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Effectiveness and Complication Rate of Percutaneous Endoscopic Gastrostomy Placement in Pediatric Oncology Patients

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ABSTRACT

Purpose: Malnutrition is a significant issue for pediatric patients with cancer. We sought to evaluate the effectiveness and complication rate of percutaneous endoscopic gastrostomy (PEG) placement in pediatric oncology patients.
Methods: A retrospective chart review was performed on 49 pediatric oncology patients undergoing PEG placement at Johns Hopkins All Children's Hospital between 2000 and 2016. Demographic and clinical characteristics, complications, absolute neutrophil count at time of PEG placement and at time of complications, length of stay, and mortality were identified. Weight-for-age Z-scores were evaluated at time of- and six months post-PEG placement.
Results: The overall mean weight-for-age Z-score improved by 0.73 (p<0.0001) from pre- (–1.11) to post- (–0.38) PEG placement. Improvement in Z-score was seen in patients who were malnourished at time of PEG placement (1.14, p<0.0001), but not in those who were not malnourished (0.32, p=0.197). Site infections were seen in 12 (24%), buried bumper syndrome in five (10%), and tube dislodgement in one (2%) patient. One patient (2%) with fever was treated for possible peritonitis. There were no cases of other major complications, including gastric perforation, gastrocolic fistula, clinically significant bleeding, or PEG-related death documented.
Conclusion: Consistent with previous studies, our data suggests a relationship between site complications (superficial wound infection, buried bumper syndrome) and neutropenia. Additionally, PEG placement appears to be an effective modality for improving nutritional status in malnourished pediatric oncology patients. However, larger prospective studies with appropriate controls and adjustment for potential confounders are warranted to confirm these findings.

Keywords: Endoscopy; Gastrostomy; Enteral nutrition; Neoplasm; Pediatrics

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Conflict of Interest
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INTRODUCTION

Cancer is the leading cause of disease-related death in children younger than 14-years-old [1]. Malnutrition is a significant comorbidity associated with cancer. The reported prevalence varies widely from 5 to 48% [2]. Malnutrition in patients with cancer is dependent on several factors: type of malignancy, extent of metastatic disease, treatment intensity, treatment duration, and side effects. Noxious effects adversely affecting nutritional status may present at any point from the time of diagnosis, during treatment, and even into survivorship [2]. Factors contributing to cancer-related malnutrition include poor oral intake, abnormal metabolism of nutrients, and adverse effects from treatments (i.e., nausea, vomiting, mucositis, and diminished appetite) [3]. Malnutrition may interfere with several processes for which childhood is a critical period, including growth, brain development, puberty, and bone formation [2]. Poor nutritional status may also adversely affect this particular population by resulting in impaired cell-mediated immunity, poor wound healing, increased risk of infection, chemotherapy intolerance, tumor relapse, lower quality of life, poorer survival outcomes, and even death [4-7].

Most guidelines recommend that children with cancer be screened for malnutrition risk during therapy; however, guidelines for nutritional rehabilitation in this population are not well defined and practices vary across pediatric cancer centers [8]. The timing and type of nutritional intervention vary both across and within institutions [8]. Available forms of nutritional intervention include enteral nutrition (EN) (nasogastric [NG], nasoduodenal, nasojejunal, or gastrostomy [G] tubes), parenteral nutrition (PN), or oral supplementation. EN has been found to be a safe and effective method of both preventing the development of future weight loss and malnutrition in cancer patients as well as reversing existing malnutrition in such patients [9]. EN provides trophic factors essential for maintenance of gastrointestinal mucosa, stimulates release of enteric hormones and gastrointestinal secretions, and improves gastrointestinal and gallbladder motility [2]. Due to its low cost and ease of implementation and discontinuation, the most common form of EN is NG tube feeding; however, NG tube feeds may be complicated by mechanical obstruction, discomfort, recurrent dislodgement, and negative cosmetic impact [10]. In the case of such barriers to nutrition, percutaneous endoscopic gastrostomy (PEG) tube insertion can be an effective alternative [11-14].

PEG placement is a minimally invasive procedure that has been shown to be a safe and effective modality for providing EN in various populations [15-18]. Studies exploring the safety and efficacy of PEG tube feedings in pediatric patients with cancer are limited, although some have suggested increased risk of complications in oncology patients due to factors such as neutropenia [7,19-21]. The primary aim of this study was to determine the efficacy of nutritional rehabilitation with PEG feedings in pediatric patients with cancer by evaluating pre- and post-PEG growth parameters, specifically weight-for-age Z-scores, as well as postoperative complications and associated risk factors.

MATERIALS AND METHODS

We performed a retrospective cohort study in children with a cancer diagnosis who received PEG tube placement at Johns Hopkins All Children's Hospital between January 2000 and February 2016. Data was extracted from the electronic medical record. This research was reviewed and approved by our Institutional Review Board (Johns Hopkins Medicine IRB #00224884).

All children between the ages of 1 month and 20 years with a malignant cancer diagnosis who underwent PEG placement at our institution by a pediatric gastroenterologist were included. PEG placement was performed by 10 different gastroenterologists. Two of the investigators evenly divided the patient records, screened their portions independently, and met to discuss unclear cases. Patients who underwent bone marrow transplant (BMT) and those with feeding tubes placed by surgery were excluded to ensure homogeneity of the analyzed population. Electronic medical records were reviewed for the following data: age at PEG placement, sex, weight-for-age Z-score at time of- and six months following PEG placement, type of PEG device placed (gastrostomy, PEG or gastrojejunostomy, PEG-J), diagnosis (cancer type), cancer relapse, length of hospital stay, conversion to gastrostomy button or gastrojejunostomy (GJ) tube, other types of supplemental nutrition given (oral or total parenteral nutrition, TPN), absolute neutrophil count (ANC) at time of PEG placement, major and minor complications within six months of PEG placement, ANC at time of complications (cellulitis, peritonitis, perforations), and mortality.

Major and minor complications were defined prior to data collection. Major complications were defined as any unplanned adverse event necessitating additional hospitalization (i.e., peritonitis requiring intravenous [IV] antibiotics, gastric bleeding requiring transfusion), any complication requiring surgical or interventional procedures (buried bumper syndrome, gastric perforation, gastrocolic fistula), or death directly caused by PEG placement, in accordance with previously published criteria [2,11,14,22]. Minor complications were defined as any superficial PEG site infection requiring antibiotics, PEG tube dislodgement, minor bleeding not requiring transfusion, or any other procedural complications not requiring urgent medical attention.

Efficacy of EN was evaluated by comparing pre- and post-PEG changes in weight-for-age Z-scores. Data were collected from measurements obtained at the time of PEG placement and up to six months (with a window of plus or minus one month) post-PEG placement. We evaluated subjects who met criteria for malnutrition based on initial weight-for-age Z-score less than –1, but also included those who were not malnourished at time of diagnosis. The decision to place PEG tubes prophylactically was made at the discretion of the treatment team due to perceived risk for malnutrition during the treatment course.

Demographic and clinical characteristics of study participants are summarized with counts and percentages. Weight-for-age Z-scores at time of PEG placement were compared with those six months post-PEG placement for all subjects using a paired *t*-test. Statistical analyses were performed using SAS ver. 9.4 (SAS Institute, Cary, NC, USA). The statistical significance level was set at $p<0.05$.

RESULTS

Patient characteristics

A total of 673 patients with neoplasm and malnutrition were identified at our institution between January 2000 and February 2016. Of the 93 who underwent PEG placement, 63 had complete pre- and post-PEG weight measurements. Fourteen patients were excluded from the study; specifically, six due to disease-related death within one to four months of receiving the PEG, three were placed on hospice shortly following PEG placement, and five relocated to another treatment center after PEG placement so medical records could not be obtained. Therefore, 49 total patients were included in the final analysis (**Fig. 1**).

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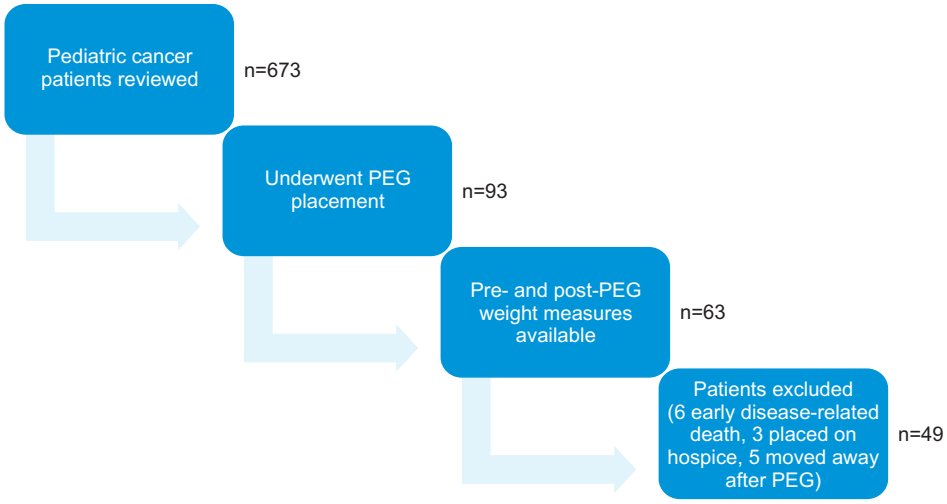

Fig. 1. Flow diagram showing patient selection.
PEG: percutaneous endoscopic gastrostomy.

Patient characteristics are outlined in **Table 1**. Of the 49 patients included, the median age at the time of PEG tube placement was 3.5 years (range of 0.1 to 18.8 years). There was a slight male predominance (57.1%, n=28). A total of 25 patients (51.0%) were malnourished at time of PEG placement, with a weight-for-age Z-score less than –1. Type of PEG tube placed included 46 (93.9%) with G tube and three (6.1%) with GJ tube. In our cohort of children with a cancer diagnosis, 25 (51.0%) patients had central nervous system tumors, 12 (24.5%) had leukemia/lymphoma, and 12 (24.5%) had solid tumors. Relapse of underlying cancer was documented in 20 patients (40.8%). Median length of hospital stay was 15 days with a range of 2 to 79 days. Conversion to Mic-Key gastrostomy or GJ was documented in 35 patients (71.4%). Other forms of supplemental nutrition included oral supplementation (18.4%, n=9), TPN (28.6%, n=14), oral supplementation and TPN (20.4%, n=10), and those with no other type of nutrition documented (32.7%, n=16).

Effect on weight-for-age Z-score is shown in **Fig. 2**. Overall, the mean Z-score improved by 0.73 (p<0.0001) from the time of PEG placement (mean Z-score –1.11) to six months post-PEG placement (mean Z-score –0.38). When analyzed separately, there was a statistically significant improvement in weight-for-age Z-score in the children who were malnourished at time of PEG placement (1.14, p<0.0001), but not in the patients who were not malnourished at PEG placement (0.32, p=0.1968).

Site complications were seen in our cohort. Of the 49 patients included, 12 (24%) developed cellulitis of the PEG site of which 11 (22%) required treatment with parenteral antibiotics and one (2%) was treated with oral antibiotics (**Fig. 3**). Other site complications included buried bumper syndrome in five (10%), and tube dislodgement in one (2%) patient. One patient (2%) with fever was treated empirically with parenteral antibiotics for possible peritonitis. There were no cases of other major complications, including gastric perforation, gastrocolic fistula, clinically significant bleeding, or PEG-related death documented.

Patients who developed cellulitis as a complication had an average ANC of 1,897 cells/uL (40% were neutropenic, with ANC <1,500/uL) at the time of PEG placement, compared to an average ANC of 4,367 cells/uL (33% were neutropenic) in those who did not develop cellulitis.

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Table 1. Patient characteristics

Variable	Value
Age (yr)	Mean=7.2
<2	16 (32.7)
2–5	11 (22.4)
6–10	7 (14.3)
>10	15 (30.6)
Sex	
Male	28 (57.1)
Female	21 (42.9)
Degree of malnutrition (weight-for-age Z-score) at PEG placement*	
None (>−1)	24 (49.0)
Any (≤−1)	25 (51.0)
Mild (−1.99 to −1)	9 (18.4)
Moderate (−2.99 to −2)	10 (20.4)
Severe (<−3)	6 (12.2)
Type of PEG tube placed	
PEG	46 (93.9)
Gastro-jejunostomy (PEG-J)	3 (6.1)
Cancer type	
CNS	25 (51.0)
Leukemia/Lymphoma	12 (24.5)
Solid tumor	12 (24.5)
Cancer relapse	20 (40.8)
Average length of hospital stay (d)	25
Underwent conversion to a gastrostomy button or GJ tube	35 (71.4)
Type of non-PEG nutritional supplementation	
Oral	9 (18.4)
TPN	14 (28.6)
Oral+TPN	10 (20.4)
None/Not documented	16 (32.7)

Values are presented as number (%) or number only.
PEG: percutaneous endoscopic gastrostomy, CNS: central nervous system, GJ: gastrojejunostomy, TPN: total parenteral nutrition.
*Percentages for mild, moderate, and severe do not add up to 51% due to rounding.

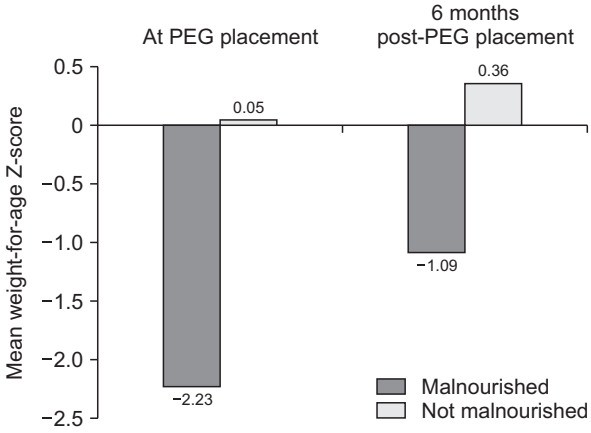

Fig. 2. Improvement in weight-for-age Z-score in patients who were or were not malnourished at time of PEG placement.
PEG: percutaneous endoscopic gastrostomy.

Of the patients who developed buried bumper syndrome, 80% were neutropenic at time of PEG placement.

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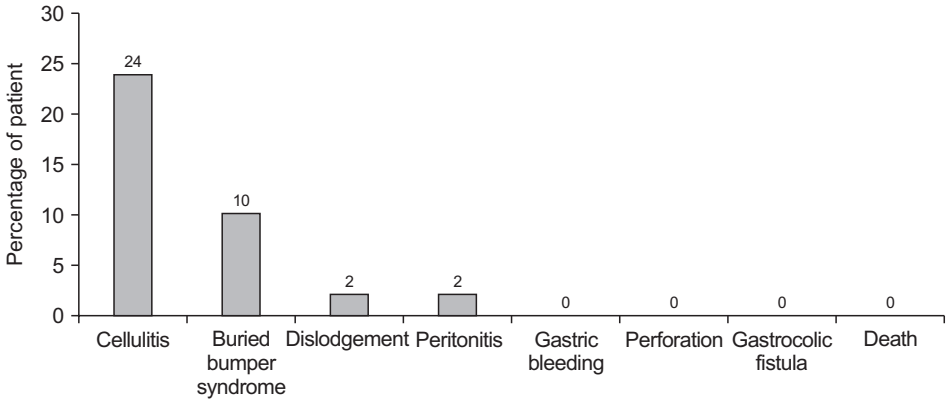

Fig. 3. Complications following percutaneous endoscopic gastrostomy placement.

DISCUSSION

Our center's experience might support EN via PEG tube as an effective modality for treating malnutrition in children with cancer. This report builds on prior studies that demonstrated effectiveness of enteral tube feeds in pediatric oncology patients over a shorter follow-up duration [23,24]. In a retrospective review of 44 hematology-oncology and BMT patients who received G tubes, Barron et al. [23] found a statistically significant weight gain from the time of G tube placement to both one and three months after placement. In a retrospective study of 103 children with medulloblastoma or supratentorial primitive neuroectodermal tumor, Bakish et al. [24] found that EN (G tube or NG tube) resulted in a statistically significant weight gain at both one and three months, while PN resulted in statistically significant weight gain at one month but not at three months, and oral supplementation did not result in a statistically significant weight gain at any time point.

Our study expands upon existing studies demonstrating effectiveness of enteral feeding at three months by demonstrating a sustained positive effect of PEG feedings over a six-month period following PEG placement. Although NG feeds may be more feasible for short term nutrition (1-3 months) based on ease of placement and removal, they may not be a practical option long term due to aesthetic concerns, discomfort (especially in the setting of mucositis), occlusion or dislodgment of the tube, and risk of otitis media and sinusitis [9,21]. In a randomized trial, NG tubes were associated with increased feeding refusal and decreased growth velocities compared to PEG [25]. Chronic NG tube use has been associated with mucosal erosion, ulceration, and prolonged hospital length of stay [26].

Our study suggests that PEG tube placement may be well-tolerated with limited complications in the six months following placement. This is in contrast to surgical placement of G tubes which have been reported to be associated with moderately high rate of complications [27]. Additionally, previous studies of parental perceptions of PEG in children suggest positive experiences related to both ease of nutrition and medication administration [28-30]. The safe and reliable delivery of enteral medications also has the potential to enhance compliance and reduce medication errors [31].

Consistent with prior reports in the literature, the most common complication associated with PEG feeds was superficial PEG site infection [7,11]. Previous studies suggest significant rates of PEG site wound infection and inflammation in children with cancer, ranging

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between 8% and 39% [2,7]. Due to risks of severe infection related to immunosuppression, children being treated for cancer are often aggressively treated with parenteral antibiotics when infections arise. This was reflected in our data, where a majority of superficial wound infections were treated with IV antibiotics.

Our study, consistent with previous studies, suggests a relationship between the development of site complications (superficial wound infection, buried bumper syndrome) and neutropenia, both at time of PEG placement and at the time of diagnosis of cellulitis [21]. This finding suggests that ANC should be considered prior to placement of PEG and that there may be increased risk of PEG site complications during neutropenic episodes. It is also possible that the use of cytotoxic drugs in the setting of malnutrition may contribute to an increased underlying risk for development of superficial infections and skin breakdown [2].

The modest risk of complications shown in this study is likely outweighed by the risk of cancer-associated malnutrition, which may result in serious infections, tumor relapse, and poorer survival outcomes, supporting the use of PEG tubes for nutritional support in this patient population. Nonetheless, standardized preventative measures should be established for post-placement care of PEG tubes to mitigate complications. Such measures may include early postoperative education on care of PEG tube, stoma, and surrounding skin, importance of regular PEG tube flushes after bolus feeds or medication administration, pump training, and anticipatory guidance in the event of accidental dislodgement. Additionally, follow-up should be scheduled with gastroenterology at time of placement to assess for complications such as local inflammation, granulation tissue, or infection [2,31].

There are several limitations to our analysis. This study describes a single-center experience, and there may exist bias in clinical outcomes related to clinical practice and procedural expertise. Additionally, we are restricted to the data available within our electronic medical record and are unable to control for potential nutritional variations, including the type and/or amount of nutritional supplementation and the standards of adherence to the use of a PEG tube. Furthermore, we were unable to distinguish between superficial skin inflammation and true infection. Moreover, we did not assess outcomes in children who had a surgically placed gastrostomy; therefore, these data could only be generalized to children with PEG placed by a pediatric gastroenterologist. Finally, this study was descriptive and retrospective in nature based on a relatively small sample size, and also lacked a comparison group of pediatric cancer patients without PEG tubes, and did not adjust for potential confounders.

Despite these potential limitations, this study suggests that PEG tube feedings may be safe and effective for the treatment of malnutrition in pediatric oncology patients. However, larger, prospective studies with appropriate controls that adjust for potential confounders are needed to confirm these results.

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