Study Protocol and Statistical Analysis Plan

Official Title:

Efficacy and Safety of Low Pressure (–4 cmH_2O) Suction Compared With Physiologic Pressure (–8 cmH_2O) Suction Using a Digital Continuous Suction System After Pulmonary Resection: A Prospective Randomized Controlled Open-label Study.

ClinicalTrials.gov Identifier:

NCT number pending

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Protocol and Statistical Analysis Plan, Version 1.2

Protocol Synopsis (English, v1.2)

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Efficacy and Safety of Low Pressure (–4 cmH_2O) Suction Compared With Physiologic Pressure (–8 cmH_2O) Suction Using a Digital Continuous Suction System After Pulmonary Resection: A Prospective Randomized Controlled Open-label Study.

Sponsor / Funding

Seoul National University Hospital (Biomedical Research Institute).

Study Period

From IRB approval through August 30, 2026.
IRB number : 2507-104-1658

Design & Setting

Prospective, randomized, controlled, open-label, parallel-group trial at a single tertiary center.

Population & Sample Size

Adults undergoing anatomical lung resection (segmentectomy or lobectomy) for confirmed or suspected lung cancer at SNUH. Planned **N=160** (80 per arm).

Objective & Hypothesis

To determine whether maintaining **–4 cmH_2O** suction on a digital chest drainage system shortens chest-tube–related recovery metrics compared with **–8 cmH_2O**, without compromising safety, and to inform an optimal pressure protocol for digital systems.

Interventions (Arms)

- **Experimental**: A digital thoracic drainage device set to continuous suction at −4 cmH_2O, initiated on postoperative day 1 after randomization. The assigned suction pressure is maintained until chest tube removal unless predefined clinical safety criteria require adjustment. Air-leak flow and drainage volume are recorded as part of routine postoperative care.
- **No interventions**: A digital thoracic drainage device set to continuous suction at

−8 cmH_2O, initiated on postoperative day 1 after randomization. The assigned suction pressure is maintained until chest tube removal unless predefined clinical safety criteria require adjustment. Air-leak flow and drainage volume are recorded as part of routine postoperative care.

Randomization & Allocation

1:1 block randomization via the institutional web system. Allocation is concealed until the end of surgery; for eligible patients on POD1, the assigned pressure is set (typically around 07:00–08:00).

Consent & Eligibility Snapshot

Written informed consent is obtained on the day before surgery. Randomization occurs **only if a measurable air leak persists on POD1** and the chest tube is not removed per routine care. Patients with **no clinically meaningful air leak on POD1 (e.g., 0–10 mL/min)** are screen-fail and remain in routine care outside the comparative analysis.

Outcomes

Primary Outcome

- **Duration of postoperative air leak (days)**
  Description: Daily air-leak flow (mL/min) recorded by the digital chest drainage system (≈6 AM). Air-leak resolution is defined as no visible air leak or <10 mL/min sustained for ≥12 hours with adequate lung expansion on chest X-ray and stable clinical status. Duration is calculated in days from randomization (POD1) to resolution.
  Time Frame: Time Frame: From postoperative day 1 randomization to the date of air-leak resolution, assessed daily, up to 30 days postoperatively or until hospital discharge.

Key Secondary Outcomes

- **Chest tube duration (days)**

  Description: Number of calendar days the chest tube remains in place during the index hospitalization.

  Time Frame: Time Frame: From the date of surgery to the date of chest tube removal, assessed during the index hospitalization for up to 30 postoperative

days.

Subgroup / Interaction of Interest

- Effect modification by **POD1 air-leak flow**: <100 vs ≥100 mL/min.

Protocolized Management Criteria

Pleurodesis (per protocol)

Prefer delayed pleurodesis. Perform at **POD6** if ≥5 days of air leak with incomplete lung expansion; if persistent, consider again around **POD10**. After pleurodesis, temporarily set suction to **–20 cmH_2O for ~24 hours**; subsequent management at clinician discretion.

Chest Tube Removal (per protocol)

Proceed when all are met:

1. Adequate lung expansion on chest X-ray (a small, asymptomatic apical pneumothorax may be acceptable);
2. **24-hour drainage ≤250 mL** and serous/serosanguinous;
3. Clinical stability.

Sample Size & Timeline

Sample Size Plan

Planned **N=160** (80 per arm), allowing an interaction test by POD1 air-leak stratum (<100 vs ≥100 mL/min) with 1:1 allocation and reasonable power (two-sided α=0.05).

Timeline (Planned)

Enrollment Aug 2025–Apr 2026; analysis Sep 2025–Jun 2026; final report Jul–Aug 2026.

Interim Analysis, Monitoring, and Data Handling

Interim Analysis & Stopping

One interim analysis at ~50% enrollment using **O'Brien–Fleming** boundaries (two-sided $\alpha \approx 0.005$ interim; 0.048 final). Consider early stop for efficacy, safety (imbalanced complications), or futility (negligible effect size). Individual-patient safety permits pressure adjustment per predefined criteria.

Data & Safety Monitoring

PI-led monitoring with designated staff; routine tracking of accrual, randomization, protocol deviations, and safety events; periodic aggregate reviews (e.g., every 20 patients or monthly).

Data Management & Privacy

Coded IDs only; no direct identifiers in research datasets; restricted access to authorized personnel; secure storage; retain ≥3 years post-study then dispose per policy.

Statistical Methods

Analysis Populations

Primary analysis follows **intention-to-treat (ITT)**. A **modified ITT** set will exclude participants with no primary endpoint ascertainment; a **per-protocol (PP)** analysis will be conducted as sensitivity.

Primary Endpoint Analysis

Compare **–4 vs –8 cmH_2O** using a **two-way ANOVA** with factors: (1) randomized pressure (–4 vs –8) and (2) **POD1 air-leak stratum** (<100 vs ≥100 mL/min), including the **interaction term**. Assess normality (Shapiro–Wilk); if violated, use an aligned-rank transform ANOVA or appropriate transformation. Report effect sizes as mean differences (or Hodges–Lehmann median differences) with **95% CIs**; **two-sided α=0.05**.

Secondary Endpoints

- Continuous variables (e.g., air-leak duration, length of stay, peak air-leak): two-sample t-test or Mann–Whitney U as appropriate; model-based two-way ANOVA mirroring the primary model will be reported as supportive.
- Categorical variables (e.g., pleurodesis performed, suction readjustment, postoperative pulmonary complications, 30-day readmission): **χ^2** or **Fisher's exact** tests; **logistic regression** (including the interaction term) as supportive.
- Re-intervention rates: analyzed similarly; time-to-event methods considered only if censoring arises.

Covariate Sensitivity

Pre-specified models may adjust for surgical approach (VATS/RATS vs open), resection type (segmentectomy vs lobectomy), and side/lobe if imbalances occur.

Missing Data

For secondary endpoints with missingness, perform **multiple imputation** (assuming missing at random) with complete-case sensitivity analyses.