

Chyme Reinfusion for Small Bowel Double Enterostomies and Enteroatmospheric Fistulas in Adult Patients: A Systematic Review Nutrition in Clinical Practice Volume 00 Number 0 xxxx 2019 1–11 © 2019 American Society for Parenteral and Enteral Nutrition DOI: 10.1002/ncp.10417 wileyonlinelibrary.com

WILEY

Sameer Bhat^{1,*} ⁽¹⁾; Puja Sharma, BMedSc (Hons)^{1,*}; Nelle-Rose Cameron, BMedSc (Hons)¹; Ian P. Bissett, FRACS¹; and Greg O'Grady, FRACS^{1,2}

Abstract

Background: High-output double enterostomies (DESs) and enteroatmospheric fistulas (EAFs) of the small bowel account for substantial patient morbidity and mortality. Management may include parenteral nutrition (PN) and prolonged admissions, at high cost. Reinfusion of chyme into the distal bowel is a proposed therapeutic alternative when the distal DES limb is accessible; however, standardized information on this technique is required. This review aimed to critically assess the literature regarding chyme reinfusion (CR) to define its current status and future directions. *Methods:* A systematic search of medical databases was conducted for articles investigating CR in adults. Articles reporting indications, methods, benefits, technical issues, and complications resulting from CR were reviewed. A narrative synthesis of the retrieved data was undertaken. *Results:* In total, 24 articles reporting 481 cases of CR were identified, although articles were heterogeneous in their structure and reporting. CR was most frequently performed for remediation of high-output DES and intestinal failure and for proximally located DES. Effluent output collection was commonly manual, with distal reinfusion more commonly automated, and with few dedicated systems. Multiple benefits attributed to CR were reported, encompassing weight gain, cessation of PN, and improvements in liver function. Technical problems included distaste, labor-intensive methods, reflux of contents, and tube dislodgement. No serious AEs or mortality directly attributable to CR were reported. *Conclusions:* CR appears to be a promising, safe and well-validated intervention for small bowel DES and EAF. However, more efficient and acceptable methods are required to promote greater adoption of the practice of CR. (*Nutr Clin Pract.* 2019;00:1–11)

Keywords

enterostomy; fistula; fistuloclysis; recycle; reinfusion

Introduction

High output of enteric contents is a common sequela of both double enterostomy (DES) of the small bowel and a subtype of enterocutaneous fistula with an exposed external orifice, termed enteroatmospheric fistula (EAF).¹ High outputs are known to precede multiple complications including dehydration and renal impairment, electrolyte disturbances, malnutrition, and intestinal failure (IF).²⁻⁴ Mortality has been reported to be as high as 30% in high-output EAFs compared with 6% having low output.⁵⁻⁷

Patients with high-output DES or EAF are commonly managed in the tertiary care setting, often as inpatients in specialist colorectal or IF units.⁸ Patients with intractable high outputs may require periods of nil per mouth, intravenous fluid therapy, medications to slow transit and reduce secretions, and potentially prolonged periods of support with parenteral nutrition (PN).^{5,9} PN is associated with substantial economic costs as well as potential secondary complications including liver dysfunction, central line– related complications, and metabolic complications such as hyperglycemia.¹⁰⁻¹⁴ Alternative or an adjunctive approach to the management of these patients is desirable.

Several studies have proposed reinfusing chyme from the proximal DES limb or EAF into the downstream bowel

*Joint first authors.

Financial disclosure: We thank the New Zealand MedTech CoRE and New Zealand Health Research Council for supporting this work.

Conflicts of interest: G. O'Grady and I. P. Bissett hold intellectual property in gastrointestinal nutrient recycling devices and are shareholders in Surgical Design Studio. The other authors have no conflicts of interest to declare.

This article originally appeared online on xxxx 0, 2019.

Corresponding Author:

Greg O'Grady, FRACS, Department of Surgery, The University of Auckland, Private Bag 92019, New Zealand. Email: greg.ogrady@auckland.ac.nz

From the ¹Department of Surgery, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand; and ²Auckland Bioengineering Institute, The University of Auckland, Auckland, New Zealand.

as a means of addressing these complications, when the distal limb is accessible.¹⁵⁻²² This technique is often referred to as chyme or succus entericus reinfusion.²³ However, the indications, methods, benefits, and any problems associated with chyme reinfusion (CR) are poorly collated in the literature at present. There is a need for clarification of the role of CR in patients with high outputs.^{24,25}

We therefore conducted a systematic search and critical review of the literature surrounding CR, with the following aims:

- 1. Summarize the currently recognized indications and methods for CR
- 2. Evaluate the clinical impact of CR
- Assess the safety of CR within the recorded experience(s)

The overall purpose was to identify priority areas and directions for future progress in this field. The focus of the current work was exclusively on adult patients bearing a small bowel DES or EAF.

Materials and Methods

Search Strategy

A systematic search of the literature was conducted in April 2019. The following search strategy was designed to capture literature reporting CR as management for patients with small bowel DES or EAF. This strategy encompassed keywords as well as Medical Subject Headings (MeSH) for DES, EAF, and reinfusion. Alternate forms of keywords were also encompassed within the search, through truncation, specific to the database search platforms. Boolean operators ("AND" and "OR") were used to combine these terms, to assist in identifying relevant articles. Details of the search string are provided in Supplementary Table S1.

The search strategy was run using the Ovid MEDLINE, EMBASE, Scopus, Cochrane, and CINAHL databases. There were no date or geographic restrictions. A manual search of the reference lists of relevant review articles was also undertaken for the purposes of identifying additional articles. A further search of the scientific literature using free text entries on Google Scholar was carried out with a similar purpose.

Screening and Synthesis of Evidence

References retrieved through the search were independently screened for full text review based on their title, abstract, and keywords by 2 reviewers. Articles selected for full text review were compared between the 2 reviewers, and discrepancies were resolved through consensus prior to full text retrieval and again before finalizing for inclusion.

Articles selected for inclusion were restricted to CR in adults (\geq 18 years) with a DES of the small bowel or EAF.

Papers relating to CR in pediatric and neonatal patients (<18 years) with a DES of the small bowel or EAF were excluded from this discussion, as were adult patients with terminal enterostomies or those with a small bowel DES without access to the distal segment. Only articles published in English, or with an English translation available, were included. There were no limitations on study design, or indication(s) for or method(s) of CR. Conference abstracts and correspondence lacking a detailed clinical description was excluded. Cases where infused contents consisted exclusively of enteral feed formulas (ie, enteral feeding via a surgically constructed fistula) or other nutrition solutions, without the reinfusion of chyme, were also omitted, as distal feeding interventions were not a focus of the present study.

The following data were then extracted from the included manuscripts by 2 independent reviewers: study characteristics; etiology resulting in DES or EAF formation; anatomical location of DES or EAF; indication(s) for CR; method(s) of CR; adjuvant therapies provided (eg, enteral nutrition or PN); influence of CR on PN therapy; quantitative outcomes (net intestinal losses, serum electrolytes, liver enzyme profiles, serum creatinine and urea, weight gain over the reinfusion duration); qualitative benefits; technical issues and complications relating to CR.

Data were recorded into a proforma spreadsheet within Microsoft Excel. Data extracted from each citation were subsequently assessed and validated for accuracy by a third reviewer. Uncertainties and inconsistencies were resolved by consensus.

Data Analysis

Given the heterogeneous nature of the included texts, a quantitative meta-analysis was not performed, and the focus of this review is a narrative synthesis of available data. Descriptive statistics were reported when possible. In view of the types of retrieved literature (detailed below), a formal appraisal of study quality was not conducted.

Results

Search Outcomes

A search of medical databases identified 165 articles, of which 70 full texts were assessed for their eligibility and inclusion (refer to PRISMA diagram; Figure 1). From these, a total of 24 articles were included for data synthesis, including 5 articles identified from a hand search and citation analysis. Characteristics of these studies are summarized in Table 1.

The literature selected for synthesis spanned a broad time interval (35 years), from 1983 to 2018, and captured diverse geographic origins (Table 1). The literature encompassed studies describing classical (manual) methods of CR as well as the innovation of novel apparatus and methods and

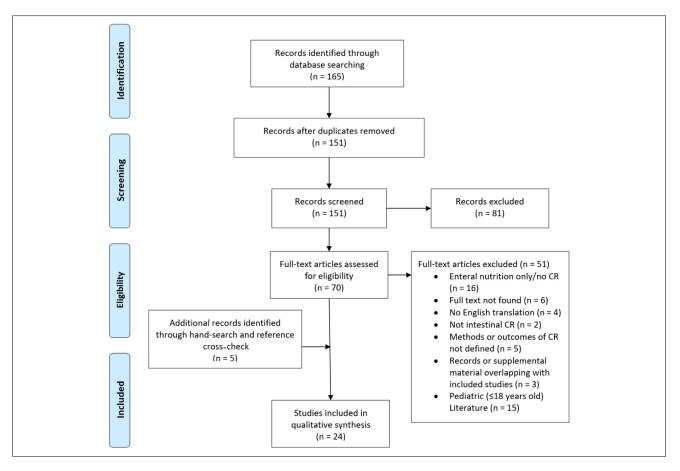


Figure 1. PRISMA flow diagram for the identification and screening of articles. CR, chyme reinfusion.

reporting a diverse range of clinical outcomes. Much of the published experience has been reported in the form of case studies or series (n = 13 papers) and retrospective cohort studies (n = 8), with few prospective studies (n = 3) and no randomized controlled trials.

Population Descriptors

CR was performed in patients with EAF in 13 studies, small bowel DES in 18 studies, and in both groups in 7 studies (refers to population data in Table 2). In total, reinfusion was reported in 481 patients, spanning a broad range of ages from 18 to 90 years, with the majority of patients being aged between 45and 60 years. Of these patients, 234 were men and 140 were women. One study, by Picot et al, accounted for a disproportionate volume of cases of CR (212 patients, or \approx 44% of all reported cases), owing to a dedicated device solution being employed in a systematic fashion (discussed further in the "Methods Employed for CR" section).¹¹

The underlying etiology resulting in small bowel DES or EAF formation was reported in 21 of the 24 texts. DES or EAF formation was most frequently observed as a consequence of peritonitis and abdominal sepsis (n = 118),

small bowel ischemia or infarction (n = 100), malignancy (n = 72), mechanical obstruction (n = 48), trauma (n = 24), and inflammatory bowel disease (n = 21). Additionally, the anatomical location of the DES or EAF was defined in 19 texts, albeit with variable consistency and clarity. A proximally located (jejunal) DES or EAF was most frequently observed, in 263 and 57 patients, respectively, whereas 8 patients receiving CR had duodenal EAF. The source data concerning anatomical descriptors of DESs and EAFs are further reported in Supplementary Table S2.

Additionally, the indication(s) necessitating CR were explicitly documented in 19 studies, with overlapping indications evident. The range of identified indications for CR, in descending order of frequency, were remediation of high DES or EAF output, IF with short (in-circuit) gut length, proximally located DES, fluid and electrolyte disturbances, malnutrition and poor weight gain, liver dysfunction and central line–related complications, metabolic derangements, and bowel rehabilitation (Table 3). In 2 texts, a definition of high-output DES or EAF was provided, which ranged from >500 mL/d to >1200 mL/d.^{10,11,26} The remaining studies, which cited high DES or EAF output as an indication for CR, did not cite a specific definition.^{15,20,23,27} For the

| Author | Year | Study Type | Study Design | Geographic Location |
|------------------------------|------|-------------------------|---------------|------------------------|
| Bissett ^{30,31} | 2000 | Cohort study | Retrospective | Nepal |
| Calicis et al ²³ | 2002 | Cohort study | Retrospective | France |
| Coetzee et al ¹⁵ | 2014 | Cohort study | Retrospective | South Africa |
| Cresci et al ²⁷ | 1997 | Case study | Retrospective | USA |
| Du Toit ¹³ | 2014 | Case study | Retrospective | South Africa |
| Gouma et al ¹⁸ | 1987 | Case series | Retrospective | Netherlands |
| Kittscha ³⁶ | 2016 | Case study | Retrospective | Australia |
| Kwun ³³ | 1999 | Case study | Retrospective | Hong Kong |
| Lefevre et al ³⁸ | 2008 | Case study | Retrospective | France |
| Levy et al ³² | 1983 | Cohort study | Prospective | France |
| Liu et al ²⁹ | 2016 | Case series | Retrospective | Taiwan |
| Maeda et al ⁴² | 1995 | Case study | Retrospective | Japan |
| McGrogan et al ³⁴ | 2012 | Case study ^a | NS | UK |
| Nagar et al ²⁰ | 2018 | Cohort study | Retrospective | India |
| Pflug et al ¹⁹ | 2013 | Case study | Retrospective | Brazil |
| Picot et al ²¹ | 2010 | Cohort study | Prospective | France |
| Picot et al ¹¹ | 2017 | Cohort study | Prospective | France |
| Prior et al ⁴¹ | 1990 | Case study | Retrospective | UK |
| Rinsema et al ³⁷ | 1988 | Cohort study | Retrospective | Netherlands |
| Sanchez-Guillen et al40 | 2016 | Case study | Retrospective | Spain |
| Wu et al ¹⁰ | 2014 | Cohort study | Retrospective | China |
| Yang et al ²⁸ | 2017 | Cohort study | Retrospective | China |
| Ye et al ³⁹ | 2013 | Case study | Retrospective | China |
| Yuan et al ³⁵ | 2011 | Cohort study | Retrospective | China |

Table 1. Characteristics of Studies Included for Narrative Synthesis.

NS, not stated.

^aAbstracts.

2 texts describing proximally located DES, the majority of patients had their proximal DES limb <120 cm from the duodenojejunal flexure.^{20,23}

Likewise, specific contraindication(s) to CR were outlined in 7 articles,^{10,11,13,15,21,23,28} with 3 studies reporting multiple reasons for patients not being reinfused.^{10,11,15} The most common reason for selecting to omit reinfusion was an inadequate length of distal bowel or the presence of a distal bowel stenosis or obstruction (n = 10), followed by complex DES or EAF anatomy (n = 9), and an intolerance to or technical difficulties with CR (n = 9 and n = 5, respectively).

Methods Employed for CR

CR methods were inconsistently reported. Where methods were reported, they usually embodied 1 of 2 basic models. The classical model comprised manual collection of DES or EAF output and either manual (syringe) or mechanical (feeding pump) reinfusion into the distal gut.

The second model for reinfusion advocated a range of novel closed-loop systems, whereby the proximal DES or EAF output was diverted and delivered to the distal limb without the need for manual intervention. These models often use aspiration pumps for collection of proximal chyme as well as peristaltic pumps (eg, enteral feeding pumps) for distal reinfusion, all involving circulation of chyme out of and then back through a stoma appliance.

There was also considerable variation in the apparatus utilized, indicating the lack of a standardized method (Table 4). The most frequently used tool was a Foley catheter, ranging from 12 to 24 French in size. Many studies used some form of peristaltic pump for reinfusion (n = 13), thereby enabling most patients to be reinfused continuously or intermittently, whereas direct bolus reinfusion was performed in 3 studies^{10,29-31} (Table 5).

A few studies reported the development of novel solutions or devices for CR. Most notable was the Enteromate system (Société Labodial, Les Clayes-sous-Bois, France), introduced by Levy et al in 1983, which employs a roller pump to aspirate intestinal output into a disposable container.³² The volume and weight of the aspirated fluid is continuously monitored and, upon reaching a preset value, an infusion pump is activated to initiate reinfusion. An updated homeuse Enteromate system was more recently utilized by Picot et al in a larger prospective study.^{11,21}

Furthermore, the process for reinfusion varied widely (Table 5). DES or EAF output from the proximal limb was filtered prior to reinfusion in 8 studies, to prevent blockage of the infusion tubing. Filtration was performed using a gauze, porous cloth, or household mesh strainer.

| Table 2. | Population | Descriptors of | of Selected | Articles. |
|----------|------------|----------------|-------------|-----------|
|----------|------------|----------------|-------------|-----------|

| Author | Small Bowel EAF (Number)/DES (Number) | Study Population Size | CR Population Size ^a | Sex (Male; Female) | Mean Age ± SD (Range) |
|-------------------------------------|---|-----------------------------|---------------------------------------|-----------------------|---------------------------------|
| Bissett ^{30,31} | EAF | 21 | 8 | | (12–58) years |
| Calicis et al ²³ | DES | 21 | 21 | 11;10 | $46 \pm 15 (18-74)$ years |
| Coetzee et al ¹⁵ | EAF and DES | 54 | 20 | 15;5 | 47 ± 16.6 years |
| Cresci et al ²⁷ | EAF | 1 | 1 | 1;0 | 26 years |
| Du Toit ¹³ | EAF and DES | 1 | 1 | 1;0 | 30 years |
| Gouma et al ¹⁸ | EAF and DES | 6 | 6 | | |
| Kittscha ³⁶ | DES | 1 | 1 | 1;0 | 70 years |
| Kwun ³³ | DES | 1 | 1 | 1;0 | 62 years |
| Lefevre et al ³⁸ | DES | 1 | 1 | 1;0 | 53 years |
| Levy et al ³² | EAF (14)/DES | 30 | 30 | | |
| - | (16) | | | | |
| Liu et al ²⁹ | DES | 6 | 6 | 3;3 | $65 \pm 9.6 (53 - 83)$ years |
| Maeda et al ⁴² | DES | 1 | 1 | 1;0 | 26 years |
| McGrogan et al ³⁴ | DES | 1 | 1 | 0;1 | |
| Nagar et al ²⁰ | DES | 35 | 35 | 26;9 | [47] ^b (19–74) years |
| Pflug et al ¹⁹ | EAF | 1 | 1 | 0;1 | 42 years |
| Picot et al ²¹ | DES | 26 | 26 | 17;9 | $57.8 \pm 13.7 (17-79)$ years |
| Picot et al ¹¹ | EAF (29)/DES | 212 | 212 | 125;87 | $61.4 \pm 14.8 (17-90)$ years |
| | (183) | | | | × /• |
| Prior et al ⁴¹ | DES | 1 | 1 | 1;0 | 58 years |
| Rinsema et al ³⁷ | EAF and DES | 8 | 8 | 4;4 | 53.4 ± 10.12 (30–62) years |
| Sanchez-Guillen et al ⁴⁰ | EAF | 1 | 1 | 1;0 | 19 years |
| Wu et al ¹⁰ | EAF | 95 | 35 | 24;11 | 50.2 ± 14.1 years |
| Yang et al ²⁸ | DES | 183 | 22 | · | 2 |
| Ye et al ³⁹ | EAF and DES | 1 | 1 | 1;0 | 41 years |
| Yuan et al ³⁵ | EAF | 82 | 41 | · | 2 |

Blank cells coincide with data points that were not reported in their respective article.

CR, chyme reinfusion; DES, double enterostomy; EAF, enteroatmospheric fistula.

^aIn several studies, only a proportion of the reported patients received CR, with the remainder either receiving no reinfusion or distal feeding with enteral formulas (fistuloclysis).

^bMedian age in years.

Dietary modification (pureed or restricted) was advocated for patients in 4 studies.^{11,21,29,33} One case study addressed the potential for blockage by blending proximal chyme in a dedicated blender.³³ Another study refrigerated the output at 4°C prior to distal reinfusion²³; alternatively, the output was infused fresh in 4 studies.^{10,28,34,35}

Clinical Outcomes

An improvement in nutrition status was routinely observed among patients receiving CR, measured by an increase in mean weight, body mass index, and Nutritional Risk Index (NRI), in 8 articles. A statistically significant nutrition improvement was reported in 2 of these studies,^{11,21} including a significant increase in NRI by 10.9 ± 9.5 (P < .001) from the largest study of 212 patients.¹¹ In 2 prominent studies, Picot et al reported a rise in plasma citrulline concentration after CR by $\approx 80\%$, which was identified as a marker of absorptive small bowel capacity.^{11,21} Of all analyzed studies, 6 reported reducing or completely ceasing PN in patients once CR had been initiated. 11,15,20,21,29,36 All but one of these showed >85% of reinfused patients as having PN withdrawn completely. 11,15,21,29,36

An improvement in liver profiles (particularly alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and bilirubin) was observed in 8 studies, with statistical significance reported in 4 of these studies.^{10,11,21,37} The restoration of liver enzymes and function was postulated by 2 groups as being related to reestablishment of the enterohepatic circulation of bile salts following reinfusion and beneficial effects on the small intestine microbiome.^{18,29}

Levy et al observed a 20% decrease in the output from the proximal limb of the DES (P < .01) when instilling a dialysate solution through the distal limb. When CR was instead performed into the distal DES limb, there was a 30% decrease in output from the proximal limb. They postulated that this was due to an inhibitory effect on the upper gastrointestinal (GI) tract secretions initiated by chyme within the distal small bowel.³² The authors compared chyme flow before CR with the ultimate fecal losses of the

| CR Indication | Number of Patients | Reference Article(s) |
|--|-----------------------|---|
| High output | 269 | Coetzee et al ¹⁵ ; Cresci et al ²⁷ ; Kwun ³³ ; Pico et al ¹¹ ; Wu et al ¹⁰ |
| IF and short bowel syndrome | 247 | Du Toit ¹³ ; Liu et al ²⁹ ; McGrogan et al ³⁴ ; Picot et al ¹¹ ; Picot et al ²¹ ; Sanchez- Guillen et al ⁴⁰ |
| Proximal DES anatomy | 56 | Calicis et al ²³ ; Nagar et al ²⁰ |
| Fluid and electrolyte imbalance | 45 | Coetzee et al ¹⁵ ; Cresci et al ²⁷ ; Kwun ³³ ; Pflug et al ¹⁹ |
| Nutrition support and poor weight gain | 23 | Coetzee et al ¹⁵ ; Cresci et al ²⁷ ; Kwun ³³ ; Sanchez-Guillen et al ⁴⁰ |
| Liver dysfunction and central line-related complications | 12 | Du Toit ¹³ ; Pflug et al ¹⁹ ; Rinsema et al ³⁷ ; Sanchez-Guillen et al ⁴⁰ |
| Metabolic derangement | 8 | Rinsema et al ³⁷ |
| Bowel rehabilitation and preparation for stoma reversal | 2 | Maeda et al ⁴² ; Prior et al ⁴¹ |
| Multiple EAF | 1 | Ye et al ³⁹ |
| Total PN reduction | 1 | Du Toit ¹³ |
| Financial barriers to care | 1 | Cresci et al ²⁷ |

Table 3. Indications for CR in Selected Articles.

CR, chyme reinfusion; DES, double enterostomy; EAF,

enteroatmospheric fistula; IF, intestinal failure; PN, parenteral nutrition.

downstream intestinal segment (from the anus, colostomy, or terminal ileostomy, depending on the anatomy) during CR, because of the difficulty in measuring chyme flow during CR. A consistent reduction in the proximal DES or EAF output after initiating CR was documented in 4 studies, all reporting statistical significance (P < .001).^{10,11,21,32}

Two studies reported favorable economic outcomes of CR, demonstrating a savings in total healthcare cost per patient.^{20,36}

Technical Issues

The most commonly reported technical issues with CR included backflow of effluent, effluent losses during the process of collection and storage, and tube blockage.^{11,13,20,23,36} Tube blockage was a problem, with Foley catheters often being employed, leading many investigators to strain contents prior to reinfusion to prevent blockage at the outlet holes.^{15,18,20,27-29,36,37} Wu et al also raised the potential for tube dislodgment, eventually leading to underfeeding.¹⁰ In this case, tube displacement was addressed by increased inflation of a retention balloon. Another tube complication

observed on a single occasion was the "swallowed" feeding tube, whereby the peristaltic activity of the distal bowel led to internal displacement of the feeding tube.¹⁰

The most prominent difficulties reported in the literature encompassed the demanding processes, hygiene, and aesthetic concerns of CR.^{10,28,33} The reinfusion process was often observed as labor intensive and unpleasant for staff and patients alike.^{15,33,36} Other challenges included maintaining patients on strict dietary regimens while being reinfused and difficulties with patient trust and acceptance of the procedure, particularly when undertaken manually.^{11,21,29,33,36}

Adverse Events and Mortality

Picot et al identified occurrence of a new fistula (n = 3) and development of distal colonic stenosis (n = 1) among a large cohort of reinfused patients.¹¹ However, these complications appeared to represent unmasking of existing pathologies or progression of underlying pathology rather than being complications of CR per se, as these were patients excluded from the reinfused group. Specific mention of no adverse events (AEs) related to reinfusion were reported in 6 articles,^{15,18,21,27,37,38} whereas 11 other studies did not report whether any AEs occurred.^{13,19,28,30-35,39,40} No studies reported any serious AEs or mortality directly associated with CR.

GI side effects were reported in association with CR in some studies, including abdominal discomfort, diarrhea, constipation, nausea, and vomiting, which were generally controlled sufficiently to enable reinfusion to be continued.^{10,20,23,29,36,41,42} However, it was not clear whether these effects were directly related to CR or the underlying etiology that resulted in DES or EAF formation, or both. One article noted that extremely rapid or bolus reinfusion may contribute to these symptoms.^{20,36}

Discussion

This study provides a comprehensive review of the current status of CR as a therapeutic intervention in adults. From 24 reported studies, CR was found to be a beneficial intervention when successfully performed and with minimal complications. CR was found to be broadly applicable for patients with small bowel DES or EAFs, and particularly for those with complications of high outputs, IF, and fluid and electrolyte imbalances.

The key benefits of CR were nutrition improvement including increase in weight gain, improvement of liver profiles, and volume reduction in DES or EAF output from the proximal limb.^{10,11,15,20,21,29,32,36} Of particular note, a very high proportion of patients (typically >85%) established on reinfusion were able to wean from PN, demonstrating substantial potential for safer care of these complex patients and at lower cost. No serious AEs relating to CR were identified, although GI side effects were common. The most

| | | Tubing | Met | Methods | |
|--|------------------------------------|---|-------------------------------|---|---|
| Author | Collection | Reinfusion | Collection | Reinfusion | Other |
| Bissett ^{30,31} | | Foley catheter (large bore) | Manual | Catheter syringe | Standard stoma bag |
| Calicis et al ²³ | | Silicone balloon rubber | Aspiration pump | (1111111111) | |
| Coetzee et al ¹⁵ | | Cautoca Foley catheter (16 Fr) | Manual (every 3 hours) | APPLIX Feeding Pump | Porous cloth; standard stoma appliance |
| Cresci et al ²⁷ Du Toit ¹³ Gouma et al ¹⁸ | | Feeding tube (unspecified) Double-lumen Foley catheter Urinary bladder catheter | Manual Infusion set (every | Feed administration set Roller pump/IV fluid | Standard stoma bag Standard stoma collection |
| Kittscha ³⁶ | | Silicone Foley balloon catheter | Aanual Manual | pump Kangaroo pump | Eakin seal; standard stoma |
| Kwun^{33} | | (12 FT) Silicone-coated Foley catheter (14 Fr) | Manual | Kangaroo feeding pump | oag Household blender |
| Lefevre et al ³⁸ Levy et al ³² | | Silicone rubber balloon | Roller pump (aspiration) | Enteromate (roller | Karaya seal ostomy |
| Liu et al ²⁹ | | Silicone Foley catheter; | Manual (6 times a day) | Feeding pump | Gauze; Karaya gum sealed |
| Maeda et al ⁴² McGrossi et al ³⁴ | lleostomy connector | surcone up cone caureter lleostomy connector | Ileostomy connector | Ileostomy connector | stoma appuance |
| Nagar et al ²⁰ | | Foley catheter (20 Fr) | Manual | Enteral feed bag | Household mesh strainer; |
| Pflug et al ¹⁹ | Double-lumen Foley | Triple-lumen Foley catheter | Manual | Diet infusion pump | VACT |
| Picot et al ²¹ Picot et al ¹¹ | Enteromate | Enteromate Simple lumen polyurethane nasogastric tube, Levine | Enteromate Enteromate | Enteromate Enteromate | |
| Prior et al ⁴¹ | Foley catheter; Silastic tubing | type (Cut 14-10) Foley catheter (20 Fr) | Manual | Peristaltic pump | Counterbalance and mercury switch; standard |
| Rinsema et al 37 | | Urinary bladder catheter | Manual (every 4 hours) | Roller pump/IVAC fluid pump | scoma bag Standard stoma collection bag |
| | | | | | (continued) |

Table 4. CR Materials and Methods.

| ntinued |
|---------|
| (coj |
| 4 |
| le |
| 9 |
| Б |

| | | Tubing | W | Methods | |
|---|---|---|---|-------------------------------------|-----------------------|
| Author | Collection | Reinfusion | Collection | Reinfusion | Other |
| Sanchez-Guillen et al ⁴⁰ | | Gastrostomy catheter (24 Fr) | Manual | Intestinal content infusion pump | Ileostomy bag |
| Wu et al ¹⁰ | Triple catheterization cannula | Gastrostomy balloon retention tube/Foley/NJ; T-shaped tube (biliarv fistula) | Aspiration pump (negative 150–200 millibars) | 4 | |
| Yang et al ²⁸ | Triple catheterization cannula | Foley catheter | Aspiration pumps | | |
| Ye et al ³⁹ | Y-type tube | PEJ catheter; Foley urethral catheter (along distal jejunal fistula port) | Manual | Enteral nutrition pump | Intestinal ostomy bag |
| Yuan et al ³⁵ | Triple catheterization cannula | Foley catheter | Aspiration pumps (negative 150–200 millibars) | | Sterile catheter bag |
| Blank cells coincide w CR, chyme reinfusion; | ith data points that were not re Fr, French catheter sizing; IV, | Blank cells coincide with data points that were not reported in their respective article. CR, chyme reinfusion; Fr, French catheter sizing; IV, intravenous; NJ, nasojejunal; PEJ, percutaneous endoscopic jejunostomy; VACT, vacuum-assisted closure therapy. | cutaneous endoscopic jejunos | omy; VACT, vacuum-assisted clos | ure therapy. |

common deterrents to CR in clinical practice were the laborintensive, demanding, and unpleasant processes for both staff and patients.^{10,15,28,33,36}

With respect to technical challenges encountered during CR, reflux of reinfused contents may decrease the efficiency of reinfusion; however, this is not problematic so long as the overall reinfusion of chyme proceeds effectively. Future research focusing on more efficient, simpler, and standardized methods of CR and related tubing could help to overcome these limitations, increasing the utility and application of CR.

Minimal research could be located on microbiological consequences of CR, which is relevant to the potential for bacterial overgrowth due to stasis of contents in a stoma appliance between recycling episodes.⁴³ However, it is notable that no complications were attributable to bacterial overgrowth in any patients in this review.

A limitation of this review was the considerable variation and heterogeneity in the structure and reporting of CR across the 24 included texts. Overall, many of the retrieved reports were largely anecdotal clinical experiences (in the form of case studies or series), as opposed to more robust trial designs. However, controlled trials are conceivably difficult to perform in this field because of the limited availability of standardized CR protocols and the relatively low number of small bowel DES or EAFs managed in many centers. It is significant that the largest study investigating CR in adult populations, which showed outstanding nutrition and biochemical results, including >90% rates of PN cessation, employed a specific device system (Enteromate).¹¹ This again indicates the substantial potential for specific devices and standardized techniques to improve CR practices and clinical outcomes in the future. In addition, some potentially promising literature reporting CR in adults had to be omitted from this review during abstract and full text screening stages due to full English translations being unavailable.44-52

This study specifically focused on CR and therefore did not evaluate the concept of distal feeding or "fistuloclysis," ie, infusing enteral feeding solutions into the distal limb of the bowel. Fistuloclysis has also been shown in reports to potentially replace parenteral feeding in these patients, with potential for significant nutrition, liver function, and other clinical benefits.^{53,54}

In conclusion, this review finds that CR is a useful and safe intervention for management of small bowel DES and EAFs. However, despite its therapeutic potential, CR has not been widely adopted internationally, principally because of a lack of an efficient, reliable, and user-friendly method. Future research should aim to standardize reporting of variables relating to CR (eg, percentage of DES or EAF output reinfused) and focus on developing less demanding and distasteful methods, to reduce the barriers to and promote greater adoption of CR.

Table 5. CR Procedures.

| Author | Bowel Patency Assessed | Straining/ Filtration | Rates: Continuous (C); Bolus (B) | Pureed or Restricted Diet |
|-------------------------------------|---------------------------|--------------------------|-------------------------------------|------------------------------|
| Bissett ^{30,31} | | | В | |
| Calicis et al ²³ | | | С | |
| Coetzee et al ¹⁵ | \sim | \sim | С | |
| Cresci et al ²⁷ | | | | |
| Du Toit ¹³ | , | v | | |
| Gouma et al ¹⁸ | Ŷ | | | |
| Kittscha ³⁶ | | N N | С | |
| Kwun ³³ | | v | - | ./ |
| Lefevre et al ³⁸ | | | | Ň |
| Levy et al ³² | | | С | |
| Liu et al ²⁹ | | \checkmark | C (hospital), B (at home) | ./ |
| Maeda et al ⁴² | | v | C | v |
| McGrogan et al ³⁴ | | | C C | |
| Nagar et al ²⁰ | ./ | | | |
| Pflug et al ¹⁹ | v | v | | |
| Picot et al ²¹ | | | С | ./ |
| Picot et al ¹¹ | | | Č | |
| Prior et al ⁴¹ | \checkmark | | C C | Ň |
| Rinsema et al ³⁷ | v | ./ | - | |
| Sanchez-Guillen et al ⁴⁰ | | v | С | |
| Wu et al ¹⁰ | | | B | |
| Yang et al ²⁸ | | \checkmark | 2 | |
| Ye et al ³⁹ | | ٠v | С | |
| Yuan et al ³⁵ | | | č | |

Blank cells relate to CR processes that were either not performed on patients or not clearly reported in their respective article. CR, chyme reinfusion.

Statement of Authorship

P. Sharma and N.-R. Cameron equally contributed to the conception and design of the research; S. Bhat, G. O'Grady and I. P. Bissett contributed to the design of the research; P. Sharma and N.-R. Cameron contributed to the acquisition of data; S. Bhat, P. Sharma, and N.-R. Cameron contributed to the analysis and interpretation of the data; S. Bhat and P. Sharma drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

References

- Marinis A, Gkiokas G, Argyra E, Fragulidis G, Polymeneas G, Voros D. "Enteroatmospheric fistulae"-gastrointestinal openings in the open abdomen: a review and recent proposal of a surgical technique. *Scand J Surg.* 2013;102(2):61-68. https://doi.org/10.1177/1457496913482252
- Arenas Villafranca JJ, López-Rodríguez C, Abilés J, Rivera R, Adán NG, Navarro PU. Protocol for the detection and nutritional management of high-output stomas. *Nutr J*. 2015;14(1):45. https://doi.org/ 10.1186/s12937-015-0034-z

- Bafford AC, Irani JL. Management and complications of stomas. Surg Clin North Am. 2013;93(1):145-166. https://doi.org/10.1016/ j.suc.2012.09.015
- Baker ML, Williams RN, Nightingale JMD. Causes and management of a high-output stoma. *Color Dis.* 2011;13(2):191-197. https://doi.org/ 10.1111/j.1463-1318.2009.02107.x
- Martinez JL, Luque-De-Leon E, Mier J, Blanco-Benavides R, Robledo F. Systematic management of postoperative enterocutaneous fistulas: Factors related to outcomes. *World J Surg.* 2008;32(3):436-443. https://doi.org/10.1007/s00268-007-9304-z
- Draus JM, Huss SA, Harty NJ, Cheadle WG, Larson GM. Enterocutaneous fistula: are treatments improving? *Surgery*. 2006;140(4):570-578. https://doi.org/10.1016/j.surg.2006.07.003
- Evenson AR, Fischer JE. Current management of enterocutaneous fistula. J Gastrointest Surg. 2006;10(3):455-464. https://doi.org/ 10.1016/j.gassur.2005.08.001
- Messaris E, Sehgal R, Deiling S, et al. Dehydration is the most common indication for readmission after diverting ileostomy creation. *Dis Colon Rectum*. 2012;55(2):175-180. https://doi.org/10.1097/ DCR.0b013e31823d0ec5
- Jeppesen PB. Spectrum of short bowel syndrome in adults: intestinal insufficiency to intestinal failure. JPEN J Parenter Enteral Nutr. 2014;38(1):8-13. https://doi.org/10.1177/014860711452 0994
- Wu Y, Ren J, Wang G, et al. Fistuloclysis improves liver function and nutritional status in patients with high-output upper enteric fistula. *Gastroenterol Res Pract*. 2014;2014:1-10. https://doi.org/ 10.1155/2014/941514

- Picot D, Layec S, Dussaulx L, Trivin F, Thibault R. Chyme reinfusion in patients with intestinal failure due to temporary double enterostomy: a 15-year prospective cohort in a referral centre. *Clin Nutr.* 2017;36(2):593-600. https://doi.org/10.1016/j.clnu.2016.04.020
- Abu-Wasel B, Molinari M. Liver disease secondary to intestinal failure. Biomed Res Int. 2014;2014:1-10. https://doi.org/10.1155/2014/968357
- Du Toit A. Nutritional management of a complicated surgical patient by means of fistuloclysis. *South African J Clin Nutr.* 2014;27(4):230-236. https://doi.org/10.1080/16070658.2014.11734515
- Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding effects on septic morbidity after blunt and penetrating abdominal trauma. *Ann Surg.* 2006;215(5):503-513. https://doi.org/ 10.1097/00000658-199205000-00013
- Coetzee E, Rahim Z, Boutall A, Goldberg P. Refeeding enteroclysis as an alternative to parenteral nutrition for enteric fistula. *Color Dis.* 2014;16(10):823-830. https://doi.org/10.1111/codi.12727
- Drenckpohl D, Vegunta R, Knaub L, et al. Reinfusion of succus entericus into the mucous fistula decreases dependence on parenteral nutrition in neonates. *Infant, Child, Adolesc Nutr.* 2012;4(3):168-174. https://doi.org/10.1177/1941406412446002
- Levy E, Frileux P, Sandrucci S, et al. Continuous enteral nutrition during the early adaptive stage of the short bowel syndrome. Br J Surg. 1988;75(6):549-553. https://ovidsp.ovid.com/ovidweb.cgi?T= JS&PAGE=reference&D=emed88&NEWS=N&AN=1988151634
- Gouma DJ, De Bruyn H, Rinsema W, Soeters PB. Pumping device for re-infusion excretions derived from a proximal jejunostomy or high output fistula. *Br J Surg.* 1987;74(8):741. https://doi.org/10.1002/ bjs.1800740832
- Pflug AM, Utiyama EM, Fontes B, Faro M, Rasslan S. Continuous reinfusion of succus entericus associated with fistuloclysis in the management of a complex jejunal fistula on the abdominal wall. *Int J Surg Case Rep.* 2013;4(8):716-718. https://doi.org/10.1016/j.ijscr.2013.04.041
- Nagar A, Mehrotra S, Yadav A, et al. Distal bowel re-feeding in patients with proximal jejunostomy. J Gastrointest Surg. 2018;22(7):1251-1257. https://doi.org/10.1007/s11605-018-3752-7
- Picot D, Garin L, Trivin F, Kossovsky MP, Darmaun D, Thibault R. Plasma citrulline is a marker of absorptive small bowel length in patients with transient enterostomy and acute intestinal failure. *Clin Nutr.* 2010;29(2):235-242. https://doi.org/10.1016/j.clnu.2009.08.010
- Tanaka A, Nakayama-Imaohji H, Shimono R, et al. Nutritional benefit of recycling of bowel content in an infant with short bowel syndrome. *J Pediatr Gastroenterol Nutr.* 2017;65(3):e75-e76. https://doi.org/ 10.1097/MPG.00000000001630
- Calicis B, Parc Y, Caplin S, et al. Treatment of postoperative peritonitis of small-bowel origin with continuous enteral nutrition and succus entericus reinfusion. *Arch Surg.* 2002;137(3):296. https://doi.org/ 10.1001/archsurg.137.3.296
- Pironi L, Arends J, Baxter J, et al. ESPEN endorsed recommendations: definition and classification of intestinal failure in adults. *Clin Nutr.* 2015;34(2):171-180. https://doi.org/10.1016/j.clnu.2014.08.017
- Kumpf VJ, De Aguilar-Nascimento JE, Diaz-Pizarro Graf JI, et al. ASPEN-FELANPE clinical guidelines. J Parenter Enter Nutr. 2017;41(1):104-112. https://doi.org/10.1177/0148607116680792
- González EM. Optimising the treatment of upper gastrointestinal fistulae optimizing the treatment of upper gastrointestinal fistulae. *Gut J Br Soc Gastroenterol*. 2001;49(suppl 4):iv21-iv28. https://doi.org/ 10.1136/gut.49.suppl_4.iv21
- Cresci GA, Martindale RG. Metabolic and nutritional management of a patient with multiple enterocutaneous fistulas. *Nutrition*. 1997;13(5):446-449. https://doi.org/10.1016/S0899-9007(97)00094-4
- Yang S, Guo J, Ni Q, et al. Enteral nutrition improves clinical outcome and reduces costs of acute mesenteric ischaemia after recanalisation in the intensive care unit. *Clin Nutr.* 2017;38(1):398-406. https://doi.org/10.1016/j.clnu.2017.12.008

- Liu MY, Tang HC, Yang HL, Chang SJ. Is jejunostomy output nutrient or waste in short bowel syndrome? Experience from six cases. *Asia Pac J Clin Nutr.* 2016;25(2):430-435. https://doi.org/10.6133/ apjcn.2016.25.2.18
- Bissett IP. Succus entericus reinfusion to treat postoperative smallbowel fistula. Arch Surg. 2003;137(12):1446. https://doi.org/10.1001/ archsurg.137.12.1446-a
- Bissett IP. Postoperative small bowel fistula: back to basics. *Trop Doct*. 2000;30:138-139. https://doi.org/10.1177/004947550003000308
- 32. Levy E, Palmer DL, Frileux P, Parc R, Huguet C, Loygue J. Inhibition of upper gastrointestinal secretions by reinfusion of succus entericus into the distal small bowel. A clinical study of 30 patients with peritonitis and temporary enterostomy. *Ann Surg.* 1983;198(5):596-600. https://doi.org/10.1097/00000658-198311000-00006
- Kwun H. Re-feeding of chymus into a high-output jejunostomy: a nursing care study. World Counc Enteros Ther J. 1999;19(4):20-28.
- McGrogan D, McCain S, Harris A, McCallion K. PMO-073 Post-operative enteral nutrition and recirculation of jejunal effluent in the management of a paraduodenal hernia: a case report. *Gut.* 2012;61(Suppl 2):A102.2-A103. https://doi.org/10.1136/gutjnl-2012-302514b.73
- 35. Yuan Y, Ren J, Gu G, Chen J, Li J. Early enteral nutrition improves outcomes of open abdomen in gastrointestinal fistula patients complicated with severe sepsis. *Nutr Clin Pract.* 2011;26(6):688-694. https://doi.org/10.1177/0884533611426148
- Kittscha J. Restoring gut continuity: reinfusion of effluent via distal limb of a loop jejunostomy. *World Counc Enteros Ther J.* 2016;36(4):28-31.
- Rinsema W, Gouma DJ, von Meyenfeldt MF, Soeters PB. Reinfusion of secretions from high-output proximal stomas or fistulas. Surg Gynecol Obs. 1988;167(5):372-376. https://doi.org/10.1002/ bapi.201410024
- Lefevre JH, Parc Y, Bennis M, et al. Multiple stomas for recurrent life-threatening gastrointestinal bleeding: report of a case. *Dis Colon Rectum.* 2008;51(11):1714-1718. https://doi.org/10.1007/ s10350-008-9220-9
- 39. Ye X, Peng N, Jiang F, et al. Subsegmental bowel enteral nutrition infusion and succus entericus reinfusion in patients with severe acute pancreatitis complicated with multiple enteric fistulae: a successful experience. *Am Surg.* 2013;79(4):E169.
- Sánchez-Guillén L, López de los Reyes R, Vives-Rodríguez E, Mato Iglesias A, Cantón-Blanco A. Enteral nutrition in Crohn's disease with a high output enteroatmospheric fistula. *Cir Esp.* 2016;94(9):547-550. https://doi.org/10.1016/j.cireng.2016.10.005
- Prior A, Downing R. A self-regulating device for continuous reinfusion of jejunostomy effluent: rapid communications in the journal of medical engineering & technology. J Med Eng Technol. 1990;14(1):21-22. https://doi.org/10.3109/03091909009028759
- Maeda K, Hashimoto M, Koh J, Yamamoto O, Hosoda Y, Morikawa Y. The use of an ileostomy connector to diminish the frequency of defecation prior to ileostomy closure in patients with a pelvic pouch. *Surg Today*. 1995;25(7):657-661. https://doi.org/10.1007/BF00311445
- Pataki I, Szabo J, Varga P, et al. Recycling of bowel content: the importance of the right timing. J Pediatr Surg. 2013;48(3):579-584. https://doi.org/10.1016/j.jpedsurg.2012.07.064
- 44. Berta JL, Piermont C, Planche E. Fistules entero-cutanees graves reinstillation du chyme dig a propos 16 obs [Serious enterocutaneous fistulas. Reinstillation of digestive chyme apropos of 16 cases]. *Med Chir Dig.* 1980;9(4):321.
- 45. Levy E, Cosnes J, Parc R, Bloch P, Huguet C, Loygue J. Reinstillation contin du chyme en reanim dig: mise en evid d'une retro-action negat sur le debit secretoire dig [Continuous reinstillation of chyme in digestive resuscitation: demonstration of negative retro-action on the digestive secretion output]. *Nouv Presse Med.* 1979;8(10):782-783.

- 46. Loygue J, Levy E, Cosnes J, Herbiere P. Nutritional problems in surgical patients in a grave condition. Enteral hypernutrition by nutripump and autoregulated reinstillation of chyme [Article in French]. *Chirurgie*. 1979;105(8):694-697. https://www.scopus.com/ inward/record.uri?eid=2-s2.0-0018619841&partnerID=40&md5=4f2 666b7401488da0b777d94e1afcc43
- Picot D, Zeanandin G, Bachmann P, et al. Management of a temporary high output enterostomy. *Nutr Clin Metab.* 2014;28(3):227-233. https://doi.org/10.1016/j.nupar.2014.06.003
- Picot D. Home succus entericus reinfusion for patients with temporary high flow enterostomy. A monocenter experience. *Nutr Clin Metab.* 2013;27(4):249-254. https://doi.org/10.1016/j.nupar.2013.09. 003
- Meng FL, Chen Y. Early enteral nutrition combined with digestive fluid reinfusion in patients with severe intestinal fistula. *World Chinese J Dig.* 2014;22(29):4530-4533. https://doi.org/10.11569/ wcjd.v22.i29.4530

- Zhu JG, Yu R, Pang LQ, Tang XJ, Zhao Y. Change of bacteria and enzymes in the drainage fluid in patients with intestinal fistulas. *Chinese J Clin Nutr.* 2011;19(6):383-386. https://doi.org/10.3760/ cma.j.issn.1674-635X.2011.06.007
- 51. Zhu J, Wang J, He Y, Zhuang H, Yang J. Application of small intestine double stoma and succus entericus reinfusion in the patients with severe intra-abdominal infection [Article in Chinese]. *Zhonghua Wei Chang Wai Ke Za Zhi*. 2015;18(7):667-670.
- Zaouche A, Khereddine T, Houissa M, et al. La reinstillation du chyme intest dans les fistules du grele [Reinfusion of intestinal chyme in intestinal fistulas]. *Tunis Med.* 1990;68(6-7):439-444.
- Ham M, Horton K, Kaunitz J. Fistuloclysis: case report and literature review. *Nutr Clin Pract.* 2007;22(5):553-557. https://doi.org/ 10.1177/0115426507022005553
- Teubner A, Morrison K, Ravishankar HR, Anderson ID, Scott NA, Carlson GL. Fistuloclysis can successfully replace parenteral feeding in the nutritional support of patients with enterocutaneous fistula. *Br J Surg.* 2004;91(5):625-631. https://doi.org/10.1002/bjs.4520