Safety, Feasibility, and Impact of Preoperative Respiratory Strength Training in Cardiac Surgical Patients

ClinicalTrials.org NCT04887415

University of Florida IRB202100993
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Study Protocol including Statistical Analysis Plan, 4/10/2022

Project Title:

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Research Personnel:

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Abstract:

The prevalence of postoperative dysphagia (swallowing impairment) is critically high in patients with cardiovascular disease who undergo cardiac surgery (CS) with estimates ranging from 3%-94%. Notably, postoperative dysphagia in CS patients has been linked to morbidity and mortality. A recent research study that prospectively examined postoperative dysphagia in a cohort of 182 CS patients revealed that CS patients who aspirated but had an effective cough response had reduced rates of pneumonia, intubation, death, and hospital readmission, and also had a shorter hospital length of stay (LOS)/reduced health care costs. These findings indicate that an effective cough response may lead to improved health-related outcomes in CS patients, implying that therapeutics focused on improving cough peak expiratory flow rate may be beneficial. Respiratory strength training (RST) is a treatment approach that has led to improvements in cough strength and effectiveness in a variety of patient populations with dysphagia. Given its effectiveness in improving pulmonary and swallow function in high-risk patients with dysphagia, implementing RST preoperatively may be an effective approach to prevent postoperative impairments in airway clearance physiologic capacity and swallowing, thereby mitigating postoperative adverse health-related outcomes. Therefore, this pilot research study will investigate the safety, feasibility, and impact of a preoperative RST program in CS patients with reduced airway clearance physiologic capacity via three specific aims: 1) Determine the safety and feasibility of a preoperative RST program; 2) Examine the impact of a preoperative RST program on expiratory, inspiratory, and airway clearance physiologic capacity; and 3) Investigate the impact of a preoperative RST program on swallowing safety and health-related outcomes in CS patients. To determine the safety and feasibility of RST, attendance at telehealth/in-person sessions, RST adherence, and adverse outcomes will be tracked. To examine the impact of RST on patient outcomes, longitudinal evaluations of breathing and swallowing will be performed, and health-related outcomes tracked. This is the first study to explore preoperative RST in CS patients to improve swallowing safety and mitigate adverse health-related outcomes. Findings will provide preliminary data to support clinical utility of preoperative RST in high-risk CS patients and will support further research in a larger cohort of CS patients to elucidate the efficacy of RST and to determine the optimal training regimen and patients who would benefit from RST.

SPECIFIC AIMS:

We seek to examine the safety, feasibility, and clinical utility of a preoperative respiratory strength training (RST) program in cardiac surgical (CS) patients with the following specific aims:

Aim 1: Test the hypothesis that a preoperative RST program will be safe and feasible in CS patients. *Approach:* CS patients will complete at-home RST with weekly telehealth sessions and one in-person session at mid-point. Attendance, RST adherence, and adverse events will be tracked.

Aim2: Test the hypothesis that a preoperative RST program will improve respiratory and airway clearance physiologic capacity in CS patients. *Approach:* Forced vital capacity, maximum expiratory and inspiratory pressure, voluntary cough peak expiratory flow, and cough spirometry metrics will be obtained before and immediately after RST. Functional measures of dyspnea and speech rate/pausing during speech will also be tracked (London Chest Activity of Daily Living scale [LCADL], Bamboo passage). Descriptive statistics and a repeated measures analysis will evaluate potential change in physiologic metrics of interest.

Aim 3: Test the hypothesis that a preoperative RST program will improve postoperative respiratory, swallowing and health-related outcomes. *Approach:* Following surgery, a fiberoptic endoscopic evaluation of swallowing will be performed and health-related outcomes examined.

Outcomes will provide needed 'proof of concept' feasibility and safety data and deliver preliminary insights into the potential role of a *proactive*, *targeted,* and *mechanistically guided* 'prehabilitation' for CS patients to improve airway clearance capacity and health-related outcomes. If hypotheses are confirmed, these data will support future large-scale clinical trials.

SIGNIFICANCE:

A reported 30.3 million Americans, or 12.1% of the population, are living with cardiovascular disease (CVD),[1] conferring an annual economic cost of ~$219 billion.[2] According to the American Heart Association, more than 1 million adults undergo cardiac surgical (CS) procedures in the United States annually, with this number expected to increase over the next decade.[3] Unfortunately, swallowing difficulty (dysphagia) is a common postoperative complication of CS that is associated with poor patient outcomes.[4–8] We recently conducted the first prospective study utilizing instrumental imaging techniques and validated swallowing outcomes in CS patients.[9] In the 182 CS patients examined with fiberoptic endoscopic evaluation of swallowing (FEES), unsafe swallowing was confirmed in 94% of patients (66% penetration, 29% aspiration) and inefficient swallowing (pharyngeal residue) in 52% (Fig. 1) following extubation.[9] Of significance was our findings that postoperative aspiration was associated with an 85-hour delay to resume oral intake, a 43% increased length of hospital stay, ~$50,000 increased cost of care, pneumonia (OR:2.6), reintubation (OR: 5.7), and death (OR: 2.8).[9] Swallowing profiles, aspiration risk factors, and associated outcomes from this study are summarized in Figure 1.

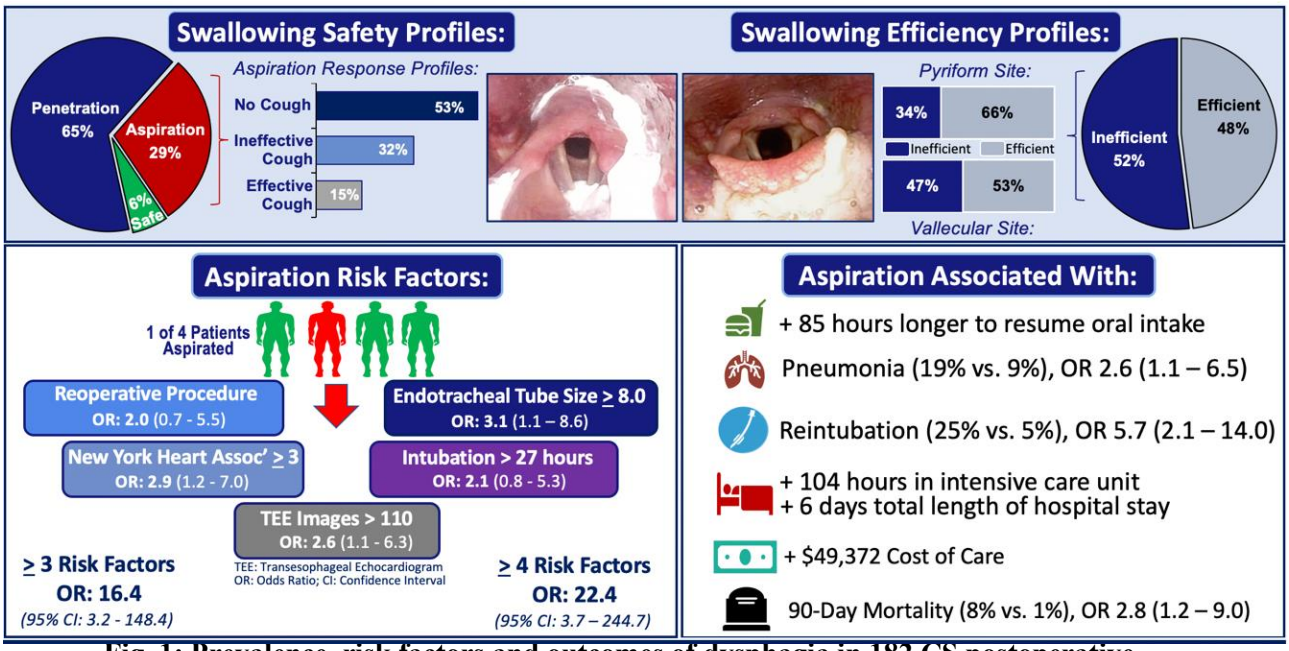

Fig. 1: Prevalence, risk factors and outcomes of dysphagia in 182 CS postoperative patients.[9]

Closer inspection of these data revealed significant differences in health-related outcomes among aspirating CS patients when stratified by cough response profiles. Specifically, aspirators who produced an effective cough to expel tracheal aspirate from the airway demonstrated significantly reduced rates of pneumonia, reintubation, mortality, readmission, LOS, and cost of care compared to aspirators who could not eject tracheal aspirate from the airway (Table 1).[9] Thus, a **CS patient's physiologic capacity to produce a strong and effective cough was a significant prognostic factor** in aspirating individuals. Given that **cough strength represents a modifiable physiologic variable**, this finding was of high clinical significance, *revealing a potential treatment target to improve CS patient outcomes* that motivate this proposal.

Table 1. CS patient outcomes stratified by cough response profiles to expel tracheal aspirate.[9]

Outcome: N (%)	CS Aspirators with:		CS Non-Aspirators:	P Value:
	Absent / Ineffective Cough	***Effective Cough:***		
Pneumonia	10/44 (23%)	**0/8 (0%)**	11/130 (9%)	**0.04***
Reintubation	13/45 (29%)	**0/8 (0%)**	7/130 (5%)	**<0.001***
90-day Mortality	4/44 (9%)	**0/8 (0%)**	1/130 (1%)	**0.04***
30-day Readmission	4/26 (15%)	**0/5 (0%)**	13/85 (15%)	0.33

Our data, combined with other published reports documenting suboptimal outcomes in aspirating CS patients,[4,5] highlight the *need for targeted interventions to improve swallowing and airway clearance abilities in CS patients that mitigate the development of associated sequelae and improve patient outcomes.* Unfortunately, no such intervention studies currently exist in the literature, resulting in gaps in knowledge and suboptimal patient care in this area.[10–12]

While many dysphagia risk factors cannot be modified, **airway physiologic capacity represents one dysphagic risk factor that can be modified (increased) via targeted exercise programs**. Respiratory strength training (RST) has been utilized across several high-risk dysphagia patient populations that is noted to improve physiologic and patient outcomes.[13–22] First applied in individuals with Parkinson's disease (PD), a 4-week RST was noted to increase cough effectiveness, swallowing safety (penetration-aspiration scale [PAS] scores), and hyolaryngeal excursion during swallowing.[13,16] Likewise, a 4-5 week RST program implemented in stroke survivors was reported to improve maximum expiratory pressure (MEP), cough peak expiratory flow, cough volume acceleration, reflexive urge to cough responses, and swallowing safety.[15,19] Similarly, in HNC patients with chronic radiation associated dysphagia, implementation of an 8-week RST program led to improved expiratory pressure generating capacity, swallowing safety, and patient reported quality of life.[14]

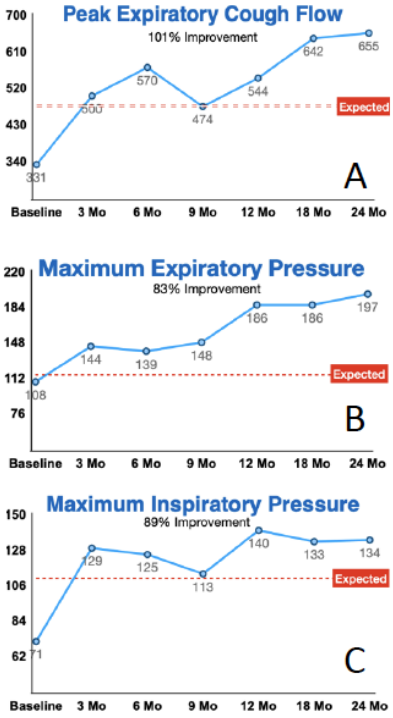

Fig. 2: RST improves physiologic capacity in a

Our group has examined the impact of early proactive RST in a progressive series of studies in individuals with amyotrophic lateral sclerosis (ALS).[17,18,20–22] Given that a reported 85% of individuals with ALS develop dysphagia, dystussia (cough impairment), and dyspnea during the disease progression,[23–26] we proposed that *proactive, targeted exercises* of the upper aerodigestive tract during the *early* stages of the disease and *prior* to the development of significant impairment would increase physiologic reserve to improve and/or maintain airway clearance physiologic capacity into inevitable disease progression. This work has noted that RST programs of varying lengths (5-weeks to 24 months) is associated with improvements in pulmonary, cough, and swallow function in patients with early stage ALS.[17,18,20–22]

For example, we implemented a combined expiratory and inspiratory RST program in an individual recently diagnosed with a bulbar onset C9Orf72 form of ALS.[20] Although this individual demonstrated safe swallowing at the time of diagnosis, peak expiratory cough flow, and maximum inspiratory pressure (MIP) physiologic capacity were significantly impaired, with the former encroaching the typical threshold considered to require reactive cough assist interventions (<270L/min). We, therefore, implemented RST, that the patient diligently completed for a two year period, with noted gains in peak expiratory cough flow (Fig. 2A), MEP (Fig. 2B), and MIP (Fig. 2C).[20] Importantly, when this individual did develop dysphagia and unsafe swallowing, he had adequate physiologic capacity to defend his airway (expel tracheal aspirate materials).

To date, **no group has examined the impact of a combined inspiratory and expiratory RST program in CS patients** targeting increased upper airway physiologic capacity before surgery that may impact postoperative patient outcomes. Here, we seek to inform current knowledge gaps by examining the utility of a proactive, preoperative RST program in a small cohort of CS patients**.** Our central supposition is that a preoperative RST program will improve a CS patient's physiologic capacity to defend the airway and thereby improve CS postoperative patient outcomes.

APPROACH:

Overview: The current *pilot* project seeks to determine the safety, feasibility, and impact of preoperative RST program in 25 CS patients who are at high risk for developing post-surgical dysphagia. Thus, this represents a 'proof of concept' study to support subsequent larger-scale clinical trials. Briefly, *Aim 1* will examine the feasibility and safety of the RST program by monitoring treatment adherence, telehealth/in-person session attendance, and closely monitoring adverse events related to RST. *Aim 2* will determine the physiologic impact of the RST program by comparing measurements of forced vital capacity (FVC), MEP, MIP, voluntary cough peak expiratory flow (PEF), and cough spirometry metrics as well as functional measures of dyspnea and (LCADL), Bamboo passage). before versus after RST (i.e., research exam 1 vs. research exam 2, Fig 3). Additionally, a FEES will be performed to index baseline swallowing and to provide secondary treatment outcomes indexed by the validated penetration-aspiration scale (PAS), dynamic imaging grade of swallowing toxicity (DIGEST), the New Zealand secretion scale (NZSS), and the Yale pharyngeal residue severity rating scale (YRS). Completion of Aims 1 and 2 will occur within one month prior to surgery (Fig. 3). *Aim 3* will involve monitoring and collection of health-related outcomes during the postoperative recovery phase and postoperative pulmonary function testing and FEES following extubation. This study timeline is depicted in Figure 3.

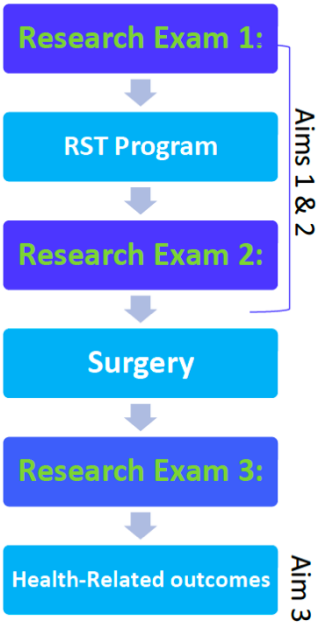

Fig. 3: Study Timeline.

Design: This study represents a *longitudinal pilot cohort study* intended to collect preliminary data regarding the safety and feasibility of a preoperative intervention program, to inform larger comparative studies that will utilize a between groups comparison. Similar study designs have been implemented in other pilot treatment studies in speech-language pathology.[17,27,28] While study designs involving group comparisons were considered for this project, the current design was chosen to ensure feasibility and a tightly conducted pilot or proof of concept study to allow detailed and rigorous outcomes and analyses. Further, consideration was given to the nature, scope, budget, and timeline of this grant mechanism intended for new investigators, and it was determined that a smaller, feasible study was most appropriate.

Participants: Twenty-five individuals undergoing cardiovascular surgery will be enrolled in this pilot project. Eligibility requirements are:

Inclusion criteria:

1. Adult 18-90 years old.
2. Not pregnant.
3. Undergoing planned cardiac surgery via sternotomy &/or extended thoracotomy & seen in the UF Health preoperative clinic.
4. Confirmed COVID-19 negative test and/or no recent COVID-19 symptoms
5. Has access to a computer, tablet, or electronic device with a stable internet connection for telehealth sessions.
6. Willing to undergo testing procedures and complete the exercise training program

Exclusion Criteria:

1. Individuals under the age of 18 or over the age of 90.
2. Pregnant women.
3. Positive for COVID-19 or symptoms of COVID-19.
4. No access to a computer, tablet, or electronic device &/ a stable internet connection for telehealth sessions.
5. Unwilling to undergo testing procedures and/or complete the exercise training program.

Recruitment: Dr. Plowman is a faculty member of the Department of Surgery, Division of Cardiovascular Surgery, and therefore has close ties with this patient population and clinical setting. Further, the ARC Lab has a strong history of successful collaborations with the cardiothoracic surgeons at the UF Heart and Vascular hospital (Drs. Jeng, Martin, Beaver, Arnaoutakis) who see patients in this preoperative clinic. Participants will be recruited from the preoperative clinic visit. Drs. Jeng and Donohue will identify eligible participants who meet inclusion criteria from clinic schedules and will approach identified individuals who will be informed of their potential eligibility to participate and asked if they would like to learn about this study. If they express interest, an approved study team member listed on this protocol will verbally detail the aims of the study, specific requirements for inclusion, and answer any questions from patients and caregivers. They will also be provided with a copy of the informed consent form to read over. Those who wish to be enrolled will sign an informed consent form, will be provided a copy of the signed informed consent form, assigned a subject identifier, and an appointment will be scheduled for their Research Evaluation 1.

Research Evaluations: CS patients will undergo three separate research examinations during this study. Before commencing the RST program, an initial research examination (pulmonary function testing, functional speech/dyspnea measures) will be completed. After completing RST and before undergoing surgery, a second research examination (pulmonary function testing, FEES, functional speech/dyspnea measures) will be completed. Finally, postoperatively, a third research examination (FEES) will be completed. The methods for the research examinations are outlined in detail below.

Research Evaluation 1: As previously described, CS patients will undergo evaluations during the preoperative phase immediately before and after the RST program. Research evaluations will take approximately 30-45 minutes to complete. During these evaluations, the following procedures and outcomes will be collected:

Pulmonary function testing (PFT): Consistent with PFT protocols and the American Thoracic Society guidelines, all PFT measures will be completed in an upright seated position with a nose clip.[29,30] FVC will be measured with a handheld spirometer (Micro I; Carefusion,Yorba Linda, California). For FVC, CS patients will be instructed to take a deep breath in, place their mouth around the mouthpiece, and blow all the air our from their lungs. MEP and MIP will be measured with the MicroRPM handheld MEP device (Micro Direct Inc., Lewiston, ME). For MEP testing, CS patients will be instructed to place their mouth around the mouthpiece and blow out as forcefully as possible. For MIP testing, CS patients will be instructed to place their mouths around the mouthpiece and breathe in as forcefully as possible. The participant will perform up to three trials of each task, inter-spaced with a one-minute rest in between. The highest value will be used for statistical analysis. Voluntary cough PEF will be tested using a handheld analog Mini-Wright Peak Cough Flow Meter (model number 3103085, Clement Clarke Int., Harlow, United Kingdom). This device is considered the gold standard Peak Cough Flow (PCF) device and is one of the only PCF devices that contains a one-way expiratory valve that prevents a participant to breathe air in from the device to reduce contamination. Additionally, we will fit the PCF meter with a Mini-Wright disposable single-use bacterial expiratory one-way valve filter mouthpiece (model number 3122064) that traps any expectorated matter or organisms ensuring a barrier to the PCF meter device. This method conforms to the American Thoracic Society (ATS) standards for PCF testing. Participants will be instructed to "cough hard like something is stuck in your throat." The participant will perform three trials inter-spaced with a one-minute rest in between. The outcome will be *Peak Expiratory Flow* ((PEF) L/min). The highest obtained value will be used. For cough spirometry testing, an oral pneumotachograph (MLT 1000; ADInstruments, Inc., Colorado Springs, Colorado) will be connected to a spirometry mouthpiece filter (MQ 304 Spirometer Filter; Vacumed; Ventura, California). Participants will be instructed to wrap their lips around the mouthpiece and "cough hard like something is stuck in your throat." Cough waveforms will be recorded using LabChart Version 7 (Microsoft Corp., Redmond, Washington) and a laptop computer devoted to this study. Cough spirometry metrics will include inspiratory phase duration, inspiratory peak flow rate, compression phase duration, expiratory rise time, peak expiratory flow rate, and cough volume acceleration. Up to three attempts will be elicited. An example of voluntary cough spirometry waveform from a previous study in our lab is provided in Fig. 5 and definitions for each outcome of interest is provided in Table 3 below.

Table 3. Definitions of cough spirometry outcomes of interest [31]

Cough Outcome:	Definition:
Inspiratory phase duration (s)	Time from onset of inspiration at 0L/s to the beginning of glottic closure or the start of the expiration onset
Inspiratory peak flow rate (L)	Peak inspiratory flow during the inspiratory phase
Compression phase duration (s)	Time to glottic opening; end of the inspiratory phase to the start of the expiratory phase
Expiratory rise time (s)	Time from the expiration phase to the peak of the expiratory flow
Peak expiratory flow rate (L)	Peak expiratory airflow during the expiratory phase of cough
Cough volume acceleration (L/s/s)	Peak expiratory flow rate /expiratory rise time

Note: L=liters, s=seconds

Functional Dyspnea Measure: Research participants will complete the London Chest Activity of Daily Living scale (LCADL), which is a standardized and validated 15-item questionnaire that measures dyspnea during activities of daily living.[32]

Speech Measure: The 'Bamboo Passage' is a validated speech testing item that consists of a 98-word paragraph.[33] It is used to determine speaking rate, and number and duration of pauses during speech. Participants will be instructed to read the passage in their normal speaking rate and loudness. Speaking rate (words per minute), number of pauses, and duration of pauses will be calculated.

A digital audio recorder (TASCAM, DR40) connected to a condenser headset microphone (AKG, Inc., HSC271) with a lapel windscreen (eBoot, Inc.) will be placed on the participants head with the headset microphone at a standardized distance of 10cm from the right lip corner. Audio recordings will be digitized at 44.1 kHz with a 16-bit quantization. Calibration of the microphone will be completed prior to each test. Speech testing items will be recorded and saved for subsequent offline analysis. Audio recordings obtained during speech testing will be blinded and rated in Audacity (Audacity 2.2.2, WordPress, 2018) for the below speech outcomes.

***Aim 2 Outcomes*:** Given our desire to index physiologic capacity, we will utilize the highest obtained outcome for FVC, MEP, MIP, cough PEF, and cough spirometry metrics at each time point before and after RST for statistical comparisons. LCADL ratings and speech measurements will also be compared before and after RST. We hypothesize that CS patients will improve FVC, MEP, MIP, cough PEF, cough spirometry metrics, dyspnea, and speaking rate/pauses post-RST.

RST Program and Telehealth/In-Person Visits:

RST Program: Enrolled CS patients will undergo a preoperative RST program immediately following Research Evaluation 1 (preoperative, pre-RST) with a targeted duration of 4-weeks that will vary dependent upon available time between the patients preop and surgery schedule. RST will be completed from the patients' home with portable expiratory and inspiratory training devices our lab has previously used: the EMST-150 or the EMST75 Lite and the IA-150 devices (Aspire Products, Gainesville, Florida, Fig. 4). The EMST 75 Lite has a resistance range of 0-75cm H_20 and the EMST-150 and IA-150 devices have a resistance range of 30 to 150cm H_20 and represent spring-loaded pressure threshold devices (Fig. 4). For completion of exercises, each device will be set to a patient's individualized 70% MEP or MIP. Following the baseline evaluation, trainers will be calibrated to the appropriate setting, and the patient will be trained on how to perform exercises. Additionally, they will be provided with a training manual that includes detailed instructions and photographs to provide reinforcement of the initial training session.

Fig. 4: Respiratory training devices. Images from https://emst150.com/product/emst150-ia150-inspiratory-adapter-bundled-combo/ (Aspire Produces, https://emst150.com/)

Participants will need to demonstrate proficiency in performing both the expiratory muscle strength training (EMST) and inspiratory muscle strength training (IMST) exercise prior to leaving the clinic and will be given a training log to record their daily sessions and a telehealth appointment card with weekly meeting dates and instructions for how to access the secure telehealth portal (a secure version of Zoom).

The RST protocol will be the previously utilized "Rule of 5's" [13] that includes training 5 days per week and performing 5 sets of 5 reps (i.e., 25 repetitions) for both expiratory and inspiratory muscle strength training. Thus, a total of 50 repetitions (25 IMST, 25 EMST) will be performed by enrolled participants. CS patients will be instructed to breathe in (IMST) or out (EMST) for several seconds until the valve audibly releases. Between repetitions, CS patients will be instructed to rest 10-15 seconds before the next repetition. After each set, CS patients will be instructed to rest for one minute before completing the next set. Repetitions will be recorded in a training log provided to the CS patients to track adherence and the quality of repetitions will be monitored during weekly telehealth sessions.

Telehealth Sessions: CS patients will complete one-five training sessions per week via telehealth with a research speech-language pathologist to ensure patients are using correct form and technique, to complete a safety and adverse event check, to answer any questions patients may have, and to assist with adherence issues. The number of telehealth visits per week will be determined based on individual patient factors including 1) patient performance of the RST program, and 2) patient requests for additional training/clarification. The research speech-language pathologist may recommend up to 5 telehealth visits per week and/or patients may request additional telehealth sessions (up to 5 per week) if they have questions or require additional support to perform the RST exercises correctly. EMST/IMST devices will also be recalibrated weekly using the Borg Category Ratio 10 Scale to measure perceived effort of the RST exercise equal to 70% MEP/MIP (Borg scale score of 7/10). The Borg Category Ratio Scale has been used in the limb literature and demonstrated accuracy in measuring %repetition max (RM). For example, a score of 2 is approximately 20% of a RM and a score of 7 is approximately 70% of a RM.[34] To ensure patient privacy, telehealth sessions will take place in a private room using a UF secure telehealth platform (a secure version of Zoom). Attendance for weekly telehealth sessions will be tracked.

In-Person Visit: CS patients will also have one in-person visit within participants' homes or the research laboratory (DG-136) with a study team member at the mid-point of the RST program to ensure patients are using correct form and technique, to complete a safety and adverse event check, to answer any questions patients may have, and to assist with adherence issues. EMST/IMST devices will also be recalibrated by retesting MEP and MIP and setting the devices to 70%. LCADL ratings and functional speech measures (bamboo passage) will also be obtained.

Training Logs: CS patients will fill out daily training logs to track RST repetitions (adherence) and to note any adverse events related to RST. The PI will calculate the total number of repetitions completed by each participant at the conclusion of the training period.

Aim 1 Outcomes will include patient adherence to RST, attendance at telehealth/in-person treatment sessions, and adverse events associated with RST. We hypothesize that RST will be safe, well-tolerated, and feasible in CS patients as measured by high adherence to RST, attendance at all telehealth/in-person sessions, and no reported adverse events.

Research Evaluation 2:

After completing the RST program and prior to surgery, CS patients will undergo PFTs, read the bamboo passage, and complete the LCADL as they did during Research Evaluation 1. Additionally, they will undergo a standardized Fiberoptic Endoscopic Evaluation of Swallowing (FEES). The second research evaluation will take approximately 45 minutes to complete.

Fiberoptic Endoscopic Evaluation of Swallowing (FEES): CS patients will undergo a FEES exam in a dedicated room (UB 1707, UB 1739) in the preoperative clinic or the ARC lab before and after the RST program using an Olympus flexible video HD Rhino Laryngoscope (ENF-V3) connected to a portable video processor and light source (Olympus CV170). To ensure patient comfort, a water-soluble lubricant (Aplicare sterile lubricating jelly 82-280) and, per participant preference, a topical numbing-agent (i.e., lidocaine hydrochloride jelly USP, 2%) will be applied to the naris, and the laryngoscope will be passed trans-nasally through the nasopharynx and hypopharynx until an optimal position is obtained.[35] The topical numbing agent will be used per participant preference and pending physician authorization.

During laryngoscope advancement, the participant may be asked to hum or say "eeeeee" to help visualize anatomy and placement of the laryngoscope. A standardized FEES protocol will be used that includes a combination of voicing and swallowing tasks. Once optimal scope positioning is confirmed, the participant will be asked to perform a series of voicing tasks to allow assessment of laryngeal and vocal fold movement that include: 1) sustained vowel "ah" 2) vowel/sniff alternating task; 3) cheek puff task; 4) breath hold task; and 5) a pitch glide of the vowel "e". CS patients will be given 5ml Gatorade x2, 10ml Gatorade x2, comfortable cup sip x2, teaspoon pudding x2, cracker x2, and M&Ms x3. A liquid that is colored needs to be used so that it may be visualized during swallowing. Gatorade will be the typical option but if a participant has dietary restrictions or a dislike for Gatorade other options will include grape juice or milk. To ensure patient safety, swallowing trials will be discontinued after two episodes of gross aspiration or if a patient is unable to clear >70% of the bolus. At the completion of the swallowing trials, the laryngoscope will be carefully removed.

Recordings will be saved on a USB200 recording device with an encrypted hard drive. The FEES images will be labeled with the participant identification study number and immediately transferred onto the Aerodigestive Research Core laboratory server to ensure data is not lost. This is a secure server and only individuals within the lab included on this IRB will have access to saved and coded files. The video images will remain on the encrypted hard drive until the end of the study and then they will be deleted. The transferred recordings will be kept on our secure server for five years following the completion of the study. Additionally, if abnormalities are noted that would be pertinent to the participant's medical care (for example, vocal fold paralysis or aspiration), our study team will alert the medical team (attending physician or nurse caring for the participant) that an abnormality was detected.

Swallowing Ratings:

Duplicate blinded ratings of the validated PAS, DIGEST, NZSS, and YRS will be performed by two experienced raters to index swallowing safety and efficiency (Tables 4-7). If a discrepancy occurs, a consensus meeting will be held with four experienced raters to finalize a rating.

Table 4: The validated penetration-aspiration scale (PAS) scores and definitions used to index swallowing safety.[40,41]

Group:	PAS	Definition:
Non-Penetrator/ Aspirator	1	Material does not enter the airway
	2	Material enters the airway, remains above the vocal folds, ejected from airway
Penetrator	3	Material enters the airway, remains above vocal folds, not ejected from airway
	4	Material enters the airway, contacts the vocal folds, and is ejected from airway
	5	Material enters the airway, contacts vocal folds, and is not ejected from airway
Aspirator	6	Material enters the airway, passes below vocal folds, ejected out of the airway
	7	Material enters the airway, passes below vocal folds, not ejected despite effort
	8	Material enters the airway, passes below vocal folds, no effort made to eject

Table 5. The validated Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) scale.[36]

Efficiency Grade and Definition	Safety Grade and Definition				
	0, PAS 1-2	1, PAS 3-4 any; 5-8 single or trace	2, PAS 5-6 intermittent or chronic, 7-8 intermittent/not gross	3, PAS 7-8 chronic and not gross or gross and not chronic	4, PAS 7-8 chronic and gross
0, <10% residue	**0**	**1**	**2**	**3**	**3**
1, 10-49% residue	**1**	**1**	**2**	**3**	**3**
2, 50-90% residue cracker	**1**	**2**	**2**	**3**	**3**

3, 50-90% residue pudding/liquid or >90% any	**2**	**2**	**3**	**3**	**4**
4, >90% residue all	**3**	**3**	**3**	**4**	**4**

Table 6. The validated New Zealand Secretion Scale (NZSS) scores used to assess the location, amount, and response to secretions during FEES.[37]

Category	Score	Symptom
Location	**0**	Nil significant pooled secretions in pyriform fossae or laryngeal vestibule
	1	Secretions in pyriform fossae (above 20%)
	2	Secretions in laryngeal vestibule (beyond healthy lubrication of mucosa)
Amount in pyriform fossae	**0**	Nil significant pooled secretions in pyriform fossae (0–20%)
	1	Secretions in pyriform fossae, not yet full (20–80%)
	2	Secretions filling (80–100%) or over spilling pyriform fossae/interarytenoid space
Response	**0**	Secretions in pyriform fossae or laryngeal vestibule effectively cleared
	1	Ineffective attempts to clear or no response to secretions in pyriform fossae
	2	Ineffective attempts to clear secretions from laryngeal vestibule
	3	No response to secretions in laryngeal vestibule

Table 7. The validated Yale Pharyngeal Residue Severity Rating Scale (YRS) scores used to assess the location, amount, and severity of residue.[38]

Vallecula Residue		
Score	**Definition**	**Severity**
I	No residue (0%)	None
II	Trace coating of the mucosa (1-5%)	Trace
III	Epiglottic ligament visible (5-25%)	Mild
IV	Epiglottic ligament covered (25-50%)	Moderate
V	Filled to epiglottic rim (>50%)	Severe
Pyriform Sinus Residue		
I	No residue (0%)	None
II	Trace coating of the mucosa (1-5%)	Trace
III	Up wall to quarter full (5-25%)	Mild
IV	Up wall to half full (25-50%)	Moderate
V	Filled to aryepiglottic fold (>50%)	Severe

Postoperative Research Evaluation 3:

Following completion of the RST program and after cardiac surgery, patients will undergo a standardized FEES evaluation that will take approximately 30 minutes and health-related outcome measures will be tracked. For postoperative FEES examinations, the PI will ensure patient readiness and safety by completing a cognitive screen (Richmond Agitation-Sedation Scale score of 0)[39] and by determining the patient's respiratory status is stable (Sp02 >90%, off CPAP/BiPAP for >30 minutes, respiratory rate <30 bpm). Table 8 shows a checklist for determining patient readiness for participating in a postoperative FEES.

Following confirmation that the participant is appropriate to proceed to swallowing testing, the research SLP will the same standardized FEES protocol as described in the preoperative research exams and will be performed at the participant's bedside. Postoperative FEES examinations will be performed within 72 hours of extubation with CS patients sitting upright in bed. During this period, the participant's vital signs will be monitored and although not

anticipated, testing will cease if a significant change is observed (Sp02<90, BR>30, spike in blood pressure or overt signs of distress) or if the participant wishes to end testing early.

Table 8: Checklist for determining patient readiness for postoperative FEES.

Domain:	Criteria:
Alertness & Cognition:	✓ Richmond Agitation- Sedation Scale of 0 ✓ Oriented to time and place ✓ Alert and able to attend to conversation and follow commands
Stable Respiratory Status:	✓ Able to remain off CPAP or BiPAP support for >30 minutes ✓ Demonstrates a respiratory rate <30
Physical Ability:	✓ Ability to sit upright for testing

Swallowing measures: Two blinded judges will independently rate swallowing safety and efficiency using the validated penetration-aspiration scale (PAS), dynamic imaging grade of swallowing toxicity (DIGEST), the New Zealand secretion scale (NZSS), and the Yale pharyngeal residue severity rating scale (YRS).[36–38,40,41] These scales are described in detail above in Tables 4-7.

Health-related outcomes: We will collect information on enrolled participants' medical history via the University of Florida Heart and Vascular hospital electronic medical records (Epic, Epic Systems Corporation, Verona, WI). Variables of interest may include previous history of dysphagia (y/n), previous cardiothoracic surgery (y/n), type of previous cardiothoracic surgery, previous cardiothoracic surgery notes, year of previous cardiothoracic surgery, dysphagia following previous cardiothoracic surgery (y/n), instrumental swallow evaluations after previous surgeries (y/n), primary surgery diagnosis, etc. Following surgery, enrolled participants will be closely monitored, and the following variables of interest will be tracked: time to oral diet, length of ICU and total hospital stay, intubation duration, extubation fast track status (y/n), pneumonia status, reintubation status, 30-day readmission status, and 90-day mortality status Epic. Given the nature of our therapy, additional metrics that provide insight into CS patients' pulmonary or swallow function may be extracted from respiratory therapists', speech-language pathologists, or other health care provider notes. These metrics may include things such as DLCO, respiratory rate, intubation duration, negative inspiratory force, instrumental swallow evaluation imaging (e.g., videofluoroscopy, FEES), etc. In addition to obtaining medical information from patients' charts, test results from research evaluations can be made available upon request to aid in medical care and reduce risk of repetitive testing.

Aim 3 Outcomes will include the postoperative PAS, DIGEST, NZSS, and YRS scores and the aforementioned health related outcomes of interest. We predict to see low rates of unsafe swallowing, and in those who do aspirate, we predict that they will demonstrate an adequate cough response to remove tracheal aspirate (PAS of 6). Further, we predict to observe low rates of pneumonia, reintubation, 30-day readmission, and 90-day mortality, as well as decreased time to oral intake and LOS for enrolled participants during their recovery.

Sample size justification: Given that this is a pilot study to determine primarily safety and feasibility data to determine whether a large-scale clinical trial is warranted, a justification based on statistical power to test hypotheses strictly at the α=0.05 level is not appropriate. The findings from this exploratory study will be used to perform future sample size and power calculations to examine the safety, feasibility, and impact of preoperative RST in a larger cohort of CS patients.

Statistical analyses: Descriptive statistics, magnitudes of estimates, and spaghetti and needle plots that visualize individual-level data across time points will first be utilized to summarize data in this small cohort and prior to performing conventional analyses and hypothesis testing.

Aim 1: Attendance, RST adherence, and adverse events will be summarized descriptively with frequency counts and percentages.

Aim 2: Descriptive statistics and an appropriate repeated measures analysis based on the distribution of data will be used to evaluate potential change in FVC, MEP, MIP, voluntary cough peak expiratory flow, and cough spirometry metrics, speech rate, number of pauses, duration of pauses, LCADL ratings across time points (pre-RST vs. post-RST).

Aim 3: Descriptive statistics will be used to summarize swallowing safety profiles postoperatively (frequency histogram, mean, mode, range of PAS, DIGEST, NZSS, YRS scores), and logistic regression will be used to compare swallowing safety and efficiency across timepoints.[42] Postoperative rates of pneumonia, reintubation, duration of intubation, intubation fast track status, any related respiratory therapy outcomes, 30-day readmission, mortality, and time to oral intake/hospital LOS, etc. will be summarized descriptively (frequency counts, %) and compared to our historical data set in CS patients.

Data Management and Quality Control: Research Electronic Data Capture (REDCap) will be used to enter and store data for the current study, which is a secure web-based application hosted at the University of Florida. REDCap has a variety of features that streamline data entry and processing including the ability to download and export data directly to commonly used statistical analyses software. The ARC lab has successfully used REDCap for data collection, storage, and analyses for other research studies

Table 9. Summary of Study Outcomes and analyses by specific aim.

AIM:		STUDY VISIT	OUTCOMES:	ANALYSIS:
Aim 1	Feasibility & safety of RST	RST at-home program, Telehealth appts/In-person visit	# RST reps completed /# prescribed, # sessions completed /# scheduled, Adverse events.	Frequency counts, percentages.
Aim 2	Physiologic impact of RST	Research Exam 1, Research Exam 2	FVC, MEP, MIP, Cough PEF, Cough spirometry metrics, Speech rate, number of pauses, duration of pauses, LCADL ratings	Descriptive statistics, Repeated measures ANOVA (or non-parametric dep' distribution)
Aim 3	Postoperative health-related outcomes	Research Exam 3, 90-days postoperatively	Swallowing safety and efficiency, intubation duration, pneumonia, reintubation, 30-day readmission, 90-day mortality, time to oral intake, hospital LOS (ICU and total), relevant respiratory therapy outcomes	Frequency counts, Percentages, Logistic regression.

Data Safety Monitoring Plan (DSMP): Dr. Jeng will provide medical oversight for this study and we will utilize standard IRB oversight to monitor any adverse events or protocol deviations. The UF-IRB will review the human subject protocol and will monitor the quality of research occurring under the approved protocol during annual continuing reviews. The IRB must approve the protocol annually, as the study progresses. Data safety monitoring will occur during weekly meetings to review Adverse Events (AE) and Protocol Deviation Logs with the PI and study team. In the event of an unanticipated adverse response, the participant's physician will be immediately notified, and the participant will be seen for a complete evaluation. Data, adverse events, and individual subject safety are monitored throughout each subject's evaluation as well as during weekly laboratory meetings with the PI and study team that adhere to the UF IRB regulations for reporting of AE's and protocol deviations.

Potential Risks: All participants will be required to pass a COVID-19 Test (i.e., COVID-19 negative) that is performed as standard of care in all surgical patients prior to being allowed to participate in this study. Thus, the risk for personal working on this project, in addition to potential cross contamination of equipment will not be a factor.
The following risks will be disclosed to all participants prior to obtaining their consent to participate:

a) A Fiberoptic Endoscopic Evaluation of Swallowing (FEES) can result in in discomfort, gagging or vomiting. Although extremely rare other complications that have been reported can include vasovagal episode (0.06%

reported incidence), laryngospasms (0.03% reported incidence), or epistaxis (0.3% reported incidence). The reported incidences of these adverse reactions to FEES are based on published reports in 6,000 patients.[35]

b) Aspiration (material in trachea) is always a possible risk during the FEES exam, as the test is intended to detect aspiration during swallowing.
c) There are no documented complications of voluntary cough spirometry or pulmonary function testing.
d) While RST has been safe and well-tolerated in a variety of patient populations,[13,14,16–18,20,21] there is a chance it could result in dizziness, lightheadedness, fatigue, or shortness of breath.

Potential Benefits: Subjects may potentially benefit from participation through improved breathing, cough, and/or swallowing function. Participating in this study will also include an instrumental swallowing evaluation following surgery and may lead to the early identification of any swallowing impairments to minimize adverse effects of swallowing difficulty and to initiate preventative measures for risk of choking, respiratory difficulty and/or pneumonia post-operatively. Additionally, study participation may lead to sooner oral intake of food, liquids, and medications while in the hospital as a result of comprehensive swallowing testing being performed post-extubation.

Conflict of Interest: There is no conflict of interest to disclose for any study team member that is specifically relevant to this study.

Summary and Conclusions: This pilot study represents the first examination of the feasibility, safety, and physiologic impact of a targeted preoperative RST program in a small group of high-risk CS patients to prevent postoperative dysphagia and associated adverse outcomes. By carefully examining detailed aspects of physiology and health-related outcomes in a feasible design for this grant mechanism, the PI will collect high quality data to support her K99-R00 NIH grant application. These preliminary data will further inform future intervention paradigms in this challenging patient population where there is no current standard of care or evidence guided intervention guidelines for either pre or postoperative dysphagia management.[11,12]

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