Published in final edited form as:

JPEN J Parenter Enteral Nutr. 2015 September ; 39(7): 860–863. doi:10.1177/0148607114538058.

Factors Affecting Spontaneous Closure of Gastrocutaneous Fistulae after Removal of Gastrostomy Tubes in Children with Intestinal Failure

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Abstract

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Background—Children with intestinal failure (IF) frequently require gastrostomy tubes (GT) for long-term nutritional support. Risk factors for persistent GCF in pediatric IF patients are largely unknown but may include underlying nutritional status and duration of indwelling GT.

Materials and Methods—Records of IF patients having undergone GT removal and allowed a trial at spontaneous closure (Spon.) were reviewed. Nonparametric continuous variables were analyzed using the Wilcoxon rank sum test. Post hoc analysis was performed to identify the optimal threshold of GT duration predicting probability of Spon. identified using Receiver Operating Characteristic (ROC) curve analysis.

Results—59 children with IF undergoing GT removal were identified. Spon. occurred in 36 (61%) sites, while 23 (39%) underwent operative closure at a median 67 days after GT removal. The duration of indwelling GT was significantly shorter in the Spon. group (11.5 vs. 21 months, $P=0.002$). Of 33 GT indwelling for ≥ 18 months, 28 (85%) closed spontaneously, compared to only 9/26 (35%) with duration >18 months ($P < 0.001$). With GCF persisting beyond 7 days only 21% (6/28) sites closed spontaneously, however this dropped to 6% (1/18) cases with concurrent GT duration > 18 months.

Conclusions—Of the risk factors evaluated, only prolonged GT duration was associated with an increased likelihood of Spon. failure. It is significantly less likely in pediatric IF patients where GCF persists > 7 days particularly if the duration of GT is >18 months. Relatively earlier operative closure should be considered in this group.

Introduction

Gastrostomy tubes (GT) are frequently used in children with intestinal failure (IF) for long-term enteral nutritional support. Contemporary management of IF aims at expedited weaning from parenteral nutrition (PN) and establishment of enteral autonomy.¹ Enteral access devices are therefore an essential component of therapy as they offer the ability to provide enteral nutrition to patients who are not able to tolerate or absorb sufficient calories orally.² Supplemental tube feeding are particularly useful as a bridge from parenteral to full oral nutrition and may thus help to reduce the duration of PN and its associated complications including intestinal failure associated liver disease (IFALD).³

While the removal of a GT often marks successful transition to all oral feeding, a landmark event for the family of a child with IF, the elation of the event is frequently mitigated by the frustration of a persistently leaking GT site. Though near uniform spontaneous closure of the tract after GT removal is seen in adults,⁴ in children a substantial number persist as gastrocutaneous fistulae (GCF) and may ultimately require operative closure.⁵ These differences in rates of persistent GCF between pediatric and adult patients are likely related to the relative differences in the abdominal wall thickness. With relatively similar diameter of the access devices the significantly longer GCF tracts, among adult patients, are associated with a much higher likelihood of spontaneous closure.

The malnutrition that frequently accompanies patients with IF may theoretically place them at higher risk for this complication. Furthermore children with IF who have been recently weaned from PN recently appear to be at a higher risk for various micronutrient deficiencies, further compounding the problems associated with this group.⁶ In previous studies

nutritional status has not appeared to be associated with the likelihood of development of persistent GCF,⁷ however, none of these studies specifically focused on an IF cohort, in whom malnutrition is likely more prevalent and therefore may have an impact on the risk of this complication.

Due to the relative frequency of persistent GCF, interdisciplinary teams involved in the care of pediatric IF patients are frequently challenged with the need to not only identify patients who would require operative closure rather also identify the time at which a persistent GCF is unlikely to close spontaneously and thus offset the risk of early operative intervention by the morbidity associated with persistently leaking GT site.

Thus, the aims of this study were to (1) describe the incidence of persistent GCF after GT removal in children with IF, (2) identify risk factors for failure of spontaneous closure, and (3) quantify the relationship between duration of leak and likelihood of spontaneous closure in order to identify the optimal timing of elective operative closure.

Materials and Methods

Following IRB approval, records of patients enrolled in a multidisciplinary intestinal rehabilitation program between July 1996 and February 2013 were reviewed to identify patients who had undergone GT removal. Patients who underwent immediate operative closure due to physician or family preference were excluded. Potential risk factors for persistent GCF were recorded [age at insertion, weight at insertion, gender, technique of insertion (operative or endoscopic/percutaneous), age at removal, weight and weight-for-age Z-score at removal, and presence of local complications such as presence of granulation tissue or history of site infection]. Statistical analysis was performed using IBM SPSS Version 21.0. Nonparametric continuous variables were analyzed using the Wilcoxon Rank Sum test and categorical variables were compared using the Fisher's Exact Test. Post-hoc analysis was performed to identify the threshold duration of indwelling gastrostomy tubes predicting probability of spontaneous closure using a Receiver Operating Characteristic (ROC) curve. The resulting groups (above and below threshold value) were compared using Kaplan-Meier Curves via Greenwood's formula.

Results

Of 296 IF patients reviewed, 67 patients were identified who underwent GT removal, 8 children underwent immediate operative closure as a result of provider or family preference and were excluded from the analysis, leaving a total of 59 patients who were allowed a trial of spontaneous closure. Among these patients, 36 (61%) GT sites spontaneously closed. Median time to closure was 7 days with a range of 1–287 days. 30 (83%) closed within 7 days, 1 (3%) at 14 days, and 5 (14%) persisted beyond 30 days. Operative GCF closure was performed in all the remaining 23 patients (39%).

Patients with sites that spontaneously closed were compared with those who underwent operative closure. Characteristics of the two groups are summarized in Table (1). Univariate analysis revealed that duration of indwelling GT was significantly longer in patients who underwent operative closure ($P=0.009$). There were no statistically significant differences

between the spontaneous and operative closure groups in terms of age, weight at insertion, gender, technique of insertion, age at removal, weight-for-age Z (WAZ) score at removal, or history of local wound complications (infections or granulation tissue). The multiple logistic regression model identified duration of indwelling GT as an independent predictive factor associated with probability of spontaneous closure adjusting for median weight and age at the time of removal ($P=0.01$). On multivariable analysis WAZ did not appear to be a significant factor influencing spontaneous closure even with the addition of 8 patients excluded from the analysis due to immediate operative closure ($P=0.75$).

Youden's Index⁸ in an ROC curve analysis identified 18 months duration of indwelling GT as the optimal threshold predicting likelihood of spontaneous closure with the greatest sensitivity and specificity [area under the curve(AUC)= 0.74; $P=0.002$, Figure 1]. Of the 33 GT indwelling for 18 months, 28 (85%) closed spontaneously, compared to only 11 of 28 (39%) with duration >18 months ($P=0.0004$). Kaplan-Meier curves with Greenwood's formula indicated lower incidence of spontaneous closure at all time intervals after GT removal in the group where duration of indwelling gastrostomy tube was >18 months (Log Rank Test 12.6; $P=0.001$, Figure 2).

The median time from gastrostomy removal to operative closure was 67 days with a range of 7– 554 days. Of those persisting beyond 7 days, only 6 of 28 (21%) closed spontaneously (Figure 3).

Discussion

Following removal of GT in children with intestinal failure (IF), 61% of patients had spontaneous closure of the tract and 39% failed to close and thus required operative closure. Of the potential risk factors evaluated, only the duration of indwelling GT was predictive of failure of spontaneous closure. Specifically, weight-for-age Z-score at the time of removal (a surrogate for nutritional status) was not different between the spontaneous and operative closure groups. Eighty-three percent of the sites that closed did so within 7 days of GT removal and those persisting longer than 7 days were unlikely to close spontaneously.

A rigorous multidisciplinary approach to intestinal rehabilitation has been associated with a sustained improvement in mortality of intestinal failure.⁹ The routine use of progressive enteral feeding advancement is an essential aspect of therapy in this setting, with the overall goal of weaning from PN as quickly as possible. The availability of enteral access via gastrostomy or gastrojejunostomy tube allows for enteral feeding in children who may have severe oral aversion, or who may only tolerate and absorb slow, continuous feeds. However once transition to full oral nutrition is achieved and enteral access devices are no longer required pediatric IF patients are frequently met with persistent GCF, many of which require operative closure. There is no standard approach to this problem. Hence this study reviewed a single intestinal failure center experience with the ultimate goal of creating a treatment algorithm to minimize morbidity from persistent GCF.

Though malnutrition has been repeatedly shown to predict poor wound healing,^{10,11} this group of IF patients with relatively low average weight-for-age Z-scores had a similar rate

of persistent GCF when compared to other pediatric patients. Previous investigations in a variety of pediatric patient populations have demonstrated spontaneous closure rates between 55–84%, though the time allowed for spontaneous closure differed between them.^{5,7,12,13,14,15,16} Low weight-for-age Z-score (which robustly reflects overall nutritional status)¹⁷ has been previously studied as a predictor of persistent GCF in more diverse pediatric patient populations.¹⁴ In the present study, no effect of weight-for-age Z-score on the rate of persistent GCF was identified despite the fact that this cohort of patients is at a higher risk of poor nutritional status both before and after transition to full enteral nutrition.⁶ Taken together, the dual findings of a similar spontaneous closure rate in IF patients and lack of association of weight-for-age with odds of spontaneous closure within this study suggests overall nutritional status may not be associated with the probability of spontaneous GCF closure in the IF patient cohort studied.

The length of time the GT was in place is consistently noted to be an important factor predicting the development of persistent GCF after removal.^{7,12,13,14,16} This may be explained by epithelialization of the tract secondary to long-standing gastrostomy tubes. In the literature, a critical period, which has ranged from 6 months to 2 years, is reported beyond which the likelihood of spontaneous closure after GT removal decreases drastically.^{5,13,14,16} Statistical analysis of current study identified a threshold duration of 18 months beyond which the likelihood of persistent GCF was substantially higher (Figures 3 and 4).

Like in previous studies, in this group the majority of the GCFs that closed spontaneously did so within 7 days of GT removal (83%).⁷ Of those persisting longer than a week, only 21% closed of note the rate of spontaneous closure dropped to 6% if simultaneously the duration of indwelling GT was greater than 18 months (Table 2). Despite this low rate of closure, the median time to operative closure was more than 2 months after removal, implying that significant morbidity from persistent GCFs could have been avoided by early surgical intervention in 79% of patients. Therefore it may be reasonable to consider operative closure after a relatively short, 7-day trial of spontaneous healing.

In select patients however expectant management may still be chosen if the morbidity associated with a persistent GCF (skin excoriation, fluid and nutritional losses) is low. GT size and length were not available in a substantial number of patients, moreover in a vast majority of children multiple different length and diameter appliances were used over the course of treatment. Consequently GT size and length were not included in the analysis.

Conclusion

Persistent GCF after GT removal in children with intestinal failure remains a significant problem. Nutritional status does not appear to significantly effect rates of spontaneous closure. Fistulae persisting for more than 7 days are unlikely to close. Early operative intervention should thus be considered after a relatively brief trial of spontaneous GT site closure, especially in children who have had indwelling tubes longer than 18 months.

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Clinical Relevancy Statement

Persistent gastrocutaneous fistulae after removal of enteral access devices is a significant problem amongst pediatric intestinal failure patients. It would be beneficial for multidisciplinary teams involved in the care of this patient cohort to not only identify those at risk of this complication but moreover identify time point beyond which the probability of spontaneous closure for persistent gastrocutaneous fistulae is prohibitively low. Consideration of earlier operative intervention beyond such a time point would likely reduce the morbidity associated with a persistently leaking gastrocutaneous fistula.

Figure 1.

ROC Curve of Time Gastrostomy Tube in Place and Spontaneous Closure

Figure 2.
Kaplan-Meier Curves Comparing Time to Spontaneous Closure of GC Fistula Based on
Time Gastrostomy Tube in Place

Figure 3.
Spontaneous and Operative Closure Rates Stratified by Time After Removal of Gastrostomy Tube

Tables 1

Univariate Analysis Evaluating Factors Associated with Persistent GCF

Variable	Spontaneous Closure (n=36)	Operative Closure (n=23)	p-value
Median age at insertion. (Months)	4	4	0.579
Median weight at insertion. (Kilograms)	3.7	4.4	0.565
Median time appliance in place. (Months)	11.5	21	0.003
Median age at removal. (Months)	17	26	0.065
Median weight at removal. (Kilograms)	9.57	12	0.076
Mean Weight for age Z-score	-1.08	-0.80	0.385

Table 2

Proportion of Spontaneous Closure Stratified by duration of indwelling G-tube and duration of GCF

	G tube Duration 18 months	G tube duration >18 months
GCF duration 7 days	22/23 (96%)	8/8 (100%)
GCF duration >7 days	5/10 (50%)	1/18 (6%)

*
Fisher Exact Test $p=0.0001$