Gastrostomy Tubes in Children with Nonambulatory Cerebral Palsy and Neuromuscular Scoliosis: An Enemy or an Ally?

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Abstract:

Gastrostomy tubes or equivalent invasive nutritional support devices are an important component for maintaining appropriate nutrition for children with cerebral palsy who have oromotor dysfunction. Although these interventions have been shown to produce positive influences on the child's health and nutrition status, they have also been associated with increased complication rates following spinal deformity surgery. Understanding the current status of the literature on this topic as well as the gaps in knowledge are crucial to gaining a thorough understanding of the role of these feeding devices in the postoperative complication profile for these at-risk patients and avenues for future research efforts.

Key Concepts:

- Children with advanced cerebral palsy are at risk for oromotor dysfunction resulting in impaired nutritional status.
- Nutritional feeding support, in the form of gastrostomy, jejunostomy, and/or gastro-jejunostomy tubes, can significantly enhance the nutritional status of these at-risk children.
- These nutritional feeding support devices have been identified as risk factors for complications following spinal deformity surgery, yet it's unclear if the devices are actual risk factors or reflect the severe impairment of the patient and the disease.

Introduction

Cerebral palsy (CP) is a collective term indicative of a static, permanent neurologic disorder with a varying clinical presentation. Although the neurologic injury is nonprogressive, the orthopaedic manifestations are often progressive.¹ In orthopaedics, CP has been characterized using the Gross Motor Function Classification System (GMFCS) by levels I-V, with decreasing independence according to increasing level. For children

with GMFCS IV-V, characterized as nonambulatory states, these children are susceptible to progressive spinal deformity and hip subluxation/dislocation for which orthopaedic reconstructive procedures are often recommended to the caregiver in the form of spinal arthrodesis or hip reconstruction.²⁻⁴

Children in these more advanced states are also susceptible to varying degrees of central neuromotor impairment. Oromotor dysfunction is one such subtype of

central neuromotor impairment and has several inter-related factors including fine motor control, communication, and upper extremity ability that influence the extent of dysfunction.⁵ Oromotor dysfunction has been described according to the Eating Drinking Ability Classification System (EDACS) to describe ability according to safety and efficiency of eating.⁶ EDACS has been shown to correlate well to GMFCS as well as fine motor control, defined according to the Manual Ability Classification System (MACS) to describe the ability for children with CP to use their hands for daily activities.⁷ Increasing levels of upper extremity fine motor control, defined by MACS levels IV and V, is significantly associated with oromotor dysfunction and has been suggested to be a stronger predictor of impairment than gross motor control.⁵

When present, oromotor dysfunction often necessitates nutritional support in the form of gastrostomy or jejunostomy tubes.⁸ Medical research has demonstrated that the placement of gastrostomy tubes (G-tubes) significantly enhances the child's nutrition status.^{8,9} Additionally, G-tubes have been reported to be the most beneficial intervention of the child's life, producing more functional improvement than any orthopaedic intervention for children with GMFCS IV and V CP. For this reason, many caregivers strongly encourage placement of nutritional support devices early in the child's life.¹⁰

However, the presence of G-tubes has been identified as an independent risk factor for complications following spinal arthrodesis or hip reconstruction in these nonambulatory patients.^{2,3,11-16} These data stand in face of the recognized increased risk for postoperative complications for CP patients with impaired presurgical nutrition status.¹⁷ When considering orthopaedic intervention in these children, it behooves the treating surgeon to consider the presence and implication of risk factors to minimize the risk for postoperative complications. However, given these conflicting reports, the question remains whether G-tubes and their equivalent nutritional support devices are an ally in mitigating the complication rate associated with impaired presurgical nutrition, a substitutionary factor with a separate predisposition for complication development, or a reflection of the severity of neurologic involvement that is nonmodifiable. The purpose of this paper is to review the available literature on this topic.

General Considerations

Due to the underlying neurologic abnormality, feeding disorders are common in children with CP, ranging from oromotor and oropharyngeal abnormalities resulting in difficulties with chewing and/or swallowing which can ultimately produce under- or mal-nutrition statuses.¹⁸ To address this, enteral feeding through G-tubes, jejunostomy tubes (J-tubes), and GJ tubes have become more frequently utilized to address underlying malnutrition and/or failure to thrive.¹⁹ However, specified indications for when to proceed with these interventions have not been clearly defined. The use of an adjunctive classification system can aide in guiding when to proceed with nutritional support interventions. Children with EDACS IV demonstrate poor swallowing and breathing coordination and are only able to eat purees or well mashed foods, whereas EDACS V children are completely unsafe to eat or drink and are reliant upon feeding tubes for nutrition.²⁰ Additionally, children with MACS V are unsafe to handle objects and given this association with oromotor dysfunction, may be indicated for nutritional interventions.5

Presurgical nutritional status has been associated with infectious complications following spinal deformity surgery. Jevsevar and Karlin¹⁷ retrospectively reviewed 45 nonambulatory children with cerebral palsy and neuromuscular scoliosis undergoing spinal arthrodesis. The authors found that children with poor presurgical nutritional status, defined as total blood lymphocyte count (TLC) <1500 cells per cubic millimeter and albumin levels < 3.5 g/dL, were at risk for postsurgical infectious complications, consisting of 11 urinary tract infections, 9 pneumonias, 2 gastrointestinal (GI)/genitourinary infections, and 2 surgical site infections (SSI). These data led to a growing trend for evaluation of presurgical nutritional status and a recommendation for

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aggressive measures, such as perioperative feeding tube interventions,²¹ to be instituted to optimize nutritional levels.

Nutritional interventions have been shown to produce reliable gains in weight for children with severe CP.^{8,22} Sullivan et al.⁸ performed a prospective, multicenter study of 57 children with CP (43 of 57 with spastic quadriplegia), demonstrating clinically important increases in median weight z-scores with caregiver reports of significant health improvements. These improvements also extend to the nutritional level with improvements in micro-nutrient levels,²² total body protein levels,²² and augmenting bone mineral content.²³ In addition to producing improvements in a child's weight and nutrition, G-tubes also result in significant improvement in quality of life measure for caregivers.⁹ However, the breadth of evidence on this topic remains low to insufficient.^{24,25}

G-tubes and Spinal Deformity Surgery

Spinal arthrodesis has been demonstrated to produce a positive impact in a child's quality of life as well as caregiver satisfaction for children with nonambulatory CP.⁴ However, these procedures carry a high rate of postsurgical complication development with 36% of patients developing a major complication within 2 years of surgery.²⁶ These complications are most commonly represented as wound healing/infections, pulmonary complications, and GI complications, all of which have been associated with the presence of G-tubes or equivalent nutritional support devices.^{2,3,11-16,27,28}

Respiratory complications are an additional area of concern for nonambulatory children given their diminished capacity to protect their airways and predisposition to pneumonia and respiratory illnesses. Blackmore et al.²⁹ performed a cross-sectional analysis on respiratory hospitalizations and treatment in 551 children with CP ranging from 1 to 26 years of age. In nonambulatory children, the presence of a G-tube or other nutritional support device was associated with a significantly increased risk of hospitalization for respiratory illness. Sharma et al.³⁰ performed a meta-analysis including over 15,000 children undergoing spinal arthrodesis for neuromuscular scoliosis, indicating that pulmonary complications were the most commonly encountered postsurgical complication. Luhmann & Furdock³¹ retrospectively reviewed 111 children with neuromuscular scoliosis (CP diagnosis in 74.7%) treated over a 20-year period, reporting that the presence of a G-tube and the history of pneumonia were independently associated with postoperative pulmonary complications.

Nishnianidze et al.²⁷ reviewed 303 children with cerebral palsy, 89% GMFCS IV or V, undergoing spinal arthrodesis, identifying factors associated with postsurgical complications. Postsurgical complications included pancreatitis (54%), pleural effusion (42.5%), and infectious complications of all origins (10.2%). Children with a G-tube (72.2% of population) had significantly higher postoperative complication scores and a significantly increased rate of developing pancreatitis and deep wound infection. Sponseller et al.¹⁵ retrospectively evaluated a cohort of 204 consecutive children with CP undergoing spinal arthrodesis at one of seven institutions. They reported a 6.4% rate of deep wound infection, developing at a mean of 34 days following surgery. Univariate analvsis identified older age, large curve magnitude, the presence of a G-tube or GJ tube, higher serum white blood cell counts, and longer operative times as risk factors for deep infection development with only the presence of a G-tube or GJ tube as an independent predictor of postoperative deep infection, carrying a 1.9 fold risk.¹⁵ A subsequent meta-analysis further defined this association between postsurgical site infection (SSI) and G-tubes, carrying an odds ratio of 3.45 for SSI compared to patients without G-tubes. This is particularly important in that only deep infection development has been shown to independently predict less improvement in health-related quality of life scores following spinal arthrodesis.32

The risk of SSI following spinal arthrodesis has traditionally been attributed to presurgical malnutrition;¹⁷ however, this premise has been challenged by subsequent

data.^{27,33} Nishnianidze et al.²⁷ assessed the influence of presurgical TLC and albumin levels, finding no statistically significant difference in postoperative complication scores based on these laboratory studies. Furdock & Luhmann³³ found in their series of 111 children with neuro-muscular scoliosis that traditional nutrition values such as pre-albumin, albumin, TLC, and total protein were not associated with an increased incidence of SSI.

Gastrointestinal complications are an important additional subset of complications to assess in postsurgical patients, ranging from ileus to pancreatitis. Nishnianidze et al.²⁷ reported a 54% rate of developing postoperative pancreatitis following spinal arthrodesis. The presence of a G-tube preoperatively carried a 1.61-fold higher risk of developing postoperative pancreatitis. Utilizing a standardized screening regimen, Abousamra et al.¹¹ noted an overall incidence of pancreatitis as evidenced by increases in enzymes in 55% of their CP patients undergoing spinal arthrodesis. Specifically, the presence of G-tube dependence was associated with a higher risk of developing postoperative pancreatitis with these patients necessitating longer hospitalization and utilization of hospital resources.¹¹

Verhofste et al.¹⁶ performed a prospective, multicenter study of 425 children with CP undergoing spinal arthrodesis, reporting a 2.2x and 6.7x rate of GI complications in those patients with G-tube or combined Gtube/oral intake, respectively. Furthermore, they noted that those patients who retain the ability to tolerate oral feeding regimens are at further risk for dysphagia, aspiration events, and complications related to the G-tube proper. However, the authors also identified that GI complication development, to include pancreatitis, was also influenced by the fasting periods following surgery. Children with G-tubes who developed a GI complication had a longer fasting period (3 days mean fasting vs. 2 days for those without a GI complication), suggesting the feeding protocol may play a significant role in complication development.¹⁶

The importance of the postoperative fasting period has been suggested by other authors. Nishnianidze et al.²⁷ reported a 54% incidence of postoperative pancreatitis in 303 children with neuromuscular scoliosis, with a reported mean fasting period of 4.43 days following surgery. The concept of accelerated discharge pathways following spinal arthrodesis in children with nonambulatory CP has recently been investigated. Another advantage of G-tubes is the ability to restart the child's diet the day following surgery.³⁴ Bellaire et al.³⁴ reported that an accelerated discharge protocol in children with severe CP resulted in not only a significant decrease in hospital length of stay but also a decrease in the development of postoperative complications.

Characteristics of Central Neuromotor Impairment

Ultimately, the etiology of the identified risks for complication development in children with CP and a G-tube has not been definitively elucidated and is likely multifaceted. Our understanding of what defines the optimal nutritional state for these at-risk children is incomplete with significant gaps in the known science and clinical practice that require further evaluation.³⁵ Aside from the restarting of feeding following surgery, the volume and characteristics of the diet may also play a significant role. Children with severe subtypes of CP are at an inherent risk of overfeeding given their lower basal energy expenditure levels and can result in heightened body fat content.³⁶ On the other hand, some severely affected patients have athetoid or similar types of CP that cause them to have high basal energy expenditure levels. Alternative feeding regimens have been investigated with low-energy, micronutrient complete, high-fiber feeding regimens allowing children to continue to grow despite energy intakes below the 75% estimated averages and have not been associated with a disproportionate rise in fat mass or fat percentage.²² Alternatively, studies of patients undergoing prolonged parenteral nutrition have been shown to result in GI tract microbiome changes

which may predispose these patients to increased infection and metabolic complications.³⁷

However, both medical and surgical authors have opined that the presence of a G-tube may serve more as a metaphorical "canary in the coalmine" indicating the extent of overall disease severity.^{13,16,38} This viewpoint can be characterized by quantifying the extent of central neuromotor impairment in these children, characterized by feeding/swallowing disfunction, speech, respiratory function, and cortical stability.¹³ Jain et al.¹³ introduced a subclassification for GMFCS V children undergoing spinal arthrodesis defined by the presence of any of four central neuromotor impairments: seizure disorder, nonverbal status, tracheostomy, and G-tube presence. The subtypes ranged from 5.0 (no central neuromotor impairment) to 5.3 based on the number of underlying central neuromotor impairments, with 5.3 subtypes having three or four impairments. Using this subclassification system, the authors found that the rate of major postoperative complications significantly increased by GMFCS V subtype with 5.3 children having a 49% rate of major complications.

Summary

Gastrostomy tubes and equivalent nutritional interventions are commonly identified as a risk factor for complication following orthopaedic surgery, but they are also associated with significant enhancements in a child's underlying nutrition and subsequent weight gain and are reported as the most beneficial intervention in a child's life by caregivers. The extent of central neuromotor impairment for these children with severe cerebral palsy directly impacts the complication profile following orthopaedic surgery particularly with regard to spinal arthrodesis. G-tubes represent one such aspect of central neuromotor impairment in cerebral palsy and may be better considered as a nonmodifiable characteristic of a child's underlying central neuromotor impairment rather than an independent risk factor for complication. Future research should investigate the role of pre- and postsurgical feeding protocols as well as dietary content on the development of complications following surgery.

Additional Links

- Management of Spinal Deformity in Cerebral Palsy: Current Concepts Review <u>https://www.jposna.org/ojs/index.php/jposna/article/view/8</u>
- Two Surgeon Approach to Posterior Spinal Fusion in the Correction of Neuromuscular Scoliosis <u>http://www.posnacademy.org/media/Two+Sur-</u> <u>geon+Approach+to+Posterior+Spinal+Fu-</u> <u>sion+in+the+Correction+of+Neuromuscular+Scolio-</u> <u>sis/1_2d9zibsb/19139662</u>

References

1. Bohtz C, Meyer-Heim A, Min K. Changes in healthrelated quality of life after spinal fusion and scoliosis correction in patients with cerebral palsy. J Pediatr Orthop. 2011 Sep;31(6):668-73. Epub 2011/08/16.

2. Shea J, Nunally KD, Miller PE, Difazio R, Matheney TH, Snyder B, et al. Hip Reconstruction in Nonambulatory Children With Cerebral Palsy: Identifying Risk Factors Associated With Postoperative Complications and Prolonged Length of Stay. J Pediatr Orthop. 2020 Nov/Dec;40(10):e972-e7. Epub 2020/10/13.

3. Stasikelis PJ, Lee DD, Sullivan CM. Complications of osteotomies in severe cerebral palsy. J Pediatr Orthop. 1999 Mar-Apr;19(2):207-10. Epub 1999/03/24.

4. Shaw KA, Reifsnyder J, Hire JM, Fletcher ND, Murphy JS. The Effect of Spinal Arthrodesis on Health-Related Quality of Life for Patients with Nonambulatory Cerebral Palsy: A Critical Analysis Review. JBJS Rev. 2019 Dec;7(12):e1. Epub 2019/12/04.

5. Mei C, Hodgson M, Reilly S, Fern B, Reddihough D, Mensah F, et al. Oromotor dysfunction in minimally verbal children with cerebral palsy: characteristics and associated factors. Disabil Rehabil. 2020 Aug 3:1-9. Epub 2020/08/04.

6. Tschirren L, Bauer S, Hanser C, Marsico P, Sellers D, van Hedel HJA. The Eating and Drinking Ability Classification System: concurrent validity and reliability in children with cerebral palsy. Dev Med Child Neurol. 2018 Jun;60(6):611-7. Epub 2018/04/16.

7. Monbaliu E, De La Peña MG, Ortibus E, Molenaers G, Deklerck J, Feys H. Functional outcomes in children and young people with dyskinetic cerebral palsy. Dev Med Child Neurol. 2017 Jun;59(6):634-40. Epub 2017/03/09.

8. Sullivan PB, Juszczak E, Bachlet AM, Lambert B, Vernon-Roberts A, Grant HW, et al. Gastrostomy tube feeding in children with cerebral palsy: a prospective, longitudinal study. Dev Med Child Neurol. 2005 Feb;47(2):77-85. Epub 2005/02/15.

9. Sullivan PB, Juszczak E, Bachlet AM, Thomas AG, Lambert B, Vernon-Roberts A, et al. Impact of gastrostomy tube feeding on the quality of life of carers of children with cerebral palsy. Dev Med Child Neurol. 2004 Dec;46(12):796-800. Epub 2004/12/08.

10. Jain A, Sullivan BT, Shah SA, Samdani AF, Yaszay B, Marks MC, et al. Caregiver Perceptions and Health-Related Quality-of-Life Changes in Cerebral Palsy Patients After Spinal Arthrodesis. Spine (Phila Pa 1976). 2018 Aug 1;43(15):1052-6. Epub 2017/12/08.

11. Abousamra O, Nishnianidze T, Rogers KJ, Er MS, Sees JP, Dabney KW, et al. Risk factors for pancreatitis after posterior spinal fusion in children with cerebral palsy. J Pediatr Orthop B. 2018 Mar;27(2):163-7. Epub 2016/08/12.

12. DiFazio R, Vessey JA, Miller P, Van Nostrand K, Snyder B. Postoperative Complications After Hip Surgery in Patients With Cerebral Palsy: A Retrospective Matched Cohort Study. J Pediatr Orthop. 2016 Jan;36(1):56-62. Epub 2015/01/31.

13. Jain A, Sponseller PD, Shah SA, Samdani A, Cahill PJ, Yaszay B, et al. Subclassification of GMFCS Level-5 Cerebral Palsy as a Predictor of Complications and Health-Related Quality of Life After Spinal Arthrodesis. J Bone Joint Surg Am. 2016 Nov 2;98(21):1821-8. Epub 2016/11/04.

14. Matsumoto H, Simhon ME, Campbell ML, Vitale MG, Larson EL. Risk Factors Associated with Surgical Site Infection in Pediatric Patients Undergoing Spinal Deformity Surgery: A Systematic Review and Meta-Analysis. JBJS Rev. 2020 Mar;8(3):e0163. Epub 2020/04/01.

15. Sponseller PD, Jain A, Shah SA, Samdani A, Yaszay B, Newton PO, et al. Deep wound infections after spinal

fusion in children with cerebral palsy: a prospective cohort study. Spine (Phila Pa 1976). 2013 Nov 1;38(23):2023-7. Epub 2013/08/22.

16. Verhofste BP, Berry JG, Miller PE, Crofton CN, Garrity BM, Fletcher ND, et al. Risk factors for gastrointestinal complications after spinal fusion in children with cerebral palsy. Spine Deform. 2021 Mar;9(2):567-78. Epub 2020/11/18.

17. Jevsevar DS, Karlin LI. The relationship between preoperative nutritional status and complications after an operation for scoliosis in patients who have cerebral palsy. J Bone Joint Surg Am. 1993 Jun;75(6):880-4. Epub 1993/06/01.

 Bertoncelli CM, Altamura P, Vieira ER, Bertoncelli D, Latalski M, Berthet S, et al. Predictive Model for Gastrostomy Placement in Adolescents With Developmental Disabilities and Cerebral Palsy. Nutr Clin Pract. 2020 Feb;35(1):149-56. Epub 2019/05/28.

19. Somerville H, Tzannes G, Wood J, Shun A, Hill C, Arrowsmith F, et al. Gastrointestinal and nutritional problems in severe developmental disability. Dev Med Child Neurol. 2008 Sep;50(9):712-6. Epub 2008/08/30.

20. Paulson A, Vargus-Adams J. Overview of Four Functional Classification Systems Commonly Used in Cerebral Palsy. Children (Basel). 2017 Apr 24;4(4). Epub 2017/04/27.

21. Jaivin JS, Banta JV, Milanese A, Hight DW, Alexander F. Peri-operative jejunostomy-tube feeding in reconstructive spinal surgery. Dev Med Child Neurol. 1991 Mar;33(3):225-31. Epub 1991/03/01.

22. Vernon-Roberts A, Wells J, Grant H, Alder N, Vadamalayan B, Eltumi M, et al. Gastrostomy feeding in cerebral palsy: enough and no more. Dev Med Child Neurol. 2010 Dec;52(12):1099-105. Epub 2010/10/23.

23. Arrowsmith F, Allen J, Gaskin K, Somerville H, Clarke S, O'Loughlin E. The effect of gastrostomy tube feeding on body protein and bone mineralization in children with quadriplegic cerebral palsy. Dev Med Child Neurol. 2010 Nov;52(11):1043-7. Epub 2010/05/26.

24. Ferluga ED, Sathe NA, Krishnaswami S, McPheeters ML. Surgical intervention for feeding and nutrition

difficulties in cerebral palsy: a systematic review. Dev Med Child Neurol. 2014 Jan;56(1):31-43. Epub 2013/06/07.

25. Gantasala S, Sullivan PB, Thomas AG. Gastrostomy feeding versus oral feeding alone for children with cerebral palsy. Cochrane Database Syst Rev. 2013 Jul 31;2013(7):Cd003943. Epub 2013/08/01.

26. Yaszay B, Bartley CE, Sponseller PD, Abel M, Cahill PJ, Shah SA, et al. Major complications following surgical correction of spine deformity in 257 patients with cerebral palsy. Spine Deform. 2020 Dec;8(6):1305-12. Epub 2020/07/29.

27. Nishnianidze T, Bayhan IA, Abousamra O, Sees J, Rogers KJ, Dabney KW, et al. Factors predicting postoperative complications following spinal fusions in children with cerebral palsy scoliosis. Eur Spine J. 2016 Feb;25(2):627-34. Epub 2015/09/28.

28. Dekker A, Crawford HA, Stott NS. How DoComplications Within the First 30 days after SpinalDeformity Surgery in Children with Cerebral Palsy AffectLength of Stay? Clin Orthop Relat Res. 2021 Feb1;479(2):366-75. Epub 2020/05/14.

29. Blackmore AM, Bear N, Blair E, Gibson N, Jalla C, Langdon K, et al. Factors Associated with Respiratory Illness in Children and Young Adults with Cerebral Palsy. J Pediatr. 2016 Jan;168:151-7.e1. Epub 2015/11/02.

30. Sharma S, Wu C, Andersen T, Wang Y, Hansen ES, Bünger CE. Prevalence of complications in neuromuscular scoliosis surgery: a literature meta-analysis from the past 15 years. Eur Spine J. 2013 Jun;22(6):1230-49. Epub 2012/10/23.

31. Luhmann SJ, Furdock R. Preoperative Variables
Associated With Respiratory Complications After Pediatric
Neuromuscular Spine Deformity Surgery. Spine Deform.
2019 Jan;7(1):107-11. Epub 2018/12/28.

32. Eguia F, Nhan DT, Shah SA, Jain A, Samdani AF, Yaszay B, et al. Of Major Complication Types, Only Deep Infections After Spinal Fusion Are Associated With Worse Health-related Outcomes in Children With Cerebral Palsy. Spine (Phila Pa 1976). 2020 Jul 15;45(14):993-9. Epub 2020/03/10.

33. Furdock R, Luhmann SJ. The value of preoperative labs in identifying "at-risk" patients for developing surgical site infections after pediatric neuromuscular spine deformity surgery. Spine Deform. 2020 Jun;8(3):517-22. Epub 2020/01/12.

34. Bellaire LL, Bruce RW, Jr., Ward LA, Bowman CA, Fletcher ND. Use of an Accelerated Discharge Pathway in Patients With Severe Cerebral Palsy Undergoing Posterior Spinal Fusion for Neuromuscular Scoliosis. Spine Deform. 2019 Sep;7(5):804-11. Epub 2019/09/10.

35. Foster BA, Lane JE, Massey E, Noelck M, Green S, Austin JP. The Impact of Malnutrition on Hospitalized Children With Cerebral Palsy. Hosp Pediatr. 2020 Dec;10(12):1087-95. Epub 2020/11/07.

36. Sullivan PB, Alder N, Bachlet AM, Grant H, Juszczak E, Henry J, et al. Gastrostomy feeding in cerebral palsy: too much of a good thing? Dev Med Child Neurol. 2006 Nov;48(11):877-82. Epub 2006/10/19.

37. Pierre JF. Gastrointestinal immune and microbiome changes during parenteral nutrition. Am J Physiol Gastrointest Liver Physiol. 2017 Mar 1;312(3):G246-g56. Epub 2017/02/06.

38. Romano C, van Wynckel M, Hulst J, Broekaert I, Bronsky J, Dall'Oglio L, et al. European Society for Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Neurological Impairment. J Pediatr Gastroenterol Nutr. 2017 Aug;65(2):242-64. Epub 2017/07/25.