Title: No Post Intubation Laryngeal Symptoms (No-PILS)
NCT05383417
Date: April 12, 2023

## Study Protocol

### Description:

Single center randomized controlled trial with 100 subjects who will be intubated for already planned surgeries. The participants will be randomized into the control group or the clip group. The clip group will have a small clip (the endotracheal tube support device, also known as EndoClip) placed on the endotracheal tube to reduce the pressure on the vocal cords and larynx. This endotracheal tube support device is made from a FDA approved biocompatible material. The University of California San Diego Institutional Review Board (“IRB”) approved this study (IRB #800842).

The control group subjects will undergo their planned procedure with no intervention during intubation. The clip group will undergo their planned procedure as normal but with the EndoClip placed on the endotracheal tube by the assigned anesthesia attending physician or trained clinician. The EndoClip is placed once the tube is secured and the ventilator circuit is connected. While extubating the patient, the endotracheal tube will be removed with the EndoClip attached and a picture of the tube will be taken to record the clip location.

Before the planned procedure, the investigators will survey the participants to get a baseline for any pre-existing laryngeal symptoms. The same survey will be administered after the procedure when the participants are awake and alert (‘Day 0’), 24 hours (‘Day 1), 48 hours (‘Day 2’), and 1 week (‘Day 7’) after the procedure. The survey will ask the participant to indicate "yes" or "no" for whether they are experiencing a sore throat, throat pain, oral pain, difficulty speaking, difficulty swallowing, changes in their voice, pain while speaking, and pain while swallowing. If they have indicated "yes" for any of the symptoms, the participants will also be asked to rate the severity on scale from 0 (no pain/difficulty) to 10 (severe pain/difficulty). If they indicate “no”, this will be considered a score of 0 for the respective outcome variable.

Other data points will also be collected in this study that are related to the intubation and participant's airway. The investigators will record the total time of the procedure and the length of time the clip is placed on the endotracheal tube. For each participant in the clip group, the investigators will also record the time it takes to place the clip on the endotracheal tube. Each participant's airway will be evaluated, and the investigators will record the thyromental distance, Mallampati score, history of difficult intubation, and the size of the endotracheal tube used. Lastly, data from each participant's intubation will be collected including number of attempts before successful intubation, incidence of dental injury, incidence of lip injury, laryngeal view on Cormack-Lehane scale, and any noted trauma upon extubation.

At any point during the study, the participant can withdraw from the study. All study participants will be identified according to a number assigned at the beginning of the study, using key code.

### Study Design:

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| Study Type: | Interventional |
| Primary Purpose: | Prevention |
| Study Phase: | Closed |
| Interventional Study Model: | Parallel Assignment |

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| | 2 arm parallel trial where one group will receive the endotracheal tube clip (EndoClip) during general endotracheal anesthesia and the other group will not (control) |
| Number of Arms: | 2 |
| Masking: | Double (Participant, Outcomes Assessor)<br><br>Patient will not be aware of their treatment arm. Investigator and Care Provider will be aware of treatment arm but data analysis (outcomes assessor) will be blinded to treatment groups. |
| Allocation: | Randomized |
| Enrollment: | 100 [Actual] |

**Arms and Interventions:**

| Arms | Assigned Interventions |
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| Experimental: EndoClip<br><br>Clip applied to endotracheal tube. | Device: EndoClip<br><br>Clip attached to mid portion of the endotracheal tube.<br><br>Other Names:<br><br>• Endotracheal tube clip<br>• Endotracheal tube support clop<br>• Endotracheal tube support device |
| No Intervention: No Clip<br><br>No clip applied to endotracheal tube. | |

**Outcome Measures:**

Primary Outcome Measure:

1. Sore throat on a scale from 0 (no sore throat) to 10 (worst possible sore throat). Subjects will indicate whether they are experiencing a sore throat or throat discomfort on a questionnaire. If they indicate 'yes' they will be asked to mark the severity of their symptoms on a scale ranging from 0 (no sore throat) to 10 (worst possible sore throat). Participants will be asked to report on their symptoms prior to intubation, after intubation on the day of discharge, 24 hours after intubation, 48 hours after intubation, and 1 week after intubation.
   [Time Frame: Baseline to 1 week after intervention]

2. Change in voice on a scale from 0 (no voice change) to 10 (most severe voice change). Subjects will indicate whether they are experiencing a change in voice (i.e. deep and/or hoarse voice, worse than their usual voice quality) on a questionnaire. If they indicate 'yes' they will be asked to mark the severity of their symptoms on a scale ranging from 0 (no voice change) to 10 (most severe voice change). Participants will be asked to report

on their symptoms prior to intubation, after intubation on the day of discharge, 24 hours after intubation, 48 hours after intubation, and 1 week after intubation.
[Time Frame: Baseline to 1 week after intervention]

3. Difficulty swallowing on a scale from 0 (no difficulty swallowing) to 10 (complete inability to swallow). Subjects will indicate whether they are experiencing difficulty swallowing on a questionnaire. If they indicate 'yes' they will be asked to mark the severity of their symptoms on a scale ranging from 0 (no difficulty swallowing) to 10 (complete inability to swallow). Participants will be asked to report on their symptoms prior to intubation, after intubation on the day of discharge, 24 hours after intubation, 48 hours after intubation, and 1 week after intubation.
[Time Frame: Baseline to 1 week after intervention]

4. Pain in the mouth on a scale from 0 (no mouth pain) to 10 (worst possible mouth pain). Subjects will indicate whether they are experiencing mouth pain on a questionnaire. If they indicate 'yes' they will be asked to mark the severity of their symptoms on a scale ranging from 0 (no mouth pain) to 10 (worst possible mouth pain). Participants will be asked to report on their symptoms prior to intubation, after intubation on the day of discharge, 24 hours after intubation, 48 hours after intubation, and 1 week after intubation.
[Time Frame: Baseline to 1 week after intervention]

5. Difficulty talking on a scale from 0 (no difficulty talking) to 10 (complete inability to talk). Subjects will indicate whether they are experiencing difficulty talking on a questionnaire. If they indicate 'yes' they will be asked to mark the severity of their symptoms on a scale ranging from 0 (no difficulty talking) to 10 (complete inability to talk). Participants will be asked to report on their symptoms prior to intubation, after intubation on the day of discharge, 24 hours after intubation, 48 hours after intubation, and 1 week after intubation.
[Time Frame: Baseline to 1 week after intervention]

6. Pain in the neck/chest on scale from 0 (no neck/chest pain) to 10 (worst possible neck/chest pain). Subjects will indicate whether they are experiencing pain in the anterior or low region of the neck and/or chest on a questionnaire. If they indicate 'yes' they will be asked to mark the severity of their symptoms on a scale ranging from 0 (no neck/chest pain) to 10 (worst possible neck/chest pain). Participants will be asked to report on their symptoms prior to intubation, after intubation on the day of discharge, 24 hours after intubation, 48 hours after intubation, and 1 week after intubation.
[Time Frame: Baseline to 1 week after intervention]

**Eligibility:**

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| Minimum Age: | 18 Years |
| Maximum Age: | |
| Sex: | All |
| Gender Based: | No |
| Accepts Healthy Volunteers: | Yes |
| Criteria: | Inclusion Criteria:<br>• Patient undergoing general endotracheal anesthesia with an endotracheal tube |

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| | • Patient is not undergoing a procedure in the head and neck region<br>Exclusion Criteria:<br>• Patient with pre-existing severe sore throat, voice change, or trouble swallowing<br>• Patient undergoing surgery in the head and neck region |

**Statistical Analysis Plan**

Our statistical plan is outlined below.

- ● **Null Hypothesis**:

**NH1)** Reducing the force on the vocal cords will not change the laryngeal symptoms in participants who underwent Endotracheal Intubation
**NH2)** Reducing the force on the vocal cords will not change the duration of laryngeal symptoms in participants who underwent Endotracheal Intubation

- ● **Alternate Hypothesis**:

**AH1)** Reducing the force on the vocal cords will change the laryngeal symptoms in participants who underwent Endotracheal Intubation
**AH2)** Reducing the force on the vocal cords will change the duration of laryngeal symptoms in participants who underwent Endotracheal Intubation

We will use IBM SPSS Statistics, version 28.0.1.1 (14). Student's t-test will be used to compare symptom severity at each time point while Pearson's chi-square test will be used to compare the incidence of throat symptoms across groups. Multiple regression analysis will be used to evaluate demographic and anesthesia variables as predictors of throat symptoms. The odds ratio (OR) and their 95% confidence interval (CI) will be reported for each covariate included in the model. The level of significance ($p$) to be considered is 0.05.