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Effect of NPO status on aspiration risk in pediatric patients undergoing procedural sedation

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Abstract:

Objective: To conduct a review of literature to determine if no solid food or liquids by mouth for more than or less than six hours impacts the incidence of pulmonary aspiration during procedural sedation in pediatric patients. **Methods:** A PubMed search was conducted utilizing the following terms: "sedation, fasting, and aspiration" and "NPO, pediatrics, and pre-procedural." Filters included: "within five years," "review articles," and "English." Articles were then screened and assessed for eligibility based on pediatric population, NPO status, procedural sedation, and risk of pulmonary aspiration. **Results:** Two prospective observational studies and one retrospective review were selected. Beach et al.[8] and Clark et al.[10] found no statistically significant difference between NPO status and the incidence of pulmonary aspiration. Andersson et al[11] found that allowing clear liquids up until called to the operating room does not increase the risk of pulmonary aspiration when compared to patients who fasted more than two hours. **Conclusion:** Overall, these studies found that NPO status does not independently increase the risk of aspiration. Future studies need larger sample sizes in order to properly assess the risk of pulmonary aspiration in pediatric patients undergoing procedural sedation.

Table 1. Acronyms used in this review.

ASA	American Society of Anesthesiologists
NO	Nitrous Oxide
NP	Nurse Practitioner
NPO	Nil Per Os
PA	Physician Assistant
PSA	Procedural Sedation and Analgesia
PSRC	Pediatric Sedation Research Consortium
6-4-2 Regimen	NPO of six hours for solid foods, four hours for non-clear fluids, two hours from clear fluids

Introduction:

The American Society of Anesthesiology (ASA) recommends that pediatric patients complete preoperative fasting prior to surgeries requiring sedation. Preoperative fasting, also known as nil per os (NPO), is defined as no food or fluids by mouth before a procedure.[1] Expert opinion suggest that fasting is warranted to help ensure patient safety by reducing the risks of vomiting and pulmonary aspiration during an elective surgery requiring sedation. Pulmonary aspiration is defined as aspirating stomach contents after administration of anesthesia, during the surgical procedure, or the period immediately following the procedure.[1]

The American Society of Anesthesiologists' current guidelines for an elective surgery requiring sedation are for a minimum NPO status of six hours for solid foods, four hours for non-clear fluids, and two hours for clear fluids (also known as the "6-4-2 regimen").[1,2] These

guidelines replace outdated pre-surgical guidelines that recommended NPO status begin midnight the day before surgery or an NPO status greater than 6-8 hours.[3] Studies have found that a prolonged fast, such as NPO after midnight, led to increased risks of electrolyte imbalances, insulin resistance, dehydration, and patient discomfort.[2] The shorter preoperative fasting period, recommended by the new ASA guidelines, has demonstrated similar patient safety without increasing risks associated with prolonged fasting.[4] However, even when fasting time is elucidated, patients tend to fast for longer periods due to operation delays. As a result, patients are put at an increased risk for the complications listed above.[4]

There are several types of sedation. General anesthesia is defined as a controlled, unconscious state where a patient's protective reflexes are not intact and the patient cannot maintain their airway on their own.[5] When general anesthesia is given, the reflexes that prevent aspiration and regurgitation of the patient's stomach contents are reduced.[6] Due to a reduction in these protective reflexes, preoperative fasting is recommended before surgery that requires general anesthesia, in order to reduce the gastric volume and acidity.[3] In doing so, preoperative fasting decreases the risk of pulmonary aspiration.[3] Pulmonary aspiration is a serious complication and is defined as contents of the gastrointestinal tract entering the lower respiratory tract.[3]

The focus of this research was to investigate the risks of pulmonary aspiration in patients undergoing procedural sedation with shorter fasting times. Procedural sedation is defined as a conscious sedation where sedatives are administered with or without analgesics, while still maintaining cardiorespiratory function.[7] During procedural sedation, the reflexes that prevent aspiration are not inhibited and the patient maintains some level of consciousness.[7] However, research is limited in regards to procedural sedation and the risk of aspiration. As a result, fasting guidelines used for elective sedation, such as general anesthesia, are typically also followed for procedural sedation. Therefore, further investigation as to whether or not the same risk of aspiration applies to procedural sedated patients' needs to be evaluated. Due to the complications associated with prolonged fasting prior to procedures, it is important to know the risk of pulmonary aspiration during procedural sedation with shortened fasting times.

Pulmonary aspiration is a rare, but serious complication that can occur when someone is put under sedation. The occurrence of pulmonary aspiration during procedural sedation ranges from one in hundreds to one in thousands, and is dependent upon a variety of risk factors.[8]

Pulmonary aspiration can result in increased morbidity, longer hospital stays, pneumonitis, pneumonia, hypoxia due to obstruction, brain damage, surgical airway, acute respiratory distress syndrome, and death.[9] Airway related death due to pulmonary aspiration is relatively rare and occurs in about one in 350,000.[9] Due to the rarity of this serious complication, studies have not had the power to properly assess the risk of aspiration during procedural sedation.[8] Currently, NPO guidelines are based upon a few studies, but mostly expert opinion and general consensus because there are not enough published studies to base the guidelines on.[8]

Due to the unknown risk of pulmonary aspiration in pediatric patients undergoing procedural sedation, the ASA continues to state that practitioners should follow perioperative guidelines, despite the insufficient evidence. This is to ensure the safety of patients from major airway complications; but fails to take into account the post-operative complications mentioned previously. The NPO guidelines recommended by the ASA are a shorter duration than the NPO duration recorded for many patients. ASA recommends no solids for at least 6 hours, however, many patients are either told to go much longer than this or end up fasting longer due to delayed procedures.[4] Despite studies that contradict the need for prolonged fasting, surgeons still continue to recommend an NPO status greater than the current preoperative fasting guidelines of two hours for clear liquids and six hours for solids.[4] An unnecessary extended fast puts the patient at risk for increased mortality and other complications.[4] The aim of this review is to determine if an NPO status greater or less than six hours impacts the risk of aspiration during procedural sedation in pediatric patients.

PICO:

Population: Pediatric patients requiring procedural sedation for elective procedures
Intervention: No food or liquids by mouth less than 6 hours before undergoing procedural sedation
Comparison: No food or liquids by mouth more than 6 hours before undergoing procedural sedation
Outcome: Pulmonary aspiration

CLINICAL QUESTION: Among pediatric patients requiring procedural sedation does no solid food or liquids for less than 6 hours, as compared to no solid food or liquids for greater than 6 hours, increase the risk of pulmonary aspiration?

METHODS:

In September of 2017 a search was conducted of the PubMed database using the search terms "sedation, fasting, and aspiration" as well as a search with terms "NPO, pediatrics and pre-procedural." The filters "full-text articles," "within five years," "review articles," and "English" were used. These two searches resulted in a total of 42 articles. There were three duplicates. The articles were screened and 29 were removed. These articles were removed because they were studies that were not related to elective procedures, studies that focused on the effect of chewing gum, articles that were not studies, or articles published prior to 2012. The remaining ten articles were screened and seven were removed due to not addressing procedural sedation and focusing on emergency sedation. Three articles were found to be acceptable. The studies include one retrospective review and two prospective observational studies. Inclusion criteria included: written in English, published in the last five years, pediatric patients undergoing elective procedures, aspiration risk as an outcome, procedural sedation, and recorded duration of NPO. Exclusion criteria includes: emergency procedures, adults, and studies that do not address the risk of aspiration. The PRISMA is shown in Figure 1, outlining how the articles were obtained.

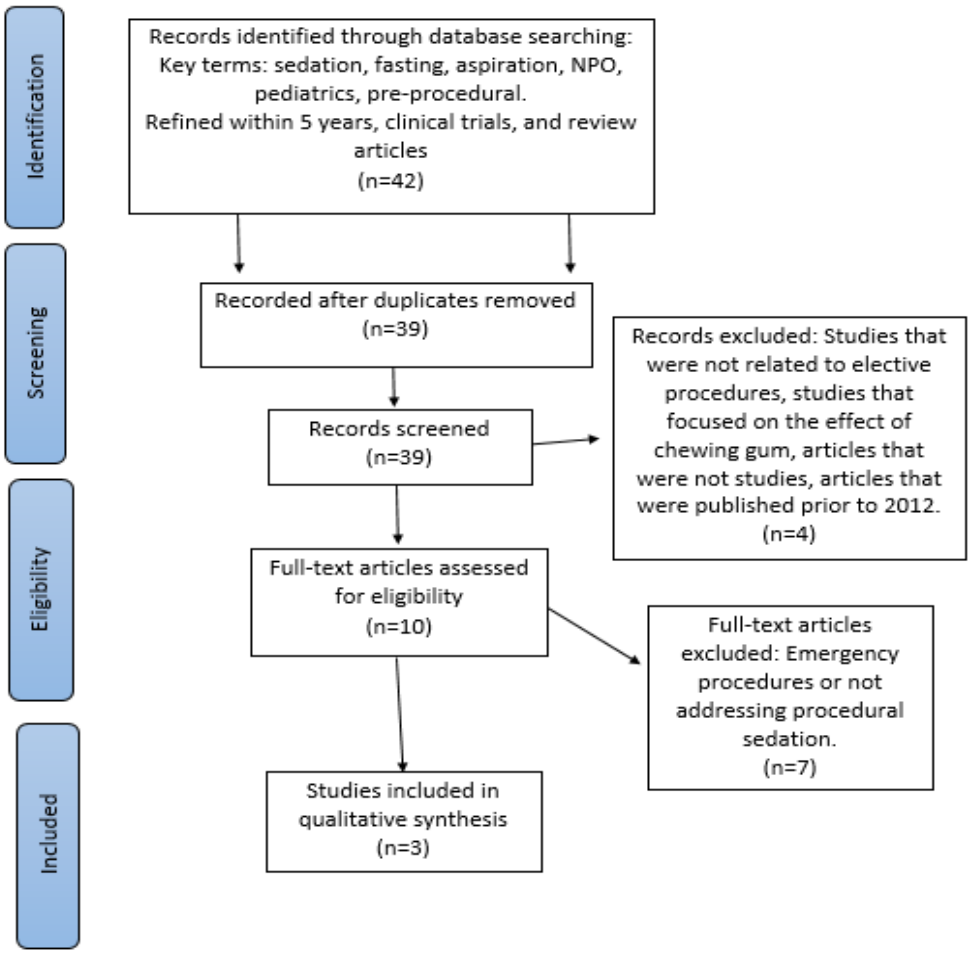

Figure 1. Prisma demonstrating how articles were obtained for this review.

Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097.

Study 1:

The risk of shorter fasting time for pediatric deep sedation. Clark et al.[10]

Objective:

To identify an association between various fasting times and procedural sedation and analgesia (PSA) related complications when conducted outside an operating theatre.[10]

Study Design:

This was a prospective cohort study of patients comparing the duration of fasting to procedure related complications, most specifically airway-related complications. This study was performed at a tertiary care university hospital in one pediatric suite. Eligible patients were 2 months to 18 years of age undergoing elective procedures performed by a pediatric critical care provider. Elective procedures included are listed in Table 2. This study investigated the risk of procedural sedation and aspiration in patients who entered deep sedation. Deep sedation was defined as a level 3 or 4 on the University of Michigan Sedation Scale (UMSS), depicted in Table 3. Levels of sedation vary during a single procedure; therefore, patients who reached even a short duration of deep sedation were included. The study included only healthy patients to ensure that the risk of aspiration was not confounded by other variables. Healthy was defined as an ASA class of I or II. Patients with an ASA class of III or higher were excluded. ASA criteria is listed in Table 4. Additional inclusion and exclusion criteria are depicted in Table 5.[10]

Table 2. Elective Procedures included in Clark et al.[10]

Procedure	Number
Auditory Brainstem Response	60
Botox Injection	212
Computerized tomography scan	205
Bone Marrow aspiration and biopsy	44
Magnetic Resonance Imaging	1060
Electroencephalogram	249
Echocardiogram	36
Lumbar Puncture	208
PICC insertion	18
Minor surgical procedures	448

Table 3. University of Michigan Sedation Scale (UMSS).[10]

Grade	Classification
0	Awake and Alert
1	Minimally sedated; tired/sleepy, appropriate response to verbal conversation and/or sound
2	Moderately sedated; somnolent/sleeping, easily aroused with light tactile stimulation or a simple verbal command
3	Deeply sedated; deep sleep, arousable only with significant physical stimulation
4	Unarousable

Table 3. American Society of Anesthesiologists physical status classification.[10]

Class I	Healthy patient
Class II	Mild systemic disease without functional limitation
Class III	Patient with systemic disease causing functional limitation
Class IV	Severe life threatening systemic disease
Class V	Moribund patient not expected to survive without the operation

Table 4. Patient Inclusion and Exclusion Criteria for Clark et al.[10]

Inclusion Criteria
Electively performed deep sedation procedures in their pediatric suite Procedures performed by pediatric critical care providers 2 months to 18 years of age Undergoing deep sedation as defined as a level 3 or 4 on the University of Michigan Sedation Scale ASA class of I or II
Exclusion Criteria
ASA class ≥ III Moderate sedation as defined as a sedation level (< 3 on the UMSS) Subjects undergoing esophagogastroduodenoscopy Procedures performed urgently or in an inpatient setting Patients who had any oral intake less than four hours prior to surgery were excluded Patients who chose not to participate

Subjects were called the day before their procedure and instructed to fast for at least 4 hours prior to their scheduled procedural sedation and analgesia (PSA). To avoid confusion patients were not given any additional instructions regarding oral intake prior to PSA; which included not specifying whether or not the fast included both liquids and solids. The patients were divided into two groups based on their reported fasting time when they arrived, 4-6 hours or more than 6 hours. Procedures performed during the study are included in Table 2. Patients were informed that demographics were being recorded to determine the safety and efficacy of PSA. Patients who chose not to participate were excluded from the study. [10]

Patients were assessed by a board certified pediatric critical care provider and deemed fit for sedation. This included a focused medical exam, ASA scores, and medical history. During the procedure the patient's vital signs, level of sedation, and procedure progress were recorded every 3-5 minutes. The medication used for sedation was recorded and 77% of the procedures used propofol. Following the procedure this assessment occurred every 10 minutes, for at least one hour, until the patient's level of consciousness returned to baseline. All data and

complications were recorded and stored in a secured electronic database. They classified these complications as: an oxygen desaturation of less than 90%, apnea, prolonged recovery time- defined as sleeping for more than an hour after procedure, crying for more than 30 minutes after procedure, hypotension, IV fluid administration, nausea or emesis, arrhythmia, allergic reaction, and pulmonary aspiration. These complications were broken down into two main categories: major and minor airway complications. Minor complications were determined to include: oxygen desaturation that required repositioning, oxygen, or suctioning. Major complications included oxygen desaturation with a period of apnea, pulmonary aspiration, airway support, and positive pressure ventilation. If a patient had more than one complication they were categorized based on the more severe complication. Secondary outcomes were also assessed. Patient identifiers were not recorded, but their demographics were. These included the patient's age, gender, weight, diagnosis, and procedure performed. Statistical analysis of the recorded data was performed using a Pearson Chi-square to determine if any of the results arose due to chance and binary logistic regression tests to predict the probability of the outcome based on the variables. A two-sided p score of less than 0.05 was deemed statistically significant. [10]

Study Results:

This study took place between January 2013 and September 2015. During this time there were 3,134 PSAs. Only 2,487 patients met the inclusion criteria and were included. The patient demographics are recorded in Table 6. There were no cases of pulmonary aspiration in the study. There were a total of ten complications researched in the study: desaturation to <90% SpO_2, apnea, prolonged recovery time, crying, hypotension, IV fluid administration, nausea or emesis, arrhythmia, allergic reaction, and pulmonary aspiration. The overall complication rate was 15%. One hundred and four of the participants had a major complication, 4% of both the short and long fasting groups. The results of this study indicate NPO status does not influence the incidence of major or minor complications during procedural sedation (p-values > 0.05). There was not a statistically significant difference in the incidence of complications between the 4-6 hour NPO group and the >6 hour NPO group. Secondary outcomes are listed in Table 7.[10]

Table 5. Clark et al.[10] Patient Demographics.

Age	*n* (%)
0-12 months	200 (8)
1-10 years	1865 (75)
11-Up	422 (17)
Gender	*n* (%)
Male	1440 (58)
Female	1047 (42)
Fasting Time	*n* (%)
4-6 hours	1007 (40)
>6 hours	1480 (60)

Table 6. Results of secondary outcomes in Clark et al.[10]

Complications	**Patients (N=2487) NPO Status**		**Odds Ratio**	**Confidence Interval (95%)**	**P-value**
	4-6 hours (n=1007)	**>6 hours (n=1480)**			
Minor Airway Complications	77	89	0.773	0.563-1.060	0.109
Major Airway Complications	6	10	1.135	0.411-3.133	0.808

Study Critique

The study was well-designed and documented. It was not, however, a randomized control trial, but rather a prospective cohort study. A prospective cohort study follows a group of people before the outcome occurs. A major problem with these studies are confounding variables affecting the final conclusions of the study, which are discussed in more detail below. In addition to pulmonary aspiration, the study investigated both major and minor complications related to fasting time. This allowed for a more comprehensive assessment of the risks associated with a shortened NPO status. Pulmonary aspiration is a rare incidence, and the sample size in this study, 2,487 patients, may not have been large enough to accurately assess the risk. As a result, the effect of NPO status on aspiration could have not been adequately assessed by the study. These patients were also all located in one medical provider's office, and this limits the population to a specific area. This study attempted to control for confounding variables as much as possible. All patients underwent a pre-sedation evaluation with medical history, ASA scores, and a focused medical exam. This was done in order to deem patients appropriate for sedation. All patients

were monitored for one hour following sedation regardless of their NPO statues. Patients between the ages of two and eighteen undergoing elective pediatric procedures with an ASA status I or II were included. While under sedation patients needed to achieve deep sedation, level 3 or 4. In regards to confounding variables, this study did not specify NPO duration or type, type of sedative and dose, or the type of surgery performed. All of these have different impacts on the complication risk during procedures. The type of food that could be eaten prior to sedation was not specified or recorded. Knowing what the patients ate or drank prior to the PSA is an important aspect in determining the risk of aspiration. All foods are not created equal in their risk of aspiration. Without knowing what patients ate prior to PSA, these results are unsatisfactory for determining the risk of aspiration. Differences in the types of oral intake prior to PSA would improve future results. Finally, this study did not address one specific procedure or form of sedation. Propofol was most commonly used (77% of the time) but the dosage was not recorded. Researchers attempted to control for the level of sedation using the University of Michigan Sedation Scale, however, sedation levels are hard to accurately assess. Therefore, even brief levels of deep sedation were included in the study. These findings cannot be generalized to all patients undergoing procedural sedation because different procedures and sedatives are associated with different risks of aspiration. The authors did not disclose any conflicts of interest or financial sponsorship.

Study 2:

Major Adverse Events and Relationship to Nil per Os Status in Pediatric Sedation/Anesthesia Outside the Operating Room: A Report of the Pediatric Sedation Research Consortium. Beach et al.[8]

Objective:

To investigate the link between patient and procedure factors and adverse pulmonary outcomes that occur during procedural sedation.[8]

Study Design:

This study was a prospective cohort observational study that evaluated the largest cohort to date, 140,000 patients, for major adverse events in pediatric patients undergoing sedation based on NPO status. The goal of this study was to determine if there were links between NPO status and pulmonary aspiration, pulmonary adverse events, and major adverse events in

pediatric patients. Forty-two institutions participated in the analysis. These institutions included a variety of hospitals all of which obtained independent IRB approval. Periodic audits were required to ensure the integrity of the research. Data was collected through a database created by the Pediatric Sedation Research Consortium, PSRC. The PSRC was established in 2003 and is a group of institutions dedicated to improve pediatric sedation practices. The participating institutions share prospective observational outcome data through the database. Participants for this study were found using an internet-based data collection tool to screen for specific complications. Patients were between the ages of less than one month to a maximum of 18 years. Demographics are listed in Table 8.[8]

Table 7. Study 2 Patient Demographics Beach et al.[8]

Age	**Number of Participants (N)**
Neonate <1 month	197
Infant 1 month-1 year	18,869
1-5 years	67,007
6-11 years	33,488
12-18 years	19,585

Inclusion criteria for the study included pediatric patients undergoing procedural sedation/anesthesia. Any pharmacological intervention made to ease an invasive procedure or test on a pediatric patient outside of the operating room was considered procedural sedation. Some form of sedative medication had to be given to qualify for the study. Procedures performed were further separated based on NPO status. These were recorded in Table 9 and an inconclusive list of medications used was recorded in Table 10. [8]

Table 8. Procedures Performed and Patient NPO Status. Beach et al.[8]

Procedure	**NPO (N=82,546)**	**Not NPO (N=25,401)**	**Missing NPO (N= 31,195)**
Airway (bronchoscopy)	713	202	369
Bone (fracture reduction)	1,699	949	554
Dental	485	70	94
Foreign Body Removal (nose, ear, or skin)	9	5	9
Gastrointestinal (upper or lower endoscopy)	9,794	638	2,619
Neurology (EEG)	4,623	4,476	1,923

Oncology (lumbar puncture or bone marrow)	14,226	2,199	4,254
Radiology (MRI or CT scan)	44,168	17,963	18,789
Sexual Abuse Examination	15	3	8
Surgical (Minor Procedure)	6,881	1,914	2,548

Table 10. Medications Used During Sedation and NPO Status. Beach et al.

Medication	**NPO**	**Not NPO**
Sedatives	81,948	24,998
Ketamine	5,305	2,050
Midazolam	18,133	6,021
Propofol	62,779	18,685

Table 11. Definition of Aspiration according to Beach et al.[8]

Event	Associated with at least one of the following:
Noted emesis OR Food material found in the oral/pharyngeal cavity	New cough New wheeze Increased respiratory effort Change in chest radiograph indicative of aspiration Need for oxygen therapy after recovery from sedation

This study did not record the depths of sedation stating it would be difficult to accurately determine the exact depth of sedation and then correlate patient outcomes. There was no need for consent because there was no intervention. Patients were separated into groups based on their self-reported NPO status. NPO was broken into three groups and included: no solid food for at least 8 hours, no non-clear fluids for at least 6 hours, and no clear fluids for at least 2 hours. Anything by mouth, less than these specified time frames, was not classified as NPO. Aspiration as defined by this study is recorded in Table 11. Outcomes investigated included pulmonary and major adverse events. Major adverse events included pulmonary aspiration, death, cardiac arrest, or unplanned admission to the hospital. The study investigated two main outcomes: pulmonary aspiration and major adverse events in relation to NPO status.[8]

Study Results**:**

Data was collected between September 2, 2007 and November 9, 2011. Of the 139,142 patients included in the study, NPO status was known for 107,947. There were 25,401 patients who reported they were not NPO. Data was analyzed using a logistic regression. There were a total of 75 major complications, and pulmonary aspiration occurred ten times. Aspiration rates per 10,000 people were 0.97 with NPO and 0.79 without NPO, shown in Table 13**.** The results were not statistically significant, and they demonstrated there is not a relationship between NPO status and complications. A multivariate exploration was then used to investigate the observational nature of data. Variables associated with an increased risk of major complications based on NPO status were included. Variables included age, ASA status, provider, propofol use, and diagnosis criteria. The adjusted comparison demonstrated certain factors are associated with an increased risk of adverse events. These included an age less than one year, emergency procedures, neurologic diagnoses, post-trauma, and those undergoing radiology procedures. Despite adjusting for age, ASA status greater than II, propofol use, provider, and emergent status, there remained no relationship between NPO status and major complications. In regards to patients with missing NPO status, multiple imputation was performed. Multiple imputation is a statistical technique that is used to analyze data that is incomplete. In this study the multiple imputation used to accommodate for the missing information about their NPO status included: imputing their NPO status, ASA physical status greater than II, and specifics regarding their emergency status. With adjustments for unknown NPO status there remained to be no statistical significance between NPO status and pulmonary adverse events in relation to procedural sedation. The patients with unknown NPO status were analyzed as both all NPO and all not NPO. Extensive results are listed in Tables 12 and 13. All p-values were greater than 0.05 and there was no significant relationship between NPO status and major pulmonary events, specifically aspiration.[8]

Table 9. Study 2 Aspiration and Major Complication Events. Beach et al.[8]

Aspiration	Patients (N=139,142)	Events
NPO	82,546	8
Not NPO Solids	23,817	2
Not NPO non-clears	899	0
Not NPO Liquids	685	0
Unknown NPO	31,195	0

Major Complications	Patients (N=139,142)	Events
NPO	82,546	46
Not NPO Solids	23,817	15
Not NPO non-clears	899	0
Not NPO liquids	685	0
Unknown NPO Status	31,195	14

Table 13. Study 2 Results. Aspiration Risk and Major Complications. Beach et al.[8]

Aspiration:	**Confidence Interval (95%)**	**Odds Ratio**	**P-Value**
Unadjusted Results	0.08-4.08	0.81	0.79
Results adjusted for all missing NPO data was assumed not NPO:	0.04-1.83	0.36	0.18
Results adjusted for all missing NPO, data was assumed NPO:	0.12-5.62	1.12	0.89
Major Complications:	**Confidence Interval (95%)**	**Odds Ratio**	**P-Value**
Unadjusted Results	0.55-1.93	1.06	0.88
Multiple Imputation data:	0.4-1.39	0.75	0.36
Results assuming all unknown NPO status were not NPO:	0.56-1.50	0.92	0.31
Results adjusted for all missing NPO data was assumed NPO:	0.59-2.0	1.12	0.70

Study Critique:

This study was a prospective cohort study. It was not a randomized control trial; leaving the study open to confounding variables. The researchers tried to limit as many confounding variables as possible by using logistic regression models. This study had the largest sample of prospectively collected sedation encounters to date that investigated the risk of major complications in pediatric patients in regards to procedural sedation. The sample size allowed for a proper assessment of the occurrence of aspiration. The population was diverse and included numerous institutions and patient populations. This allowed for NPO status to be evaluated in a variety of ways. When the original outcome measures of the study were found to have no statistical significance between NPO status and major complications, further analysis was performed to assess if there were any other variables that increase the patients' risk of complications. This study found that there was no statistically significant relationship when investigating additional variables. These results align with previous research that pediatric pulmonary events, specifically aspiration, are rare events.[8]

This study had several limitations. Their definition of a pulmonary aspiration was specific and stated that the patient had to have pulmonary symptoms or a change in their radiograph to be diagnosed with pulmonary aspiration. This could decrease the number of events identified. In addition, this study only investigated immediate perioperative risks of aspiration, and although it is unlikely, it is possible that some instances were missed. Specifics regarding the patient's diet prior to procedural sedation were unknown. There was no documentation of what meals the patient consumed prior to surgery and therefore no way to determine the effect on aspiration. The participants' NPO status were self-reported and based upon their report they were assigned to a group. The exact timing of NPO status was also not recorded. It is unknown how close the two groups were in their average NPO duration. This could impact results if they were close in duration. Self-reporting NPO status also introduces recall bias and as a result the NPO status recalled by the patient could be inaccurate. In general, self-reporting is not as reliable and can produce inconsistent results. Inaccurate NPO status recall would place participants in incorrect study groups, and alter results**.** In addition, patients with a high risk of aspiration risk, or if they severely violated the NPO orders, were not included in the study. The outcome of those procedures could add a lot of insight in regards to NPO and aspiration risk. Beach et al.[8] reported no conflicts of interest.

Study 3:

Low incidence of pulmonary aspiration in children allowed intake of clear fluids until called to the operating suite.[11]

Objective:

To determine the incidence of pulmonary aspiration in pediatric patients undergoing general anesthesia for elective procedures with unlimited intake of clear fluids prior to the operating suite.[11]

Study Design:

This was a case control study that evaluated the incidence of pulmonary aspiration in 10,015 pediatric patients with unlimited clear liquid intake prior to elective procedures. This study was conducted at Uppsala University hospital and used patient charts from January 2008-December 2013. Uppsala University hospital has a strict pre-operative fasting rule of no solids after midnight and at least 4 hour fasting for breast milk. However, they are much more lenient on clear fluids. This study aimed to assess if unlimited intake of clear fluids prior to being called

to the operating suite influenced the incidence in pulmonary aspiration. Patients were found using the patient data management system and their charts were reviewed. Charts were reviewed for instances of vomiting, regurgitation, and aspiration. This study classified aspiration events as two main outcomes: pulmonary aspiration and suspected pulmonary aspiration. Due to the retrospective nature of the study not all instances of pulmonary aspiration were confirmable. Suspected pulmonary aspiration was distinguished from pulmonary aspiration when vomiting occurred with sedation, and there were transient symptoms; however, there were no signs of respiratory distress. Transient symptoms included crackles, rales, or obstructed breathing. Pulmonary aspiration was classified based on observations of gastric contents or radiological evidence of contents in the airway.[11]

During the five-year time span this study retrospectively observed 11,535 elective procedures. Of these only 10,015 were included in the study. Inclusion criteria and exclusion criteria is listed in Table 14. Patients included were less than one year up to 18 years of age. Age breakdown for the study and patient ASA status is recorded in Table 15. Anesthesia methods for a majority of these cases was propofol and fentanyl if spontaneous ventilation with a laryngeal mask airway was planned. Alternatives were used for intubation and included thiopentone, fentanyl, and atracurium. Forms of airway management were recorded, but the type of medication was not.[11]

Table 10. Inclusion and Exclusion criteria for Andersson et al.[11]

Inclusion Criteria
- Patients less than 1 year of age up to 18 years of age - Pediatric patients undergoing general anesthesia for elective procedures
Exclusion Criteria
Children anesthetized for procedures other than surgery such as radiation therapy or radiological examinations -Procedures in the Ear, Nose, Throat, ophthalmology, or neurosurgery operating rooms, because they applied 6-4-2 fasting routine and different anesthesia methods -Emergency surgery -neonates in the neonatal intensive care unit

Table 11. Patient Demographics H. Andersson et al.[11]

Age	**Number of Participants (N)**
<1 year	822
1-5 years	4314
6-12 years	2932
13-16 years	1947
ASA Status	**(n)**
I	5851
II	3016
III	734
IV	23
Unknown	392

Study Results**:**

Data was collected between January 2008 and December 2013. There were three cases of pulmonary aspiration and fourteen incidences of suspected pulmonary aspiration. The three cases of pulmonary aspiration had post-operative chest x-rays that were consistent with aspiration. There were 14 patients who developed transient symptoms following vomiting. The charts reported that there was no evidence of gastric contents visualized in the airway or laryngeal mask. In addition, these patients did not suffer post-operative respiratory distress. In only two of these cases was a chest x-ray performed, and both x-rays did not show evidence of pulmonary aspiration. Overall, there were no long-term complications associated with aspiration or suspected aspiration, and there were no incidences of mortality observed. A total of 98 incidences of vomiting or regurgitation during anesthesia were recorded; these were not classified as aspiration or suspected aspiration. The study results concluded age and ASA status did not influence the incidence of aspiration. Andersson et al.[11] did not find an increased incidence of aspiration when compared to studies that implemented clear liquid fasting times greater than two hours. There was no reported statistical analysis of the results.[11]

Study Critique:

Andersson et al.[11] had a well-designed case control study. It was not a randomized control trial; leaving the study open to confounding variables. This study filled a gap in research by assessing the incidence of pulmonary aspiration in pediatric patients that allowed them to consume clear liquids up until being called to the operating suite. It is unknown whether at least 2 hours of fasting of clear liquids prior to general anesthesia is needed. Andersson et al.[11] stated the evidence from their research could help with decreasing the number of incidences of preoperative dehydration and hypoglycemia. Allowing clear liquids could also improve patient

comfort and decrease hemodynamic complications. Research assesses the incidences of aspiration in pediatric patients to be from 1 to 10 in 10,000 patients.[11]The researchers performed a power analysis and determined that they had sufficient power to be able to assess the risk of pulmonary aspiration.[11] This study did not have its own comparison group. Their results were compared to the findings of previous studies that strictly adhered to the 6-4-2 regime. These studies also had differing definitions and processes for diagnosing pulmonary aspiration. This study, nor any of the studies they reported as comparisons, had instances of mortality. This indicates the most severe incidences of aspiration were recorded. As a result of the lack of control group there is a decrease in the validity of the results. The assessed increased or decreased instance of pulmonary aspiration is compared to studies that had different patient populations and different definitions of aspiration. Using other studies to compare results increases confounding variables and negatively impacts the validity.

Andersson et al.[11] focused on the effect of clear liquids and aspiration. They reported a strict NPO by midnight policy for their patient, but did not specify the duration of time they fasted from solids. It is unknown how strict providers were at independently enforcing this policy. This study does not specify when, or how much, clear liquid was consumed prior to entering the operating suite. Patients in the study were given the freedom to consume liquids up until called to the operating room, but patients were encouraged to only drink when thirsty. As a result, patients could have fasted from clear liquids more than two least two hours. Each patient included in this study could have had different fasting times and different amounts of clear-liquids consumed. Andersson et al.[11] also reported there is usually at least a thirty-minute time frame between being called to the operating room and the induction of medication, which increases the clear liquid fasting time. This is likely true for most hospitals and therefore should be considered when giving patients fasting times.

Andersson et al.[11] performed their study at one specific Swedish hospital in the operating room. Results were limited to the skill sets of the hospital employees and the population they service. The operating room is an environment well equipped and prepared to handle vomiting and regurgitation. When vomiting or regurgitation occurred patients were suctioned or placed on their side to prevent incidences of aspiration. These results cannot be extrapolated to larger populations, especially those that do not occur in the operating room. For example, providers in a radiology suite are not always directly in contact with their patients, and the risk of pulmonary

aspiration could be higher due to delayed access to the patient. This study was performed in Sweden. While it is a developed nation with access to healthcare, the populations among the United States and Sweden still differ and may not be generalizable to the United States population. Andersson et al.[11] reported no conflicts of interest.

Discussion:

Two studies used in this review came to the general consensus that the risk of pulmonary aspiration during procedural sedation for those who fasted more than six hours is comparable to those who fasted less than six hours. Andersson et al.[11] came to the conclusion that fasting more than two hours from clear-fluids is comparable to NPO less than 2 hours prior to general anesthesia. None of the results showed a statistically significant relationship between NPO and the risk of aspiration. Beach et al. study concluded, based upon their p value, that there is not a statistically significant association between NPO status and risk of aspiration.[8] Pulmonary aspiration is a rare complication. Larger studies, like the Beach et al.[11], need to be performed in order to determine if the duration of fasting increases the risk of pulmonary aspiration. Of the three studies, Beach et al.[8] was the largest, with 139,142 participants, which may explain why the incidences of aspiration during procedural sedation (Table 12). Current research indicates that the risk of aspiration ranges from 1 to 10 per 10,000 patients. [8,11] Andersson et al. had 10,015 patients and three instances of aspiration in patients undergoing general anesthesia.[11] Clark et al had 2,487 participants and no recorded instances of aspiration; this suggests that their population size was not large enough to determine aspiration risk (Table 16).[10] Only one of studies did not have a population size large enough to appropriately assess the risk (Table 16). Andersson et al. determined that they had sufficient power to be able to assess the risk of pulmonary aspiration and PSA.[11] The other two studies did not perform a power analysis and as a result placed limitations of the study. However, Beach et al. had a large enough population size to appropriately assess risk of pulmonary aspiration. None of these studies showed statistical significance between NPO timing and aspiration risk. Further research is needed, especially with a larger sample size, to further reinforce the Beach et al. [8] conclusion that there is a lack of association between NPO status and aspiration.

The studies used in this review were two prospective observational studies and one retrospective study. These studies were limited because they were observational. Randomized controlled trials could have provided a better analysis on the risk of pulmonary aspiration during

procedural sedation and NPO status by looking at specific fasting times, as compared to patient reported. The question remains as to whether or not it is ethical to perform a randomized controlled trial when the risk of pulmonary aspiration during sedation, following a shorter NPO, is unknown. A randomized control trial could place patients at unnecessary risk and this would make it difficult to get approval and find willing participants. Alternatively, a very large prospective cohort study, with fasting times diligently recorded, may provide the best analysis of aspiration risk in patients undergoing procedural sedation. This format would not place patients at increased risk of complications.

Table 12. Comparison of Studies

Study	**Clark MM[10]**	**Beach, Michael L M L.[8]**	**Andersson et al.[11]**
Study Type	Prospective observational study	Prospective observational study	Retrospective review
Population size	2,487	139,142	10,015
Age of Subjects	2 months to 18 years	0 months to 18 years old	Less than 1 year to 18 years old
NPO >6 hours	1,480	82,546	All patients were on a strict NPO > 6 hours for solids
NPO <6 hours	1,007	1,584	All patients were allowed to consume clear liquids until called to the operating suite.
Aspiration	0	10	3

None of these studies reported the exact duration of patient fasting, the characteristics of the last meal, or liquid the patient consumed. The goal of fasting is to reduce the gastric volume and acidity in order to reduce the incidence of aspiration.[9] Ideally, the act of fasting would completely prevent the occurrence. However, pulmonary aspiration does occur in patients who perform a prolonged fast. The ASA recommends providers take into account the type and quantity of food patients eat prior to setting fasting guidelines.[1] The standardized fasting times do not control for the type of solid food consumed. The type of food is significant because some foods take longer to clear the stomach, such as a cheeseburger compared to crackers or a salad. Therefore, additional fasting time may be indicated for patients who consumed fried or fatty foods.[9] Recording the last meal consumed and when it was consumed will control for food

characteristics being a confounding variable for the effect of NPO status on aspiration. Research should not solely focus on NPO status as the only approach to decrease gastric volume and acidity.[1]

Andersson et al.[11] researched the effects of shortened clear-liquid fasting time on pulmonary aspiration in patients undergoing general anesthesia. Clark et al. [10] and Beach et al.[8] both examined this outcome patients undergoing procedural sedation. Due to the limited research on shortened fasting times in pediatric patients, Andersson et al.[11] was the most applicable study found for this review. With the exception of the form of sedation, the clinical question and methods were similar between the studies. Guidelines and pre-operative practices recommended by the ASA are the same for patient's undergoing general anesthesia and procedural sedation.[1] The similarity in pre-operative practices allowed for easy comparison of studies. General anesthesia is a deeper form of sedation than procedural. As discussed previously, a patient under general anesthesia is in a controlled, unconscious state where their protective reflexes are not intact and they cannot maintain their airway on their own. In this study, pulmonary aspiration occurred more frequently in the Andersson et al.[11] study (about 3:10,000) than the Beach et al.[8] study (about 1:10,000). The incidence of aspiration in this review was higher in the patients undergoing general anesthesia, but research shows that the incidence varies from 1-10 per 10,000.[11] All three studies came to the same conclusion, there is no increased incidence of aspiration based on fasting time.[8,10,11]

The higher a person's ASA physical status classification, the higher their risk of pulmonary aspiration.[9] These three studies used relatively healthy children with lower ASA statuses. Only children within classes I-III, according to the ASA physical status classification, were included in the studies (Table 5). Beach et al.[8] found there was a positive correlation with major complication and ASA physical status, age, types of procedures, and emergency sedation status. There was not a correlation between these variables and NPO status.[8] Further research into those correlations could help with understanding the risk of other complications and pulmonary aspiration in relation to NPO status. New guidelines concerning pediatric procedural sedation guidelines and NPO status could be categorized based on the patient's independent risk factors.

Conclusion:

Clark et al.[5] and Beach et al.[6] concluded there was no statistically significant difference between an NPO status less than 6 hours, compared to greater than 6 hours, and the risk of aspiration during procedural sedation in pediatric patients. Andersson et al.[11] concluded that a shortened fast for clear liquids does not increase the incidence for aspiration prior to general anesthesia. Due to the rare occurrence of pulmonary aspiration, further research on the risk of major complications during non-emergent procedural sedation in the pediatric population is needed. Future studies should include randomized controlled trials or large prospective cohort studies that focus on the risk of pulmonary aspiration in relation to NPO status in pediatric patients undergoing procedural sedation. These studies should include fasting time frames greater and less than six hours for solid foods and fasting times greater and less than two hours for clear-liquids. Studies should have larger sample sizes, in the tens of thousands, in order to adequately assess the rare event of pulmonary aspiration during procedural sedation. Beach et al's.[8] study found that NPO status is not an independent risk factor for pulmonary aspiration in individuals undergoing procedural sedation.[8] Variables to consider and control for in future studies include the level of sedation, ASA status, type of procedure, last meal, and the form of sedation and its mechanism of delivery. Further research is needed to determine how pulmonary aspiration is directly affected by NPO status. Future studies should address several limitations: sample size, types of procedures performed, the sedation used, duration of NPO, and a record of the last meals patients consumed and when.

Further research is needed to see if medications such as anti-emetics, antacids, H2 receptor antagonists, proton pump inhibitors, anti-cholinergics, or gastrointestinal stimulants decrease the incidence of aspiration. Currently, there is insufficient literature to recommend these medications for routine use, and therefore they are not recommended by the ASA.[1] These medications could decrease gastric contents and acidity, and as a result, potentially decrease the incidence of aspiration. Future research regarding these medications is indicated. If these medications were found to be effective, then patients could fast for a shorter duration. This could improve patient comfort and prevent complications.

The process, type, and form of sedation should be well documented in future studies. To determine if there is a relationship between the level of sedation and airway complications, the level of sedation should be classified and recorded. One of the studies in this review used the University of Michigan Sedation Scale, seen in Table 3, to classify levels of sedation. Future

studies should also include sedation professionals of differing experience and skill level to eliminate potential research bias. Research has shown that highly trained anesthesiologists have lower instances of aspiration when compared to sedations specialists with less experience.[12] It is unrealistic to assume that every patient will be sedated by a highly trained anesthesiologist. In order to assess the risk of aspiration as a result of NPO status, sedation specialists should vary in skill level. The medication used as the sedative is also important for future research. Propofol has been shown to decrease the lower esophageal sphincter pressure and, as a result, increases the risk of aspiration.[12] Other medications such as volatile anesthetic agents, β-agonists, opioids, atropine, thiopental, tricyclics, and glycopyrrolate have also been associated with increased risk of aspiration.[12] In addition, if a topical anesthetic is applied to the larynx, the cough reflex is inhibited and the risk of pulmonary aspiration is further increased.[12] The medication should be controlled for in order to assess the effect of NPO status on aspiration. The results of one large study using a large variety of sedatives would be impacted if one medication decreased lower esophageal sphincter more than others. This variable could be assessed for separately, however this would decrease the population size and, as a result, the power of the study. There are several factors that influence the patients' risk of aspiration, and future research controlling for the type, form, and delivery of sedation will fill the gaps in research.

More than half of airway related deaths under sedation are due to pulmonary aspiration if they are not identified and treated appropriately.[9] Due to the dire consequences of aspiration, it is imperative to conduct further research to determine if a specified NPO status does affect the risk of pulmonary aspiration. There are instances of pulmonary aspiration that remain asymptomatic.[8] Pulmonary aspiration is hard to research because the risk of pulmonary aspiration is small, and the risk of developing signs or symptoms is even smaller. Therefore, events are rare and easy to overlook. However, in the studies used in this review there were no instances of mortality.[8,10,11] This indicates that though some instances of aspiration may be missed, the most severe instances are being diagnosed and treated. The more severe instances of pulmonary aspiration are the ones that result in morbidity and mortality and are therefore the most important outcomes when assessing the effect of NPO status on aspiration risk. Missing harmless aspiration events does not influence the significance of these results as long as the most severe events are documented.

This research is important because decreasing fasting time for patients can decrease the number of patients who suffer electrolyte imbalances, insulin resistance, dehydration, and patient

discomfort.[2] Literature is lacking regarding other ways to decrease gastric contents and acidity. Further exploration is needed to determine if there is a better way to prevent aspirations, such as medications. Studies have found that NPO status alone does not increase a patient's risk of aspiration, and therefore it is important for future research to control for these variables.[12]

Future studies should aim to drastically increase their sample sizes and to control for as many variables as possible. If the control and comparison groups are as similar as possible with only the duration of NPO differing, future research would have much more significance. The goal of future research is to ensure patient safety and provide the highest quality of care to patients. These studies suggest that there is no difference in the risk of pulmonary aspiration or major complications in pediatric patients undergoing procedural sedation in relation to NPO duration. Future investigation is still needed to further validate these results. In regards to NPO status prior to PSA, we recommend that it would be safe for patients to have clear liquids up until called to the operating suite. Due to the rare incidence of aspiration in the general population and the significant complications that result, a longer NPO status may be appropriate for solid foods. We recommend a solid food fasting time of four hours, instead of six, due to no statistically significant difference in the number of complications based on NPO status. In addition, the delay of time it takes to reach the operating suite and start sedation would unintentionally prolong the fasting time. The apparent instance of aspiration and complications do not appear to increase based on NPO status, however, the instance of post-operative complications and patient discomfort does increase with prolonged fasting time. Ideally, by decreasing fasting time by two hours post-operative complications could be decreased and the incidence of aspiration and complications would not increase.

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