PUSH IT: Preventing Unnecessary Surgeon Holds on Ingestion for Tracheostomy

1. **Specific Aims**
    a. To determine if continuation of enteral feeds up to the time of tracheostomy improves nutritional status as evident by total caloric intake, and has no effect on risk of aspiration as evident by reported feed material in mouth, worsening consolidation or opacification on chest x-ray within 48 hours, increased requirement of O2/ PEEP, worsening ABG, and pneumonia within 7 days

Hypothesis

We hypothesize that continuing enteral tube feeds in critically ill intubated patients up to the time of tracheostomy does not increase risk of aspiration and may improve overall nutritional status. We also hypothesize that there is no difference in aspiration events between nasogastric and nasoduodenal enteral feeding routes or operations performed in the operating room versus in the ICU.

Statement on Impact

There are currently no standardized guidelines regarding whether intubated patients can continue enteral feeds up to the time of tracheostomy. Additionally, it is unclear whether the route (i.e. nasogastric versus nasoduodenal tube feeds) or the location of the procedure (OR vs ICU) has any implications on feasibility and safety. The purpose of this study is to implement a protocol designed to decrease the interruption of enteral feeds in critically ill patients in hopes of increasing quantitative nutritional intake and prospectively evaluate whether with feeds there is an increased risk of aspiration. We will also use our data to explore the safety and efficacy of nasogastric versus nasoduodenal feeds.

Currently at our institution holding feeds preoperatively (6 hours) for tracheostomy is physician dependent. In our recent quality improvement retrospective project, we demonstrated that patients who had feeds continued to the time of tracheostomy had no difference in pulmonary complications. We also noted that patients with feeds continued were more likely to have sacral decubitus wounds. As preoperative tube feed management is based on surgeon preference, we suspect this result is due to selection bias, in that the surgeon is more willing to continue feeds in sicker, deconditioned patients with poor nutritional status. We believe that continuing feeds up to the time of tracheostomy will decrease feed interruptions thereby increasing quantitative nutritional intake and show no difference in aspiration rates as defined by feed material in the mouth, worsening consolidation or opacification on chest x-ray within 48 hours post operatively, increased requirement of O2/ PEEP, worsening ABG, pneumonia within 7 days. Overall, we feel these benefits will ultimately lead to decreases in morbidity associated with malnutrition and will also decrease delays to the operating room.

2. Research Strategy

A. Significance:

Malnutrition is a significant problem in the critically ill, however with busy operating room schedules, we often find that feeds are interrupted repetitively prior to elective surgery. These interruptions are practiced based on the American Society of Anesthesiologist guidelines for fasting intervals for elective surgery. These guidelines, however, were not created for critically ill, intubated patients (14). Controversy around continuing feeds in intubated patients up to the time of surgery exists due to the theoretical concern for loss of airway and need for reintubation on a “full” stomach, and the consequent aspiration risk. Critically ill patients receiving enteral feeds are at risk for aspiration events at baseline with aspiration pneumonitis and aspiration pneumonia resulting in significant morbidity (17). The theoretical concern for an increased risk of aspiration with continuation of enteral feeds up to the time of surgery persists without supporting evidence (1,2,9,10). Not only is ‘to feed or not to feed’ controversial, one study by Schneider et al demonstrated that anesthesiologist, anesthesia critical care, medical critical care, and surgical critical care physicians often disagree about the length of time necessary to cease the enteral feeding of an in intubated patients before scheduled procedures such as tracheostomy (8). It is equally unclear whether nasogastric versus nasoduodenal feeds differ in their ability to administer adequate nutrition and risk of morbidity (11,12,13). Again pointing to the need for a universal evidence based guideline on perioperative enteral feeding to benefit critical care patients.

Additionally, extensive evidence demonstrates that malnutrition is harmful and associated with increased morbidity including increased ICU length of stay and overall increased hospital mortality (15, 16). Meanwhile, good nutrition in the hospital setting is associated with decreased infectious complications, reduced inflammatory cytokines, and improved wound healing (2).

This important topic has been looked at previously by small nonrandomized trials. Angotti et al compared 11 patients who underwent tracheostomy without tube feed interruption to 45 patients with feeds held 4 hours prior to tracheostomy and discovered no difference in pulmonary complications however noted the nil per os group sustained a substantial caloric deficit (10). Pousman et al performed a prospective observational cohort study to evaluate the feasibility of implementing a reduced enteral fasting protocol for mechanically ventilated patients and although no statistical difference was shown, there was a trend demonstrating increased delivery of enteral nutrition and faster achievement of nutrition goals in the intervention group (9).

To this end, the goal of the present study is to implement a protocol designed to decrease the interruption of enteral feeds in critical care patients and prospectively evaluate whether this leads to a quantitative increase in nutritional intake without increasing the risk of aspiration as defined by reported feed material in mouth, worsening consolidation or opacification on chest x-ray within 48 hours postoperatively, increased requirement of O2/ PEEP, worsening ABG, and diagnosis of pneumonia within 7 days. Additionally, we hope that increasing quantitative nutrition may decrease morbidity especially in the small subset of patients where feed interruptions occur repetitively.

If the aims of the project are achieved, the data obtained from this study will be used to create an evidence based platform from which physicians can practice. This will end the anecdotal controversy regarding perioperative tube feed management, increasing quantitative nutrition, and ultimately improving the care of critically ill patients.

B. Innovation:
This project aims to challenge and shift the current clinical practice paradigm of interrupting enteral feeding prior to tracheostomy in critically ill patients. We hope that through evidence-based medicine we can improve patient care and decrease the risks of malnutrition in the intensive care setting.

C. Approach:
Study design
To test our hypothesis, we will prospectively identify patients with critical illness requiring tracheostomy after admission to the ICU. Overall patient prognosis and indication for tracheostomy will be determined by the admitting surgeon and the critical care physician. Patients with plans for tracheostomy will be screened and informed consent (via healthcare proxy or next of kin) will be obtained for enrollment.

These patients will then be randomized to our continued enteral feeds arm up to the time of surgery versus nil per os at least six hours prior. If randomized to the continued enteral feed arm, the patients will continue to receive enteral feeds via their nasogastric or nasoduodenal tube which was placed at the discretion of the critical care physician.

We will prospectively follow the patients and evaluate their clinical outcomes including quantitative caloric delivery and specific indicators for aspiration postoperatively including reported feed material in mouth in the anesthesia record, worsening consolidation or opacification on chest x-ray within 48 hours, increased requirement of O2/ PEEP, worsening ABG, and diagnosis of pneumonia within 7 days.

We will also collect data, including: diagnosis, medical comorbidities, type of enteral feed, total hours nutrition is held preoperatively, type of nutritional access (NG vs ND), development of ventilator associated pneumonia (VAP) within 7 days, development of surgical site infection, and any adverse post-tracheostomy events. Data will then be compared in the groups.

In our statistical analysis we will also evaluate for differences between patients receiving feeds via nasogastric tube and nasoduodenal tube up to the time of the procedure. Additionally, will perform subgroup analyses of patients with different diagnoses, and a subgroup analysis on procedures performed in the operating room versus ICU.

Study Population
Our study population will be adult patients admitted to Surgical and Trauma Intensive Care Units who require tracheostomy. Retrospective studies of our trauma registry suggest at our single level one trauma center we have 50-80 qualifying patients annually. Once admitted to the ICU, evaluated, and determined to meet inclusion criteria, informed consent for enrollment into the study group will be sought. Given the severity of illness in this patient population, we expect to require the consent of the patient's health care proxy or next of kin.

Inclusion and Exclusion Criteria
Our study population will be patients admitted to the surgical or trauma ICU who are 18 years or older and require tracheostomy. Patients in whom we are unable to identify a health care proxy or next of kin to obtain informed consent and individuals who are less than 18 years of age will be excluded from this study. Those deemed to be clinically brain dead within 48 hours of enrollment or transitioned to comfort measures within 48 hours of enrollment will also be excluded. Pregnant patients and prisoners will also be excluded from the study.

Data Collected
Initial data collected upon enrollment will include relevant demographic data including comorbidities and admitting diagnosis. Recent diagnosis of pneumonia (VAP vs CAP) within 7 days of the procedure will also be recorded. Data will then be collected and will include route of enteral access, enteral feed type, enteral feed administration rate, hours enteral feeds help perioperatively, pre-operative and post-operative FIO2, preoperative and postoperative ventilator settings, ABG, and new infiltrate on chest x-ray within 48 hours post operatively. We will also review the anesthesia note to evaluate if any aspiration events occurred intraoperatively as evident by suctioning out feeds from the mouth. We will also conduct surveillance for any tracheostomy adverse events such as return to OR and surgical site infection.

Study Outcomes
Quantitative nutritional intake, aspiration events by reported feed material in mouth, worsening consolidation or opacification on chest x-ray within 48 hours, increased requirement of O2/ PEEP, worsening ABG, and diagnosis of pneumonia within 7 days.

Study Timeline
We anticipate the duration of enrollment of this study to last approximately 12 months. Erie County Medical Center is a large, urban Level 1 American College of Surgeons-verified trauma center where we see approximately 50-80 patients per year who meet inclusion criteria. We anticipate in order to have enough data to create a solid statistical analysis we would need at least an additional 3 centers with similar volume. Individual subject participation will comprise the length of their hospital stay.

We estimate that completion of primary analysis of the data from this study will be approximately two months following study closing. Data will be collected throughout the study and analyzed to assure subject safety and identification of adverse events. This will be coordinated between the designated co-investigator at each site with the primary investigator. This time frame will allow evaluation of both primary and secondary study endpoints.

Data Storage and Confidentiality
All individually identifiable health information will be de-identified prior to entry of subject data into the study database. We plan to use the RedCap data collection tool which is password protected and encrypted. Printed hard copies of data, if used, will be kept in a locked filing cabinet within the principal or co-investigators locked offices to be determined at each site. At Erie County Medical Center this is located at (David K. Miller, C405), within the Department of Surgery at ECMC. If any breach in confidentiality occurs, the principal or co-investigator will contact the Health Sciences Institutional Review Board at University at Buffalo as it is serving as single IRB.

Statistical Analysis
Standard descriptive statistics such as means, medians, standard deviations for continuous responses (length of stay, ventilator days) and frequencies for categorical responses (complications status, wound/infection status, feed type) will be estimated overall and within each group. For continuous variables, normality will be assessed using goodness of fit tests and quantile-quantile plots. For normally distributed responses, t-tests will be used to evaluate group differences, with Levene's equality of variance test determining the choice of Satterthwaite's approximation or the standard pooled variance estimator. To evaluate group differences in responses exhibiting evidence of a non-

normal underlying distribution the Mann-Whitney U test will be used. Association of categorical responses within treatment groups will be evaluated using the chi-squared goodness of fit test.

To assess differences in rates of aspiration events, a log-rank test for differences in survival curves model will be used. Assuming proportional hazards and non-informative censoring, a cox-model will be used to estimate follow-up hazard ratios for development of aspiration pneumonia between the two groups of interest. This assumption has proven reasonable in past research concerning pneumonia development. Should these assumptions not hold, an accelerated failure time model will be used instead, with odds ratios estimated rather than hazard ratios.

To detect a hazard ratio of 0.6667 for aspiration in patients receiving tracheostomy with continued enteral feeding up to the time of surgery with a type 1 error rate of 0.05 and a power level of 0.80, we require 99 case/control pairs. Pending study enrollment and creation of a multicenter trial, the study should be sufficiently powered.

Follow-up analysis will evaluate risks of tracheostomy, such as return to OR and surgical site infection. Patients who do and do not experience these adverse events will be matched using propensity score techniques using baseline data. The matched sample and standard sample will be examined using survival analysis methods to identify potential risk factors.

Provisions to Monitor Data and Ensure Safety of Subjects

To ensure safety of the research subjects, data collected during the study period will be periodically evaluated. Data regarding the primary endpoint as well as morbidity-specific endpoints will be evaluated throughout the study. Data collection for individual subjects will be an ongoing process throughout the study and will be completed on a weekly basis. The first formal data analysis will occur at one months into the study and then one month thereafter until the conclusion of the study.

The data will primarily be analyzed by a statistician affiliated by the institution and reviewed by the principal investigator and the Data and Safety Monitoring Board for the study. We will evaluate the data as described in subsection of this proposal "*Statistical Analysis"*. After analyzing the data, it will be presented to a committee composed of the principal investigator, attending surgeons, and intensivists at the primary site. At these meetings, in addition to evaluating the primary and secondary endpoints we will also review the incidence of any post-tracheostomy occurrences.

Risks to Subjects

The physical risks to subjects in this study is a minor increase over minimal risk. We will be specifically tracking and identifying any adverse events and monitoring the safety of the study via monthly statistical analysis and DSMB review. While this subject population (critically ill) is at risk for psychological and social/economic risks following severe illness/injury (PTSD, anxiety, depression, altered behavior, damage to employability, etc.), we do not foresee any direct risks of that kind due to participation.

Consent Process

Informed consent for enrollment into this study will be obtained by the primary co-investigator at each site after determining patients meeting inclusion criteria. The principal investigator at each site will be a member of the surgical or intensive care team and will be involved in the consent process. The consent process will take place after determining the patient's appropriateness for the study. This process will be completed in the intensive care unit.

The consent process will be extensively discussed with the patient's health care proxy or next of kin to ensure an understanding of the study and those consenting will be asked to expressly recite their understanding of the process. The documentation of informed consent in writing will be completed with a member of the nursing staff in attendance who will attest to the consent process.

We hypothesize that continuing enteral feeds in critically ill intubated patients up to the time of tracheostomy increases overall quantitative nutritional intake, has no increase in aspiration risk, and decreases morbidity. We also hypothesize no difference in morbidity between nasogastric and nasoduodenal enteral feeding routes and no difference in procedures performed in the operating room compared to in the intensive care setting. Our goal is to be

able to implement a new standard of care designed to decrease the interruption of enteral feeds in critical care patients thereby increasing nutritional intake and decreasing morbidity.

Data Dictionary

Pneumonia- Chest XRAY with new or progressive infiltrate, consolidation, cavitation AND either fever >38C or leukopenia (<4000 wbc) or leukocytosis (>12,000 wbc) , AND new onset purulent sputum, increased secretions, increased suctioning requirement, new onset tachypnea, dyspnea or cough, or increased oxygen requirements, ventilator demands or worsening gas exchange

VAP (ventilator associated pneumonia)- The following clinical signs and symptoms after ≥2 days of mechanical ventilation: Chest XRAY with new or progressive infiltrate, consolidation, cavitation AND either fever >38C or leukopenia (<4000 wbc) or leukocytosis (>12,000 wbc) , AND new onset purulent sputum, increased secretions, increased suctioning requirement, new onset tachypnea, dyspnea or cough, or increased oxygen requirements, ventilator demands or worsening gas exchange

SSI (Surgical Site Infection)- Infection which occurs after surgery in the part of the body where the surgery took place

Immediate adverse post-operative event- death within 24 hours of surgery, myocardial infarction within 24 hours, stroke within 24 hours, gastric contents within mouth/ emesis within 24 hours, bleeding from surgical site within 24 hours, reoperation within 24 hours

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