

<PE-AT>Initiation of Enteral Feeding Regimens Following Laparoscopic Gastrostomy Tube Placement in the Pediatric Patient

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**Outcomes Associated with Early vs. Late Initiation of Exclusive Enteral Feeding
Regimens Following Laparoscopic Gastrostomy Tube Placement in the Pediatric
Patient**

Abstract

Objectives: Despite frequent placement of pediatric laparoscopic gastrostomy tubes, no rigorous evaluation of initial feeding and advancement regimens exists. Therefore, the aim of this study was to determine whether early enteral feeding after gastrostomy tube placement is associated with increased symptoms, procedural complications, or length of stay (LOS).

Methods: In this retrospective cohort study, the records of all patients at a tertiary care pediatric hospital who had gastrostomy placement were reviewed. Only patients fed exclusively via gastrostomy were included. Feeding was monitored starting with the first post-operative feed and subsequently in 24-hour increments. Adverse events were recorded based on clinical documentation.

Results: A total of 480 patients met inclusion criteria. Patients who started feeds between 24 and 36 hours had a shorter LOS compared to those who started at 36 to 48 hours ($p=0.0072$) or >48 hours ($p<0.0001$). Patients requiring ≥ 60 hours to reach goal feeds had significantly longer LOS than the other groups. There was no difference in the distribution of the LOS based on percentage of goal feeds initiated. Subjects who required ≥ 60 hours to attain goal feeds had the most feeding complications.

Conclusions: More aggressive feeding advancement and earlier initiation of feeds were associated with decreased LOS without an associated increase in adverse clinical events.

Keywords: pediatrics; enteral nutrition; gastrostomy; length of stay

<PE-FRONTEND>

Introduction

The indications for gastrostomy tube (GT) placement in the pediatric population are extensive.¹ In the United States, there were approximately 188,000 GT placed in 2007 alone.² Fox et al. reported that, in 2009, GTs were placed at a rate of 18.5 procedures/100,000 US children.³ However, despite the frequency with which GTs are inserted, there continues to be a lack of research to guide clinicians in proper initiation and advancement of enteral feeds in pediatric patients.^{4,5}

Some of the earliest studies examining different feeding methodologies after GT placement were published in the 1980's when Keohane et al demonstrated no change in side effects with nasogastric (NG) feeds of differing osmolalities.^{6,7} Since that time, a multitude of authors have demonstrated that patients can be fed as early as 3 to 4 hours postoperatively without feeding intolerance or an increase in adverse events.⁸⁻¹³ The ESPGHAN Committee on Nutrition concluded that data is generally limited regarding best approaches for delivering enteral feeds.¹⁴

Many elements of the feeding regimen have yet to be rigorously studied. Namely, what percentage of a patient's daily calories can be given in the initial feed and how rapidly can feeds be advanced to the patient's caloric goal? Expert opinion recommends initiating feeds at 25% of goal and increasing by 25% per day such that goal feeds would be obtained on day 4 post-GT placement.^{15,16} However, others suggest attaining goal calories first in 24-48 hours by continuous feeds and then transitioning to bolus feeds.⁵ Instead of focusing on goal caloric intake, some authors have used a wide variety of volume-based recommendations.^{4,5,15,16}

Because wide variances in recommendations and published protocols exist, the aim of this study was to evaluate the outcomes associated with differing advancement of enteral

feeding post-GT placement in our patient population. Our hypothesis is that early introduction of feeding with prompt advancement to goal feeds is associated with decreased length of hospital stay without increasing adverse events and emergency department re-visits.

Materials and Methods

This is a retrospective, cohort study of patients who received a primary GT from January 1, 2010 to December 31, 2015. This study was conducted at an urban university-affiliated tertiary care pediatric hospital. It was reviewed and approved by the institutional review board (reference number 10-04880-XP) prior to study commencement. Patient records were reviewed if they were coded for the following procedures: laparoscopic gastrostomy (ICD9 43653/43.19, ICD10 ODH64UZ), open gastrostomy (ICD9 43830/43.19, ICD10 ODH60ZA), neonatal open gastrostomy (ICD9 43831/43.19, ICD10 ODH68UZ), percutaneous endoscopic gastrostomy (ICD9 43246/43.11, ICD10 ODH68UZ), laparoscopic Nissen fundoplication (ICD9 43280/44.67, ICD10 ODX44ZZ), or open Nissen fundoplication (43327/43328/44.65/44.66, ICD10 ODV40ZZ).

The following patients were excluded from the study: 1. Those who received only fundoplication without GT insertion, 2. Those who underwent GT revision or replacement, 3. Those for whom feeds from initial GT placement were unable to be monitored due to early discharge, 4. Patients who concomitantly received either oral feeds or parenteral nutrition, and 5. Patients in whom the GT was used only for medications.

The following definitions were used:

1. **Goal Feeds:** The minimum goal kCal recommended by the registered dietitian on the team unless otherwise stated by the treating physician. kCal were chosen as the measure of goal feeds over other measures (i.e. volume) based on the 2009 *ASPEN Enteral Nutrition Practice Recommendations*.⁵ In order to be considered to have

attained goal feeding, a patient was required to maintain goal feeds for a minimum of 24 hours without requiring reduction in caloric content. The only exception to this was if a patient was required to be NPO for a reason unrelated to tolerance of tube feeding, such as sedation for an MRI or other procedure. Notably, tolerance of bolus feeding was not necessary for patients to be considered to have attained goal feeding.

2. Pre-Procedural Feeds: The total kCal that the patient took in via enteral routes in the 24 hours prior to being made NPO for surgery.
3. Adverse Events: The following were considered adverse events for the purposes of our study. First, vomiting and diarrhea were tallied as the number of events recorded in nursing flowcharts or physician daily notes prior to achieving goal feeds. Given the retrospective nature of the work these were crosschecked with each other in order to avoid double counting events while also attempting to ensure that all events were included in the data. Second, feeding complications were recorded as categorical variables, counting only whether or not the patient had an adverse event. Events were recorded if a patient had them anytime from placement to discharge. Events were found by using nursing flowsheets or by Boolean searching the patient chart for the following terms: gastroparesis, dyspareisis, leak, distention, granulation, irritation, erythema, and intolerance. These complications were chosen as remarkable adverse events due to their use in previous studies.^{1,13}
4. 30-day Emergency Department (ED) visits: ED visits for GT or gastroenterological related complaints. These were found by looking in the electronic medical record (EMR) to see if they visited the ED for any reason. If the reason was related to the GT then they were included. Only ED visits at our institution were included.

The following times were used to determine data points for measuring achievement of goal feeds. The “out of operating room (OR) time” documented in the OR record was defined

as time zero. The time when the first feed was given was measured from this point. The feeds given every 24-hours from the first feed until discharge were measured to provide a snapshot of the patient's progress. Once the patient achieved goal feeds, the time from out of OR to goal feed was determined and reported as time to goal feeds (TGF). Of note, although the patient was required to stay on goal feeds for 24 hours as described previously, the time to goal feed was calculated to the first feed at goal and not the last. Length of stay represents the time from the out of OR time to the discharge time. Discharge time was defined as the time that the discharge order was signed in the EMR.

We sought to control for confounding variables in the following ways. First, patients were stratified for analysis based upon the indication for placement. The diagnoses for placement were obtained from the operative report as well as the discharge diagnoses as recorded in the discharge summary. Second, we evaluated the difference in outcome measures based upon the surgeon. Third, we compared patients based upon whether or not they had a Nissen fundoplication. Fourth, we looked at the hospital setting (intensive care units vs floor status) as a surrogate for general patient stability. Fifth, the patient's Z score was calculated using peditools.org CDC growth charts based upon the patient's weight immediately prior to surgical placement. This was compared to the the first recorded weight after attaining goal feeding. For infants <36 months old their weight was corrected for their gestational age.

Continuous variables were reported as medians and interquartile ranges (IQR), while categorical variables were summarized as frequency counts and percentages. Relationships between continuous variables were explored using Spearman's correlation, while Chi-Square test and Fisher's exact test were used to determine associations between categorical variables. To test the difference in time to hospital discharge between levels of the variables of interest,

Kruskal Wallis test was performed, with post-hoc comparisons conducted using the Dwass-Steel-Critchlow-Fligner (DSCF) method with a Bonferroni adjusted significance level. A significance level of 0.05 was used in all main analyses. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

Demographics

In total, 901 patients were identified. 421 patients were excluded for the following reasons: patient received fundoplication only (n=42), secondary gastrostomy (n=17), concurrently receiving parenteral nutrition or oral feeds (n=346), patients discharged prior to reaching goal feeds (n=12), received medication administration only via GT (n=4). Of the remaining 480 patients that we included 259 were male and 221 were female. 258 self-identified as African-American, 182 as Caucasian, 11 as Hispanic, 3 as Asian, and 26 as either other or unidentified. Our median patient age was 8.67 months with an inter-quartile range (IQR) of 3.12-30.26. 188 of our patients were in critical care settings (i.e. intensive care units (ICU)) vs 292 were on the general floor.

Patients were stratified based upon comorbid conditions listed in the discharge summary and operative note. In the event that a patient had multiple comorbidities they were classified in multiple groups. In total 63 patients had congenital heart disease, 94 had cerebral palsy, 79 had developmental delay, 82 had facial malformations, 221 had gastroesophageal reflux disease, 69 had oral aversion, 116 had seizures, and 59 had either chromosomal malformations or other diagnoses.

Associations Between Feeding Initiation, Time to Goal Feeds, and Length of Stay

Analysis of association of time to feeding initiation and length of stay (LOS) showed a statistically significant association (Table 1). Performing a post-hoc analysis, it was found that when patients started their feeds between 24 and 36 hours, they had a shorter LOS

(median 135.8 hrs) compared to those who started at 36 to 48 hours (174.6 hrs, $p=0.007$) or >48 hours (239.5 hrs, $p<.0001$). Analysis of association of amount of feeds (kCals) used at start of feeding and LOS showed no association in the LOS depending on the amount of feeds used at the start of feeding ($p=0.18$).

Analysis of association of time to goal feeds (TGF) was statistically significant ($p<.0001$) (Table 2). Patients were grouped into the following categories: those who obtained goal feeds at <12 hours, 12 to <24 hours, 24 to <36 hours, 36 to <48 hours, 48 to <60 hours and ≥ 60 hours. Post-hoc analysis showed that those in the ≥ 60 hours group had a significantly longer LOS (221.32 hrs) than those in the 12 to <24 hour group (141.8 hrs, $p<0.001$), the 24 to <36 hour group (145.2 hrs, $p=0.003$), and the 36 to <48 hour group (120.4 hrs, $p=<0.0001$).

Associations Between Time to Goal Feeds and Adverse Outcomes

No significant association between time to goal feeds and the number of ED visits was discovered. There was also no significant association in ED usage amongst patients who started at different percentages of their goal feeding regimen (Supplemental Table 1).

The lowest rates of emesis were in those who attained goal in 12 to <24 hours (8.5%) while the highest rates occurred for patients whose TGF was 48 to <60 hours (38.8%). There was an association of emesis based on TGF ($p=0.0003$) using post hoc analysis of these two groups. There was also an association amongst these two groups with feeding complications ($p=0.0017$) (Table 3).

Associations Between Comorbidities and Adverse Outcomes

Analysis on associations of comorbidities was performed. These are listed in table 4. Further analysis was performed specifically on patients with concurrent Nissen funduplications. Not surprisingly, these patients had lower post-surgical rates of emesis

($p < .0001$). However, there was no significant difference in diarrhea ($p = 0.06$), 30-day ED visits ($p = 0.90$), time to hospital discharge ($p = 0.36$), or feeding complications ($p = 0.07$).

Other Pertinent Analyses

Location of care was also associated with adverse events. Those in non-critical care settings (i.e. the floor) suffered from diarrhea (8%) more than those in critical care settings (18.2%, $p = 0.0018$) while those in critical care settings (i.e. ICU) suffered from more feeding complications (23.6%) compared to the floor (34%, $p = 0.012$). Those on the floor had a higher proportion of subjects with a time to goal feeds between 36 to < 48 hrs (24%) compared to those in the ICU (13.8%), while those the ICU had a higher proportion of subjects with a time to goal feeds ≥ 60 hrs (32.4%) compared to the floor (17.8%, $p = 0.003$). No associations were found between the 6 primary operative surgeons and rate of adverse events. We could not evaluate types of formula and associated outcomes because the data was significantly skewed toward the standard formulas. We did evaluate the difference between the pre-procedural and post-procedural Z Scores and found no statistical difference.

Discussion

The primary aim of this study was to evaluate the outcomes associated with differing advancement of enteral feeding post-GT placement. We found that early initiation of enteral feeding (between 24 and 36 hours) and earlier achievement to goal feeds were both associated with shorter LOS without increasing adverse events or post-procedural ED visits for GT problems. These results differ from some expert recommendations expressed in previous publications, which state that feeds should be advanced by 25% each day over the course of 4 days.^{15,16}

Our study results are consistent with previous findings which show that earlier feeding may be safe in children.^{8,13} Our study also suggests that starting feeds less than 36 hours post-GT placement may be an important measure for likely shorter LOS. When

comparing the 36 to <48-hour group to the 24 to <36-hour group we found a significant difference in LOS (Table 1). The data did not suggest that there were any differences in patients where they were started within 24 hours compared to the other groups. While there was no statically significant difference it is notable that patients who started on feeds at <24 hours numerically took longer to achieve goal feeds. Other studies showed no difference in time to discharge in patients who started feeds sooner.^{8,12,13} When adding this study to their work, this data supports that earlier feeds are associated with earlier hospital discharges although clear direction of when to start feeds remains unclear.

It is important to note that because this study is retrospective in nature and there was not a clear clinical practice guideline in affect during this period of evaluation, the differences we see were associations and not indicative of causation. It is possible that the association we see is a reflection of the fact that patients who were able to tolerate earlier initiation and advancement of feeding were healthier and, therefore, more likely to be discharged earlier.

Regarding the TGF it is notable that attaining goal feeds in <60 hours had no association with the LOS. However, attainment of goal feeds at >60 hours was associated with longer LOS. There was also a numerical, though not statistically significant increase in LOS for patients who attained goal feeds in <12 hours. It is also true that patients who reached goal feeds at <12 hours had a longer time to reach TGF but that this was not statistically significant. This may be attributable to the paucity of patients in our cohort who were started at feeds of <12 hours.

Patients may have tolerated feeds better because they had less severe underlying disease. We feel however as though this is not especially obvious given our data. Reasons for prolonging advancement were not significantly different in our patients. For example, patients in the ICU vs the floor had no more episodes of emesis comparatively. Also there were no increased adverse events in patients born more premature than others. Presumably,

prematurity and ICU care would indicate sicker patients yet they groups had similar outcomes. Notably, floor patients had more diarrhea than ICU level patients. It is unclear whether advancement was hindered by diarrhea or if slower advancement caused the diarrhea. If it held that sicker patients took longer to reach goal feeds we would expect this to be reversed. We feel that this research demonstrates the need for prospective studies with strict protocols for feeding initiation and advancement.

Notably, only 2% of patients within the cohort were started at $\geq 67\%$ of goal feeds. While only 10% of patients were started between 34% and $< 67\%$ of goal feeds. As suggested by other authors, it is felt that patients can likely be started closer to goal feeds than is the current standard of care.^{21,22} The mean (standard deviation) for the initial feeds as a percentage of goal was 20% (21%), while for the pre-procedural feeds the mean (standard deviation) was 87% (39%). Due to the small size of the cohort for whom higher percentage of goal feeds were started there was a limitation in the ability to draw statistical conclusions. Their data is presented in supplemental table 2.

The study also demonstrated several interesting associations outside of the primary focus. First, this study hypothesized that there would be no difference between the ED usage rates based upon how aggressively feeds were started and advanced. It was found that regardless of the time to start feeds or the TGF, that the ED usage did not increase. This suggests that patients were not being discharged prematurely after having quickly advanced feeds only to return to the ED and seek care for GT related complications such as vomiting, diarrhea, or inability to care for the site.

Second, a patient's associated comorbidities may affect their ability to tolerate feeding advancement. Patients who had cerebral palsy had an increased rate of diarrhea, emesis, and feeding complications. This may be clinically relevant as patients with cerebral palsy may have more feeding problems due to underlying gastrointestinal dysmotility. With this in

mind, it may be reasonable to be more cautious in feeding advancement of patients with cerebral palsy. More research will be needed to further evaluate this association. Patients with oral aversion had more episodes of vomiting. This may be indicative that patients with oral aversion have other underlying disease that is causing the oral aversion. It may suggest to clinicians that they should be more cautious prior to GT placement as underlying etiologies may need further investigation.

The limitations of this study should also be recognized. The most notable limitation is the retrospective nature of this work. This was particularly problematic when recording adverse events such as vomiting and diarrhea. Although nursing flowcharts were crosschecked with physician progress notes in order to limit over/under reporting this remains a significant difficulty. In the future, a prospective study is needed to better evaluate these adverse events. Since this study is retrospective it may have led to inconsistencies in charting of feedings and adverse events. In order to further delineate appropriate feeding regimens, prospective studies need to be undertaken.

Another significant limitation is variability in provider practice which may be created unrecognized bias. This leads to several challenges including providers holding feeds in clinical situations that other providers continued to feed. Another limitation described previously was the small percentage of patients who were started at or near goal feeds, this limited the ability to statistically evaluate this group separately. Notably, LOS may be affected by a multitude of factors including comorbidities. Also, we considered only the number of kCals a patient received not whether they were given bolus or continuous feeds. Finally, we did not evaluate the type of formula that patients were taking. This may also be a potential confounder.

In conclusion, in post-operative gastrostomy tube patients, earlier attainment of goal feeds and earlier initiation of feeds were associated with decreased length of stay. More aggressive

feeding regimens were not associated with increased adverse clinical outcomes. Since current published guidelines focus on expert opinion rather than data, we believe that this work will help clinicians prescribe safe and effective feeding regimens for their patients.

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Table 1: Comparison of Length of Stay across Time to Start Feed

| | Time to Start Feed | | | | p-value (Kruskal-Wallis) |
|---|----------------------|---------------------------|----------------------------|----------------------------|-----------------------------|
| | < 24 Hrs (n=61) | 24 to < 36 hrs (n=238) | 36 to < 48 hrs (n=93) | >= 48 hrs (n=88) | |
| Length of Stay (LOS), hrs, Median (IQR) | 152.7 (94, 452.5) | 135.8 (94.4, 242.5) | 174.6 (119.1, 434.8) | 239.5 (166.6, 525.5) | <.0001 |
| Post HOC using Dwass, Steel, Crithclow-Fligner with Bonferroni Correction (alpha =0.05/6=0.0083) | | | | | |
| <24 Hours | ----- | 0.8613 | 0.4981 | 0.0210 | ----- |
| 24 to < 36 Hrs | ----- | ----- | 0.0072 | <.0001 | |
| 36 to < 48 hrs | ----- | ----- | ----- | 0.0956 | |
| >= 48 hrs | ----- | ----- | ----- | ----- | |

This table evaluates the length of stay (LOS) based upon when the patients started their feeds.

Average LOS of each group as well as the interquartile ranges (IQR) are listed in the first row. Post-hoc analysis are listed in the bottom rows comparing the different groups.

Statistical significance was found when comparing patients started on feeds within 24 hours to those started at >= 48 hours. It was also found comparing the 24 to <36 hour group with both the 36 to <48 hour group and the >=48 hour group.

Table 2: Comparison of Length of Stay across Time to Goal Feeds

| Variable | Time to Goal Feeds (TGF) | | | | | | p-value (Kruskal-Wallis) |
|---|--------------------------|------------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| | < 12 hrs (n=28) | 12 to < 24 hrs (n=106) | 24 to < 36 hrs (n=88) | 36 to < 48 hrs (n=96) | 48 to < 60 hrs (n=49) | >= 60 hrs (n=113) | |
| Length of Stay (LOS), hrs, Median (IQR) | 171 (96.5, 518.6) | 141.8 (96.6, 387.3) | 145.2 (92.6, 336.5) | 120.4 (92.8, 229.9) | 164.9 (115.2, 266.5) | 221.32 (166.9, 363.9) | <.0001 |
| Post HOC using Dwass, Steel, Critchlow-Fligner with Bonferroni Correction (alpha =0.05/15=0.0033) | | | | | | | |
| < 12 hrs | ----- | 0.9915 | 0.9735 | 0.8063 | 1.0000 | 0.5661 | ----- |
| 12 to < 24 hrs | ----- | ----- | 1.0000 | 0.8275 | 0.9625 | 0.0006 | |
| 24 to < 36 hrs | ----- | ----- | ----- | 0.9788 | 0.9241 | 0.0026 | |
| 36 to < 48 hrs | ----- | ----- | ----- | ----- | 0.2603 | <.0001 | |
| 48 to < 60 hrs | ----- | ----- | ----- | ----- | ----- | 0.0240 | |
| >= 60 hrs | ----- | ----- | ----- | ----- | ----- | ----- | |

This table evaluates length of stay (LOS) based upon the time to goal feeds (TGF) . As with table 1 the LOS with interquartile range (IQR) is listed in the first row underneath each group. Groups are compared with one another in the lower portion of the table. Significance was found when comparing patients who reached goal >=60 hour with all groups except those who reached goal at <12 hours.

Table 3: Negative Outcomes by Time to Goal Feeds

| | Time to Goal Feeds | | | | | | p-value (Chi-Square Test) |
|------------------------------|--------------------|------------------------------|-----------------------------|-----------------------------|-----------------------------|----------------------|------------------------------|
| | < 12 hrs (n=28) | 12 to < 24 hrs (n=106) | 24 to < 36 hrs (n=88) | 36 to < 48 hrs (n=96) | 48 to < 60 hrs (n=49) | >= 60 hrs (n=113) | |
| Emesis | | | | | | | |
| Yes | 7 (25) | 9 (8.5) | 13 (14.8) | 20 (20.8) | 19 (38.8) | 29 (25.7) | 0.0003 |
| No | 21 (75) | 97 (91.5) | 75 (85.2) | 76 (79.2) | 30 (61.2) | 84 (74.3) | |
| Diarrhea | | | | | | | |
| Yes | 3 (10.7) | 8 (7.5) | 13 (14.8) | 16 (16.7) | 8 (16.3) | 20 (17.7) | 0.3100 |
| No | 25 (89.3) | 98 (92.5) | 75 (85.2) | 80 (83.3) | 41 (83.7) | 93 (83.3) | |
| Feeding Complications | | | | | | | |
| Yes | 6 (21.4) | 22 (20.7) | 19 (21.6) | 26 (27.1) | 11 (22.5) | 49 (43.4) | 0.0017 |
| No | 22 (78.6) | 84 (79.3) | 69 (78.4) | 70 (72.9) | 38 (77.5) | 64 (56.6) | |

This table demonstrates patients who were reported to have emesis, diarrhea, or other feeding complications based upon how quickly their feeds were advanced. Feeding complications were defined as any clinical event noted by the care team that lead to holding feeds aside from emesis and diarrhea as these are reported separately. These included gassiness, gastroparesis, dysparesis, leak, distention, granulation, irritation, erythema, and intolerance not otherwise specified. P-value compares the 12 to <24 hour group with the 48 to <60 hour group.

Table 4: Associations Between Comorbidities and Negative Outcomes

| | Negative Outcomes | | | | | | | | | | | |
|-------------------------|-------------------|---------------|--------------|------------------|---------------|--------------|-----------------|-----------------|--------------|-----------------------|-------------------|--------------|
| | Emesis | | | Diarrhea | | | 30 Day ED Visit | | | Feeding Complications | | |
| | Yes (n=97) | No (n=383) | p- value* | Yes (n=68) | No (n=412) | p- value* | Yes (n=65) | No (n=415) | p- value* | Yes (n=133) | No (n=347) | p- value* |
| CHD, n (%) | | | | | | | | | | | | |
| Yes | 13 (13.4) | 50 (13.1) | 0.9279 | 3 (4.4) | 60 (14.7) | 0.0216 | 13 (20) | 50 (12) (88) | 0.0775 | 23 (17.3) | 40 (11.5) | 0.0941 |
| No | 84 (86.6) | 333 (86.8) | | 65 (95.6) | 352 (85.3) | | 52 (80) | 365 (88) | | 110 (82.7) | 307 (88.5) | |
| CP, n (%) | | | | | | | | | | | | |
| Yes | 27 (22.7) | 67 (17.5) | 0.0219 | 29 (42.6) | 65 (15.8) | <.0001 | 16 (24.6) | 78 (18.8) | 0.2716 | 35 (26.3) | 59 (17) (17.3) | 0.0214 |
| No | 70 (77.3) | 316 (82.5) | | 39 (57.4) | 347 (84.2) | | 49 (75.4) | 337 (81.2) | | 98 (73.7) | 288 (83) | |
| DD, n (%) | | | | | | | | | | | | |
| Yes | 17 (17.5) | 62 (16.2) | 0.7509 | 18 (26.5) | 61 (14.8) | 0.0162 | 13 (20) | 66 (15.9) | 0.4076 | 26 (19.5) | 53 (15.3) | 0.2583 |
| No | 80 (82.5) | 321 (83.8) | | 50 (73.5) | 351 (85.2) | | 52 (80) | 349 (84.1) | | 294 (80.5) | 107 (84.7) | |
| Facial Anomalies, n (%) | | | | | | | | | | | | |
| Yes | 16 (16.5) | 66 (17.2) | 0.8631 | 4 (5.9) (5.9) | 78 (18.9) | 0.0081 | 7 (10.8) | 75 (18.1) | 0.1458 | 24 (18) (14.2) | 58 (16.7) | 0.7289 |
| No | 81 (83.5) | 317 (82.8) | | 64 (94.1) | 334 (81.1) | | 58 (89.2) | 340 (81.9) | | 109 (82) | 289 (83.3) | |
| GERD, n (%) | | | | | | | | | | | | |
| Yes | 36 (37.1) | 185 (48.3) | 0.0483 | 34 (50) | 187 (45.4) | 0.4797 | 27 (41.5) | 194 (46.7) | 0.4334 | 72 (54.1) | 149 (42.9) | 0.0276 |
| No | 61 (62.9) | 198 (51.7) | | 34 (50) | 225 (54.6) | | 38 (58.5) | 221 (53.3) | | 61 (45.9) | 198 (57.1) | |
| Oral Aversion, | | | 0.0222 | | | 0.0037 | | | 0.8030 | | | 0.9725 |

| | | | | | | | | | | | | |
|----------------|--------------|---------------|--------------|---------------|---------------|---------------|---------------|---------------|--------|---------------|---------------|--------|
| n (%) | | | | | | | | | | | | |
| Yes | 21 (21.6) | 48 (12.5) | 2 (2.9) | 67 (16.3) | 10 (15.4) | 59 (14.2) | 19 (14.3) | 50 (14.4) | | | | |
| No | 76 (78.4) | 334 (87.5) | 66 (97.1) | 345 (83.7) | 55 (84.6) | 356 (85.8) | 114 (85.7) | 297 (85.6) | | | | |
| Seizure, n (%) | | | | | | | | | | | | |
| Yes | 26 (26.8) | 90 (24.5) | 0.4970 | 28 (41.2) | 88 (21.4) | 0.0004 | 16 (24.6) | 100 (24.1) | 0.9276 | 37 (27.8) | 79 (22.8) | 0.2471 |
| No | 71 (73.2) | 293 (75.5) | | 40 (58.8) | 324 (78.6) | | 49 (75.4) | 315 (75.9) | | 96 (72.2) | 268 (77.2) | |
| Other, n (%) | | | | | | | | | | | | |
| Yes | 15 (15.5) | 44 (11.5) | 0.2868 | 3 (4.4) | 56 (13.6) | 0.0327 | 8 (12.3) | 51 (12.3) | 0.9966 | 21 (15.8) | 38 (11) | 0.1485 |
| No | 82 (84.5) | 339 (88.5) | | 65 (95.4) | 356 (86.4) | | 57 (87.7) | 364 (87.7) | | 112 (84.2) | 309 (89) | |

*All p-values correspond to Chi-Square Test. This table demonstrates the association between comorbidities and negative outcomes. If

patients had more than one of the indications above, they were classified in each category. Congenital Heart Disease (CHD), Cerebral Palsy (CP), Developmental Delay (DD), Gastroesophageal Reflux Disease (GERD). Emergency Department (ED).