake intubation. Although these patients could potentially benefit from the intervention, they will not be considered in this trial due to differences in the clinical conditions and technical requirements.
Recruitment	5	Patients will be selected directly from the usual surgical scheduling flow at Hospital Alma Máter, either on the same day their elective surgeries are scheduled or at the pre-anesthesia consultation. No campaigns or additional efforts will be undertaken to recruit participants outside this context.
Setting	5	Hospital Alma Máter de Antioquia, a tertiary-level center serving urban and rural populations primarily from the department of Antioquia, Colombia, caring for individuals covered by both contributory and subsidized health schemes.
Organization	4	The organization of the trial largely coincides with usual practice, since the personnel involved are anesthesiologists with standard specialized training in airway management and videolaryngoscopy. However, videolaryngoscopy is not a routine component of all operating rooms in Colombia; therefore, in centers that do not have the device, acquisition or arrangement of this additional resource will be required.
Flexibility in delivery of the intervention	4	Administration of the intervention will allow standard patient care with respect to anesthetic induction. Clinical judgment will guide neuromuscular relaxation (drug and dose). The time to initiate intubation is specified according to the drug chosen; this does not depart from what a trained anesthesiologist normally does. Up to three attempts with the same technique are allowed, and switching devices or performing additional maneuvers is permitted at the anesthesiologist's discretion, reflecting the flexibility of routine care. There are no restrictions on co-interventions, allowing the professional to apply any complementary measures deemed appropriate. For monitoring, a basic record of the procedure will be kept (number of attempts, assigned technique, intubation time, procedure video, and any

		device change or maneuver) and drug administration.
Flexibility in adherence	3	The trial mandates use of the assigned device on the first attempt and classifies as major deviations any device change, third-party intervention, or non-permitted co-interventions, which leads to exclusion from the per-protocol analysis. In addition, we standardized the procedure and required training with competency verification (CUSUM), measures that enhance adherence beyond routine practice. However, protocol deviations at the anesthesiologist's discretion are permitted.
Follow-up	4	For the primary outcome, no follow-up will be conducted after delivery of the intervention; however, the adverse event (safety) outcome entails follow-up 1 hour after extubation, which often is not part of usual care and represents additional personnel. No additional follow-up is planned for the other outcomes.
Primary outcome	4	The primary outcome will be first-attempt intubation success. Its importance lies in avoiding multiple intubation attempts and potential associated complications, which directly impacts patient safety (7,12). In addition, it is a commonly used indicator as a quality metric in both clinical practice and research (82). However, although it is highly relevant to anesthetic practice, it is not as directly patient-centered as outcomes tied to the patient's experience or postoperative recovery.
Primary analysis	4	Primary outcome analysis will be per protocol because this is a non-inferiority trial; however, intention-to-treat sensitivity analyses will be performed.

Table 7. PRECIS-2 ratings

d. Step 4: Review the PRECIS-2 wheel

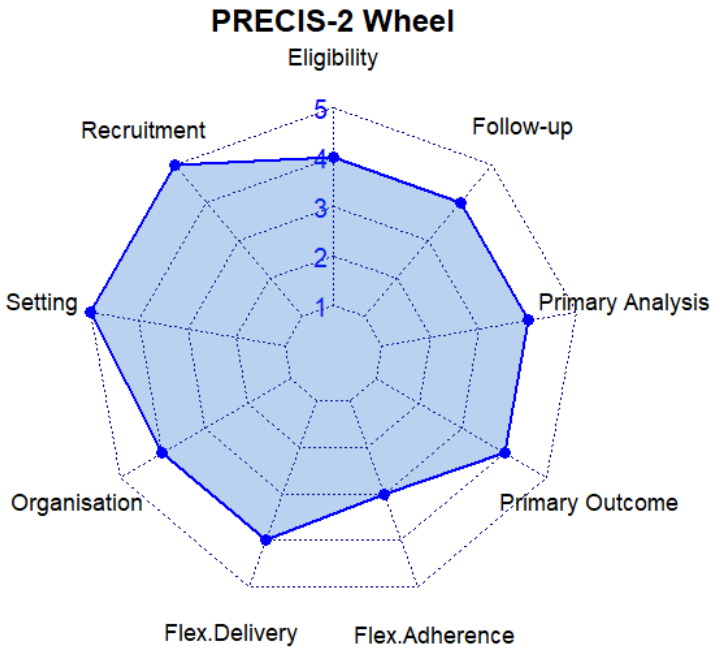

Figure 2. PRECIS-2 graphical tool. Taken and adapted from: Loudon K, et al. The PRECIS-2 tool designing trials that are fit for purpose. BMJ;350:h2147

36. Appendix C. List of operational sites.

Site name	Address	Site type	Number of operating rooms	Services included in the trial	Assigned investigators
Hospital Alma Máter – Hospital-based	Calle 69 #51C–24, Medellín, Sevilla neighborhood	High-complexity hospital	14 operating rooms	Main recruitment center	
Hospital Alma Máter – Ambulatory site	Carrera 51A #62–42, Medellín, Prado neighborhood	Ambulatory surgical center	4 operating rooms		

37. Appendix D. Operational table of variables

Variable	Operational definition	Nature	Scale	Unit or code
eda	Age	Quantitative continuous	Ratio	Years
gen	Gender	Qualitative	Nominal	0. Female; 1. Male
pes	Weight	Quantitative continuous	Ratio	Kilograms (kg)

tal	Height	Quantitative continuous	Ratio	Centimeters (cm)
imc	Body mass index (BMI)	Quantitative continuous	Ratio	Kilograms per square meter (kg/m^2)
pro	Place of residence	Qualitative	Nominal	0. Rural; 1. Urban
mal	Mallampati	Qualitative	Ordinal	1. I; 2. II; 3. III; 4. IV
pre	Number of previous surgeries	Quantitative discrete	Ratio	Integer
den	Dentition status	Qualitative	Ordinal	0. Good; 1. Poor; 2. Edentulous
asa	ASA classification	Qualitative	Ordinal	1. I; 2. II; 3. III; 4. IV; 5. V; 6. VI
sta	Patient status	Qualitative	Nominal	0. Outpatient; 1. Inpatient
rie	Surgical risk	Qualitative	Ordinal	0. Low risk; 1. Moderate risk; 2. High risk
mod	Surgical specialty/model	Qualitative	Nominal	0. General surgery; 1. Orthopedic; 2. Urologic; 3. Gynecologic; 4. Neurosurgical; 5. Plastic surgery; 6. Otorhinolaryngology; 7. Ophthalmology; 8. Vascular; 9. Other
tec	General anesthesia technique	Qualitative	Nominal	1. Balanced —

				halogenated agents; 2. Total intravenous
tq	Surgery time	Quantitative continuous	Ratio	Minutes (min)
ta	Anesthesia time	Quantitative continuous	Ratio	Minutes (min)
ti	Intubation time	Quantitative continuous	Ratio	Seconds (s)
lar	Type of laryngoscope used	Qualitative	Nominal	0. C-MAC; 1. Laringocel; 2. Direct laryngoscope
pog	Percentage of Glottic Opening (POGO)	Quantitative continuous	Ratio	0 to 100%
nii	Number of intubation attempts	Quantitative discrete	Ratio	Integer
Frv	Best laryngeal view (Fremantle)	Qualitative	Ordinal	F = Full; P = Partial; N = Not visible
frf	Ease of intubation (Fremantle)	Qualitative	Ordinal	1. Easy; 2. Modified; 3. Unattainable
sat	Operator satisfaction	Qualitative	Ordinal	1–5
sgp	Perception (SAGAT)	Qualitative	Dichotomous	1. Yes; 2. No
sgc	Comprehension (SAGAT)	Qualitative	Dichotomous	1. Yes; 2. No
sgy	Projection (SAGAT)	Qualitative	Dichotomous (with open-	1. Yes; 2. No

			ended description if applicable)	
ext	Place of extubation	Qualitative	Nominal	1. Operating room; 2. ICU; 3. Recovery room; 4. Inpatient ward; 5. Other
adv	Dental loss (Adverse event)	Qualitative	Dichotomous	1. Yes; 2. No
adl	Mucosal injury (Adverse event)	Qualitative	Dichotomous	1. Yes; 2. No
add	Postoperative sore throat (Adverse event)	Qualitative	Dichotomous	1. Yes; 2. No
tmd	Thyromental distance	Quantitative continuous	Ratio	Centimeters (cm)
srd	Sternomental distance	Quantitative continuous	Ratio	Centimeters (cm)
tmh	Thyromental height	Quantitative continuous	Ratio	Millimeters (mm)
nc	Neck circumference	Quantitative continuous	Ratio	Centimeters (cm)
iid	Inter-incisor distance	Quantitative continuous	Ratio	Centimeters (cm)
csm	Cervical spine mobility n	Qualitative	Ordinal	1. Normal; 2. Reduced; 3. Fixed
upt	Upper-lip bite test	Qualitative	nominal	I-III

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