This submission includes:

1. Original statistical analysis plan

Statistical Analysis Plan (SAP)

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1. 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	x	x
Male	x	x
Weight, kg		
Height, cm		
BMI, kg/m²		
Place of residence, n (%)		
Urban	x	x
Rural	x	x
Mallampati classification — n (%)	x	x
I	x	x
II	x	x
III	x	x
IV		
Number of previous surgeries	x	x
Dentition status — n (%)		
Good	x	x
Poor	x	x
Edentulous	x	x
ASA classification — n (%)		
ASA I	x	x
ASA II	x	x
ASA III	x	x
Patient status — n (%)		
Outpatient	x	x

Inpatient	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	 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 (1,2).

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

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).

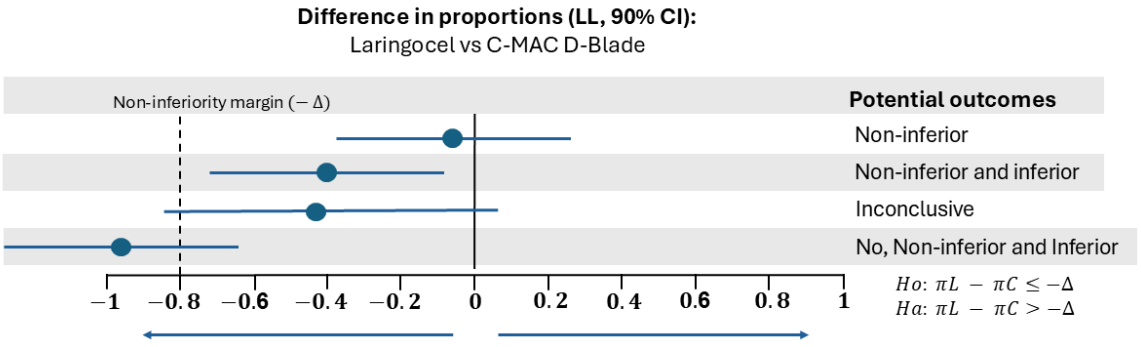

Figure 1. Potential outcomes for the difference in proportions between Laringocel and C-MAC D-Blade. LL: lower limit of the 90% CI.

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	$Ho: \pi L = \pi C$ $Ha: \pi L \neq \pi C$	Proportion of participants with	Exploratory

	situational awareness		loss of situational awareness by group, difference in proportions (95%)	
	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:

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

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 (3), intubator experience (4,5), body mass index (6), thyromental and sternomental distances, thyromental height, limited cervical motion (7), 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:

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

And the difference in proportions will be $\hat{\Delta} = \hat{P}_1 - \hat{P}_0$ 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 (8).
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 (9).
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 (10,11).
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

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