Short bowel syndrome: Surgical therapy

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ABSTRACT: Many surgical solutions to short bowel syndrome have been proposed; however, none has proven to be uniformly successful. Some of these solutions, combined with optimal medical management, may represent the patient's only hope for survival without parenteral nutrition. Most forms of surgical therapy are supportive and aim at controlling three basic pathophysiological defects: decreased intestinal transit time, gastric hypersecretion, and reduced functional mucosal surface area. Conservative resection and, thus, prevention of short bowel syndrome remains the best form of treatment at present. In the future, small bowel transplantation may prove to be an important advance in therapy; however, this remains largely experimental due to continued problems with rejection. Can J Gastroenterol 1990;4(4):167-173

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Syndrome de l'intestin court: Traitement chirurgical

RESUME: De nombreuses solutions chirurgicales ont été proposées pour traiter le syndrome de l'intestin court mais aucune n'a remporté un succès uniforme. Certaines, combinées à un traitement médical optimal, représentent peut-être le seul espoir de survie du patient sans le recours à l'alimentation parentérale. La plupart des interventions chirurgicales apportent un traitement de soutien et visent à contrôler trois défauts physiopathologiques de base: diminution du transit intestinal, hypersécration gastrique et réduction de la surface fonctionnelle de la muqueuse. La résection conservatrice, c'est-à-dire la prévention du syndrome de l'intestin court, reste donc la meilleure forme de traitement pour le moment. Dans l'avenir, la transplantation du grêle sera peut-être un progrès thérapeutique important; dans une large mesure, cette intervention reste toutefois expérimentale, les problèmes de rejet continuant à se manifester.

As a common cause of short bowel syndrome is surgical resection, it is not surprising that many surgical solutions to short bowel syndrome have been proposed. Although none has been uniformly successful, some have proved to have merit when used in conjunction with medical therapy, and often represent the patient's only chance to become independent from parenteral nutrition.

The best form of surgical 'treatment' remains that of prevention with conservative resections (1). Even the retention of a few extra centimetres of bowel can have a profound influence on the intestine's ability to adapt, and thus on the eventual prognosis. Many authors have advocated construction of multiple ostomies with a second look procedure for all marginal bowel which may be viable (1-3).

Surgical treatment can be classified into three categories based on pathophysiological processes: slowing transit time; decreasing gastric secretions; and increasing the effective mucosal surface area (4).

SLOWING INTESTINAL TRANSIT

Surgical therapy to decrease intestinal transit time is based on the construction of a partial small bowel obstruction. Many different methods have been devised; however, all are unpredictable in their eventual effect. Most of the complications which arise from each method are due to bowel obstruction.

Antiperistaltic segments: Reversal of intestinal segments to create antiperistaltic regions was originally described by Mall in 1896 (5). He reversed variable segments of small bowel in three dogs, two of which died of bowel obstruction, while the third lived for three months. At laparotomy two months later, the segment showed retention of reversed peristalsis. Through the use of glass beads as markers, Mall also demonstrated a delay in intestinal transit time. The procedure was viewed as impossible until the
In summary, intestinal reversal to create an antiperistaltic region and delay transit is one of the more common surgical interventions used in the treatment of short bowel syndrome. The ideal length in the adult seems to be 10 to 15 cm with placement as distally as possible. Nevertheless, inconsistent results and difficulty in predicting which patients are likely to respond have consistently dampened enthusiasm for this approach.

Recirculating loops: The recirculating loop is an extension of intestinal reversal and was first suggested by Stafford et al in 1959 (16). Mackby in 1965 (17) showed an improved survival in dogs when a recirculating loop was combined with a separate antiperistaltic segment. Altman (18) in a controlled experiment on 20 dogs found that animals with recirculating loops had better fat absorption but lost more weight, and often died due to anorexia compared with controls. In a separate study comparing recirculating loops to segmental reversals, the latter were more often technically successful and had fewer complications (19). Although a further report of successful clinical application of the recirculating loop was submitted in 1975, the procedure has fallen into general disfavour due to the strong evidence against its being superior to a simple reversal and to the fact that the procedure is complicated, uses long lengths of bowel and is fraught with complications causing a high mortality rate (20).

Colon interposition: Colon interposition has also been used in the treatment of short bowel syndrome. Use of the colon has three main advantages: an intrinsically slow peristalsis; decreased likelihood of causing obstruction due to the fact that colon can be placed isoperistaltically; and no requirement for the use of small bowel which is already compromised in residual length. Initially, antiperistaltic colonic segments were used and shown to be of benefit in a dog model (21). In 1967, Trinkle and Bryant (22) placed a 5 cm antiperistaltic segment of transverse colon in a three-week-old infant after massive resection for a mid gut volvulus. Although the patient died, she initially gained weight and had an increase in transit time with a decrease in stool frequency. Later, isoperistaltic colon interposition was investigated by Hutcher (23,24). In a series of experiments with beagle puppies, he showed increased survival with the interposition of a 15 cm segment of isoperistaltic colon both pre-ileal and pre-jejunal after a 90% small bowel resection. The animals in both cases attained approximately 70% of their expected growth with a decrease in mortality and morbidity compared with controls. Garcia et al (25) interposed a 24 cm segment of isoperistaltic colon to a 15 cm length of small bowel with an intact ileocecal valve in a human patient. After an adaptive period, intestinal transit time increased from 10 to 105 mins and the patient was able to maintain adequate nutrition by oral feeding. In this patient, the development of a D-lactic acidemia was postulated to be due to bacterial overgrowth. Comparison of iso- and antiperistaltic colonic interposition was examined by Lloyd (26,27) using a 90% small bowel resection in the rat. In a series of experiments, he found that antiperistaltic colonic interposition effectively prolonged transit time but had other unpredictable effects. Some animals acquired a small bowel obstruction and had, on average, lower body weights with only a slight increase in the absorption of albumin and no change in the absorption of fat compared to controls. He concluded that there was no advantage to antiperistaltic interposition over isoperistaltic and, indeed, there may be disadvantages. Further studies in dogs by Carner (28) showed that the insertion of a 20 cm length of antiperistaltic colon made no difference in xylose absorption, 24 h fat excretion, bowel transit time or average weight loss. Although his numbers were small, he concluded that antiperistaltic colonic interposition was of no benefit.

Glick et al in 1984 (29) published a series on six infants in which a proximal isoperistaltic segment of colon was used to treat short bowel syndrome. The segments were 11 to 15 cm in length and three of the infants survived while the others died of sepsis and total parenteral...
similar construction (34-38).

been predictable. Sculler (31) at­

Experimental valves: The recogni­
tion that the presence of an il­
crease, the acidification of the lumen of the intestine would hinder the action of the digestive enzymes, and the resultant osmotic and volume load would further compound the fluid, electrolyte and nutrient losses already occurring in the compromised bowel.

The realization that patients with previous vagotomies and gastrectomies were more tolerant of massive resection led to the use of these procedures for the control of gastric hypersecretion in short bowel syndrome. Today, with the emergence of the H2 receptor antagonists and the realization that gastric hypersecretion is probably temporary, there is no place for the surgical treatment of gastric hypersecretion.

**INCINERATING THE EFFECTIVE MUCOSAL SURFACE AREA**

Attempts at increasing the effective mucosal surface area has led to three completely different approaches: the growth of neomucosa; bowel lengthening and tapering procedures; and small bowel transplantation.

Neomucosa: Neomucosa was originally investigated by Cywes in 1968 (43) and Binnington in 1974 (46). They observed that the serosa of neighbouring bowel could be used as a bed to stimulate the growth of a mucosal covering. In a series of experiments on dogs and pigs, they found that if the small bowel was opened along its antimesenteric
border and sutured to the serosa of a neighbouring piece of bowel in a longitudinal intestinal patch, the intervening serosa would be covered with a mucosa which was proven to contain enzyme levels similar to normal mucosa (46). The functional nutrient absorptive ability of this mucosa, however, was not known.

An exhaustive series of experiments by Thompson (47-50) culminated in a paper in 1988 which seemed to summarise neomucosa (51). He observed that intestinal patching had an inhibitory effect on intestinal adaptation in dogs subjected to 75% intestinal resection and intestinal patching. His data showed a decrease in overall growth of the intestine and in villus height. Transit time was prolonged but the animals lost weight and had lower albumin levels. Furthermore, the increase in intestinal mucosal surface area was insignificant. It would seem that neomucosa has little if anything to offer in the treatment of short bowel syndrome at the present time.

**Tapering and lengthening procedures:** Intestinal tapering and lengthening procedures have met with much more success. Tapering was originally proposed when it was noted that bowel proximal to an atretic segment always became so markedly dilated that reanastomosis was difficult. Peristalsis was felt to be functionally ineffective. Initially, the antimesenteric border was opened and a longitudinal strip of bowel was removed before re-approximating the bowel. The calibre of the remaining bowel was reduced so that anastomosis was easier and peristalsis was aided due to apposition of the bowel wall during peristalsis. Patients treated in this way did indeed gain weight, and many were able to come off total parenteral nutrition (52). The major drawback to this procedure was that it necessitated the loss of valuable mucosal surface area. A modification of this technique called 'plication' (internal infolding) performed along the antimesenteric border was compared to antimesenteric excision by Ramanujan (53). He found that plicated bowel was eventually incorporated into the bowel wall and was better structurally and functionally after artificially induced bowel dilatation in a dog model.

In 1980 Bianchi (54) described in a pig model an elegant procedure called intestinal lengthening. The procedure is based on the premise that the blood supply to the small bowel runs in an alternating fashion around each side of the bowel. This allows an avascular plane to be developed between the two leaves of the mesentery such that a GIA stapler can be passed down the centre, dividing the bowel into two parallel tubes. These can be approximated end-to-end in an isoperistaltic fashion to give a segment which is twice as long but only half the diameter of the original bowel. The procedure was first used clinically by Boeckman and Traylor (55) on a child with short bowel syndrome from a gastroschisis with bowel necrosis. The child was left with 39 cm of small bowel anastomosed to the transverse colon. This grew to a length of 50 cm over the ensuing years; however, the child weighed only 9.2 kg at four years of age. Following a Bianchi procedure, the patient required total parenteral nutrition for a further 10 weeks but was progressed to a full diet and did not require artificial nutrition after this time.

Aigrain in 1985 (56) published a report of another infant with short bowel syndrome who had an intestinal lengthening procedure done. Postoperatively, she remained on total parenteral nutrition for four weeks but was then able to progress to a regular diet. He modified the procedure to some extent by re-anastomosing the lengthened bowel in a helical formation to prevent traction on the mesenteric vessels. The problems encountered postoperatively included bacterial overgrowth proximal to the lengthened loop, nutritional intolerance and gastroesophageal reflux. Bacterial overgrowth was felt to be due to poor peristalsis in the proximal dilated duodenum which was not tapered. Oral tolerance of feeding was complete by eight months, although continuous tube feed supplementation still maintained a large proportion of the caloric intake. Urecholine was used to combat the reflux with complete success.

Thompson et al in 1985 (57) were unsuccessful in their attempt to apply the Bianchi procedure to a child with the short bowel syndrome. After dividing the bowel they re-anastomosed it, only to have one segment of the lengthened bowel become nonviable. Interestingly, the patient apparently improved clinically and the authors attributed this to the resultant tapering of the remaining segment of bowel.

A direct comparison of the efficacy of intestinal lengthening relative to other surgical treatments of short bowel syndrome has been performed in a pig model by Sigalet et al (unpublished data). They compared isoperistaltic colon interposition and intestinal lengthening. While both groups showed superior weight gain to control animals receiving no treatment, intestinal lengthening was found to be superior to isoperistaltic colon interpositioning.

Intestinal lengthening appears to be a viable alternative in the surgical treatment of short bowel syndrome. Application of this procedure seems to be tailored to the subset of the population in which the residual bowel has dilated so markedly that peristalsis is relatively ineffective (58). The advantages include the fact that no mucosal surface area need be sacrificed; a slowing of transit time is obtained without causing a functional obstruction; and normal peristalsis is restored to a previously dilated segment.

**Small bowel transplantation:** Successful small bowel transplantation may be the ultimate treatment for short bowel syndrome. The technical feasibility was first established experimentally in the late 1960s by Lillhei in a dog model (59). His procedure consisted of transplanting the entire small intestine with vascular anastomosis between the respective mesenteric vessels of the graft and host. His autografts survived indefinitely, but the allografts all rejected in a matter of days. At present, the major obstacle is still rejection, as the large amount of lymphoid tissue present in the transplanted organ makes it extremely immunogenic (60,61). Control of rejection can be approached by either general immunosuppression of
the host or by alteration of the immunogenicity of the donor organ. Numerous methods of temporary control of rejection have been accomplished in the dog model using conventional host immunosuppressive therapy. Unfortunately, both azathioprine and prednisone interfere with mucosal cell replication and thus the function of the graft (60). Antilymphocyte serum alone has been shown to be insufficient in averting rejection in dogs (62).

The development of the immunosuppressive agent, cyclosporine, attracted new interest. Mono drug therapy with cyclosporine in a rat model (15 mg/kg/day) given for four weeks postoperatively can prevent rejection (63). Recently, low dose cyclosporine (5 mg/kg/day) given over two weeks has also prevented rejection in rats (64). Unfortunately, the results in large animal models have not been as successful. Renick et al in 1982 (65) demonstrated that intramuscular cyclosporine (25 mg/kg/day) would prolong survival in a transplanted dog from a mean of 12.5 to 103.8 days. The importance of parenteral administration of the drug was underlined in an extension of this work by Craddock et al (66) who demonstrated that dogs with incontinuity grafts given oral cyclosporine survived for less than one month (66). This emphasized the fact that absorptive function of an allograft is initially suboptimal, and immunosuppressive therapy should be accomplished parenterally. Further studies by Ricour (67) and Grant (68) in pigs confirm these findings. The addition of prednisone to cyclosporine therapy has been shown in dogs to improve survival over cyclosporine alone (69); however, these results have not been consistently reproduced. High dose cyclosporine therapy may not be without its own problems; a reversible impairment of intestinal absorption with a protein-losing enteropathy has been described in dogs (70). Experimental attempts at passive immune enhancement (antidonor antibody) have been entirely unsuccessful in prolonging survival (61).

Attempts at reducing the immunogenicity of the graft tissue have met with failure. Schaut (60) irradiated the graft tissue prior to transplantation in rats with no increase in graft survival. When lymph nodes from the graft were examined microscopically there was considerable lymphocyte depletion but many lymphocytes were still present. This failure to eradicate all lymph tissues may explain the lack of success. Much of the immunogenicity of the graft is felt to be due to the class II antigen-bearing cells. A new approach using pretransplant administration of monoclonal antibodies to class II antigens is being investigated. This method has already been shown to prolong graft survival of pancreatic islet transplants (71). Other approaches include pretransplant blood transfusions and segmental grafts (72,73). The latter is a direct attempt to decrease the immunogenic load which, in turn, has resulted in lower cyclosporine doses necessary to prevent rejection. Another complicating factor in intestinal transplants is that one of the first functions to fail with rejection is the mucosal barrier. This enables the translocation of bacteria into the submucosa and, eventually, into the blood stream with resultant sepsis. If the rejection process proceeds to this point, it is irreversible.

Small bowel grafts contain large amounts of lymphoid tissue which creates the potential for graft versus host disease. Some authors feel that this is a laboratory phenomenon due to the heavy immunosuppression of the host immune system. Most, however, feel that rejection and graft versus host disease are not mutually exclusive and can coexist (74). Graft versus host disease can manifest itself even if rejection is prevented by cyclosporine (75). This is contrary to other organ systems in which graft versus host disease can be prevented by large doses of immunosuppressive agents. The use of antilymphocyte serum to pretreat the donor along with cyclosporine treatment to the recipient has been shown to uniformly prevent graft versus host disease in rats (76).

In addition, there remain technical problems associated with small bowel transplantation at present. Most early graft failures are due to arterial and venous thrombosis of the graft and intestinal volvulus (65,77). The incidence of the latter can be decreased by ensuring proper orientation of the transplanted bowel. Monitoring the in vivo function of the graft to ensure early detection of rejection is difficult. Functional tests of water, sodium and sugar absorption with repeated small bowel biopsy have been proposed as the most reliable methods (78). A recent study by Banner et al (79) suggests that subclinical rejection can persist in the intestinal wall - in the submucosa and muscle - undetectable by mucosal biopsy alone. Additional technical problems centre around short term graft preservation. Presently, intravascular flushing with a balanced salt solution containing fructose in combination with hypothermia will provide up to 18 h of preservation (61). This has also been shown to decrease graft immunogenicity (80).

At present, small bowel transplantation remains an experimental alternative in the treatment of short bowel syndrome (61,62). Control of rejection is still the major obstacle to successful transplants. Clinical experience with small bowel transplantation and cyclosporine therapy remains limited. Nine patients (including four children with multivisceral grafts) have undergone small bowel transplantation under cyclosporine coverage. Four have survived, although three have had their grafts removed. The remaining five have all died due to sepsis, hemorrhage or unknown causes (81).

CONCLUSIONS
Management of the short bowel syndrome continues to be a difficult clinical problem. Over the long term, the clinician depends on intrinsic adaptation of the residual intestine and this, in turn, is dependent on length, type and functional state of the residual bowel along with the presence or absence of an ileocecal valve and colon. The mechanisms of adaptation are not entirely understood, thus preventing active interventional therapy to accelerate adaptation. As the most common cause of short bowel syndrome is...
while the adaptive process is occurring, and is directed at controlling or improving three pathophysiologic problems: decreased intestinal transit time; gastric hypersecretion; and reduced functional mucosal surface area. Initial therapy should be medical with consideration of surgical intervention only after therapeutic failure. Patience is very important as clinical improvement due to adaptation can be expected for up to two years.

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