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Original article

Management of entero-atmospheric fistulas by chyme reinfusion: A retrospective study

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SUMMARY

Background & aims: High output entero-cutaneous fistulas may lead to intestinal failure with parenteral nutrition (PN) as the gold standard treatment to prevent dehydration and malnutrition. However in case of entero-atmospheric fistula (EAF) with the distal limb of the fistula accessible, chyme reinfusion (CR), a technique that restores artificially digestive continuity can be performed until the surgical repair. Our aim was to study the efficacy of CR in EAF regarding nutritional status, intestinal function, PN weaning and liver tests.

Methods: Retrospective study of 37 patients admitted for EAF and treated by CR from 1993 to 2017. Delays were expressed in median (25%-75% quartiles) and other data on mean ± SD.

Results: Location of EAF: jejunum (29), ileum (8). The length of the upstream intestine was estimated in 21 patients: 19 had a bowel length <150 cm of which 16 had less than 100 cm. During CR, mean digestive losses decreased from 1734 ± 578 to 443 ± 487 ml/24 h ($p < 0.000001$), nitrogen absorption increased from 45.3 ± 18.6 to 81.8 ± 12.9% of ingesta ($p < 0.001$). The percentage of patients with plasma citrulline <20 μmol/l decreased from 71 to 10%. PN was stopped in all patients within 3 (0–14) days after CR initiation, 2 patients required an intravenous hydration and 20 had an additional enteral support. The nutritional status improved: albumin (33.1 ± 5.1 g/L *vs* 28.4 ± 6.5, $p < 0.001$), NRI (decrease of the number of patients at risk of severe malnutrition from 22 to 10 ($p < 0.001$)). The number of patients who had one or several liver tests abnormalities (>2 N) decreased from 94 to 41% ($p < 0.001$).

Conclusion: When the efferent part of the small bowel is accessible, CR is a safe and inexpensive method that restores bowel function. In most cases, it makes it possible to stop PN and helps to improve the nutritional status until surgical reconstruction.

1. Introduction

Entero-cutaneous fistula (ECF) is defined as a communication between the gastrointestinal tract and the atmosphere. Entero-atmospheric fistula (EAF) is a clinical form of ECF in which the small intestine is exposed as a stoma, most often through a loss of substance in the abdominal wall. Spontaneous closure is considered impossible [1]. The therapeutic management of EAF is often very challenging and is associated with a prolonged stay in surgical or intensive care units until the surgical restoration of intestinal continuity. Up to 75–80% of fistulas develop after surgery (anastomosis leakage or bowel injury) [2]. In other cases, fistulas occur spontaneously in the setting of radiation enteritis, malignancy or inflammatory bowel disease. Although the outcome of EAF has improved over the past decades due to advances in nutrition and in the management of sepsis, mortality and morbidity are high with reported mortality ranges from 6% to 33% [3]. There is consensus on the need to treat infections and to develop an aggressive nutritional therapy. Some acronyms summarize these guidance principles: the six points of the S.O.W.A.T.S

Abbreviations: ECF, entero-cutaneous fistula; EAF, entero-atmospheric fistula; PN, parenteral nutrition; CR, chyme reinfusion; IF, intestinal failure; IF2, type 2 intestinal failure; IVS, intravenous support; FE, fluids and electrolytes; NRI, nutritional risk index; CNDA, coefficient of nitrogen digestive absorption; CFDA, coefficient of lipids digestive absorption.

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[4] guidelines proposed by the Maastricht group (Sepsis control, Optimisation of nutritional status, Wound care, Anatomy of the bowel and the fistula, Timing of surgery, Surgical planning) or the S.N.A.P. strategy from the Salford Unit in UK (Sepsis, Nutrition, Anatomy, Plan) [5]. This strategy aims to decrease mortality, optimize local and systemic conditions to promote successful surgical treatment and avoid post-operative recurrence, insofar as mortality rate of these surgical procedures is high compared to other elective surgical procedures [6].

Defined by daily digestive losses equal or above 500 ml, high output EAF are complicated by a greater mortality than low output fistulas [7]. They behave like type 1 short bowel syndrome of the anatomical classification [8]. They may be responsible for intestinal failure (IF), defined as a "reduction of gut function below the minimum necessary for macronutrients absorption and/or water and electrolytes, such that intravenous supplementation is necessary to maintain health and/or growth" [9].

In case of EAF, the intestinal failure is type 2 (IF2), which corresponds to a prolonged acute condition, often in metabolically unstable patients, who require complex multidisciplinary care including active nutritional management and complex wound care, until the surgical repair. It is generally not recommended until 3–6 months after the initial surgery [2,4,10], although the optimal timing of the reconstructive surgery is not clearly defined [11]. During this period, nutritional therapy is a challenge because enteric fluid losses result in malnutrition and electrolyte disorders. Parenteral nutrition and/or hydration support (IVS) remain the gold standard treatment for the compensation of fluids, electrolytes and nutrients losses. However, when the downstream efferent segment of the small bowel is accessible and present intact intestinal absorptive capability, chyme reinfusion (CR), a technique that restores artificially digestive continuity by an extra-corporeal circuit of the chyme, may be an alternative to parenteral nutrition (PN) after the initial period of resuscitation. Because it is safe and inexpensive compared to parenteral nutrition, ASPEN [12] and ESPEN [13] now mention chyme reinfusion and distal feeding by "fistuloclysis" (administration of enteral nutrition in the efferent limb of the small bowel fistula) among the treatment strategy [14–17]. However, despite being developed in the late 1970's [18], chyme reinfusion is not a widespread technique and literature data are limited [19]. To our knowledge, only a few series or case reports focused on chyme reinfusion in the indication of EAF [20–23].

We report our experience of CR in the indication of EAF through a retrospective study of 37 patients on nutritional status improvement, liver tests and parenteral supports weaning.

2. Materials and methods

2.1. Population

Our department is a tertiary centre specialized in digestive and nutritional rehabilitation, including intestinal failure. All patients admitted for a high output EAF on the small bowel with at least 2 orifices visible within an abdominal wall dehiscence are considered for CR if they require IVS and if they are stable haemodynamically with no sign of sepsis. The indication of CR generally corresponds to a fistula output of at least 1200 ml/24 h. Abcesses contraindicate CR if they result from a fistula or if they are responsible for transit disorders or ileus. Other inclusion criteria were absence of progressive peritoneal carcinosis, agreement of the patient to carry out CR and to accept blended food.

We classified the fistulas according to their presentations on the abdominal wall as following: fistulas with everted hole as a loop ileostomy or fistulas with separated orifices.

2.2. Methods

2.2.1. Chyme reinfusion

Continuous CR was performed with specific peristaltic pumps and probes. The automate (Enteromate II® Labodial 78,340 Les Clayes sous Bois, France) and the portable pump (Enteromate portable) are able to operate 24 h a day for several weeks. They allow the extracorporeal circulation of the chyme, in a close system reduced to a probe, from the collection bag to the reinfusion probe, without manipulating it. Jejunal chyme was continually aspirated from the collection bag using a peristaltic pump and infused into the diverted downstream small bowel. The dead space of the extracorporeal circuit was lower than 50 ml and did not cause any volemic deprivation. We followed our "clinical pathway", a protocol that describes all the steps involved in conducting and monitoring a CR, for all professionals involved, from admission to return home.

2.2.2. Levin tube placement and preparation of CR

In order to start CR, a flexible F14 to 16 Levin feeding tube without balloon, made of thin-walled, high-caliber polyurethane was inserted in the efferent limb of the fistula for 15–20 cm. Placement of the tube and absence of abnormality of the distal part of the small bowel was checked by a contrast radiologic examination with 50 ml of an iodized contrast solution. It was used to estimate its length, evaluate its motor function, check the emptiness of the colon, and look for stenosis and fistulas.

Once the tube was inserted and the radiological control performed, we stopped antidiarrheal drugs and we infused 1000 ml of an oral rehydration solution with 10 or 20 g of macrogol to remove any stool residues or fecaloma, and antibiotic decontamination (one colimycine dose in the hydration mixture). The solution was administered by an enteral feeding pump at a maximum low rate of 50 ml/h, during one day, to be renewed if necessary or supplemented by an enema. We checked that it did not trigger pain or fever. Then we started CR.

2.2.3. Nutrition and drugs

All oral solid food was pureed to avoid clogging the tubing. When necessary, additional enteral nutrition was provided through a naso-gastric, gastrostomy or jejunostomy tube if present or "en Y″ in the CR probe. IVS were decreased or stopped based on inlet-outlet balances, diuresis and weight monitoring. Delayed or extended-released drugs have been avoided and replaced by their adapted galenic equivalent. If necessary, they were inserted into the downstream "en Y″ probe (e.g. laxatives).

2.2.4. Data collection

The clinical and biological data were collected prospectively and recorded in a specific Access database registered at the French Committee for Computing and Freedom CNIL (N° 1452427).

Height and weight were measured at admission; then, weight was measured twice a week during the hospitalization. Body mass index (BMI = weight [kg]/height [m]^2), weight loss at admission as compared to usual weight (100*(usual weight-actual weight)/usual weight) and Nutritional Risk Index (NRI = 1.519*Alb+41.77* weight/usual weight) where Alb was plasma albumin concentration, were calculated. Severe malnutrition risk was defined as NRI<83.5, moderate malnutrition risk as 83.5 ≤ NRI≤97.5, and absence of malnutrition risk as NRI>97.5.

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Oral intakes were quantified twice a week using Nutriciel® software, which calculated nutritional intake (energy, proteins, carbohydrates, lipids) from meal orders and actual ingesta from visual estimates of serving sizes consumed. Urine and fistula outputs were quantified daily. During CR, anal stools were weighed daily during the first 3 or 4 days; after the initial period they were weighed only when their number was ≥3/day. In practice, the patient is invited to have a bowel movement on a commode chair, whose collection bucket is covered with a garbage bag (waterproof and very light). The patient throws the toilet paper in a garbage can (or in the toilet) and not in the bucket. The stools of the 24 h are thus collected (a lid on the bucket limits the diffusion of odours).

Blood samples were collected for all patients at their admission, before initiation of CR and repeated during CR at the discretion of the prescriber according to clinical evolution. The biological tests were carried out by the same laboratory. Plasma values of liver tests, i.e. alanine amino-transferase (ALAT), aspartate amino-transferase (ASAT), alkaline phosphatase (AP) and gamma-glutamyl-transpeptidase (GGT), higher than two times the normal values were considered as increased. When possible, intestinal nitrogen and fat outputs were measured over three consecutive days, before the initiation of CR, and at least three weeks after CR initiation. Nitrogen and fat faecal concentrations were measured according to the Kjeldahl's [24] and the Van de Kamer's [25] methods, respectively. Nitrogen and fat fecal outputs were expressed as the mean daily nitrogen or fat fecal outputs in g/day. Contemporary oral protein and fat intakes were determined using Nutriciel® software. Nutritional food intakes (oral, enteral and parenteral) were expressed as kcal/kg actual body weight/day and g/kg actual body weight/day for energy and protein, respectively. The coefficients of nitrogen (CNDA) and fat (CFDA) digestive absorption were the proportion of ingested protein and fat not recovered in the stools, and were calculated as: CNDA = (1-(intestinal nitrogen (g/day)/protein intake (g/day)/6.25)*100 and CFDA = (1-(steatorrhea (g/day)/fat intake (g/day))*100. Values higher than 85% were considered as physiological.

From 2008 onwards, fasting plasma citrulline concentration was determined simultaneously with the CNDA and CFDA within the three days before and after CR initiation. Simultaneously, creatinine clearance was calculated with the Cockcroft's formula for 1.73 m^2 because alteration of renal function prevents from interpreting plasma citrulline. Plasma citrulline concentration was determined using reverse-phase high performance liquid chromatography (HPLC). As Crenn et al. [26] showed that a plasma citrulline below 20 μmol/l was predictive of IF, we choose this threshold to define a low plasma citrulline.

The location on the jejunum or ileum and the length of the intestine upstream were determined mainly by the surgeon's report, the clinical history and the imaging. The length of the intestine downstream was estimated on radiological opacification x-ray images by estimating the distance between two flexions at 30 cm and using the length of the catheter introduced into the intestine. The sum of the lengths of the upstream and downstream intestinal segments was done if both data were known.

2.2.5. Statistical analysis

Statistical analyses were performed with Excel spreadsheet program and Statistical Tools For High-Throughput Data Analysis (http://www.sthda.com/). The durations were expressed as median (interquartile ranges 25%–75%). Alb, citrulline, NRI, liver tests before and during CR, were expressed as mean ± SD and compared by paired Student's t test and distribution of malnourished patients by Chi2 test.

2.2.6. Ethical statement

This work was conducted in accordance with the declaration of Helsinki.

3. Results

3.1. Patients recruitment and characteristics

From 1993 to 2017, according to the inclusion criteria, 66 consecutive patients had EAF. We excluded 16 in whom the downstream segment was not accessible, 3 because the downstream intestine was only colon, 4 because of a flow rate <1200 ml/24 h initially or becoming so under CR, 2 because of the worsening of the parietal wound condition after 3 days. Four patients had started CR and had to stop it due to a pathology on the downstream segment not diagnosed in the initial imaging (ileal stenosis 1, colorectal stenosis 1, fistula on the downstream segment 2). The remaining 37 patients were included (Fig. 1). All patients had EAF located on the small intestine. We included a patient who had a fistula of the 2nd duodenum upstream of a complete obstacle, drained by a large Pezzer tube, the CR being performed in a jejunostomy.

Demographics and aetiology of small bowel resection are summarized in Table 1.

3.2. Surgical procedure and subsequent small bowel anatomy

Most frequently, fistula occurred in the setting of an emergency surgery for perforation. No fistula occurred spontaneously, all were postoperative. Nineteen patients had undergone colonic or rectal resection, among them 7 with a terminal ileostomy; 6 had undergone an upper digestive tract surgery. EAF were mainly (n = 30, 82%) due to peritonitis and mechanical occlusion. In both cases, volvulus in wall hernias or perforations on parietal prosthesis material are frequent aetiology (n = 12/30). One patient had a postoperative recurrence of EAF and was treated with CR for both periods (Table 2).

Most fistulas (78%) were located on the jejunum, only one patient was treated by CR for a duodenal fistula. Twelve patients have had a small bowel resection during a previous surgery or during the surgical procedure that led to the fistula. The downstream intestinal segment was amputated in 19 patients who had undergone colonic or rectal resection, including 7 with terminal ileostomy; 6 had undergone upper gastrointestinal tract surgery, 1 oesogastrectomy, 2 Finsterer gastrectomy for cancer, 3 gastric bypass.

The length of the upstream intestine was estimated in 21 patients: 19 had a bowel length <150 cm of which 16 had less than 100 cm. By adding the lengths of the afferent and efferent intestinal segments of the fistula, the total small bowel length was 224 ± 72 cm (data for 20 patients) of which 17 were greater than 150 cm and 3 between 100 and 150 cm. One patient had a jejunal fistula, an intermediate segment of more than 120 cm ending in a second ileal fistula. He was treated by a double jejuno-jejunal and ileo-ileal CR.

3.3. Intestinal function

CR increased the length of the functional intestine. It was associated with a dramatic improvement in intestinal function. The intestinal losses were reduced by 74% ($P < 0.000001$) and the number of patients with output higher than 1000 ml/24 h decreased from 35 (97%) to 3 (8%) ($P < 0.0001$). CNDA and CFDA were measured before and after CR initiation in 10 and 5 patients, respectively. Intestinal nitrogen absorption improved by 81%, lipids absorption by 103% and steatorrhea decreased by 78%. The number

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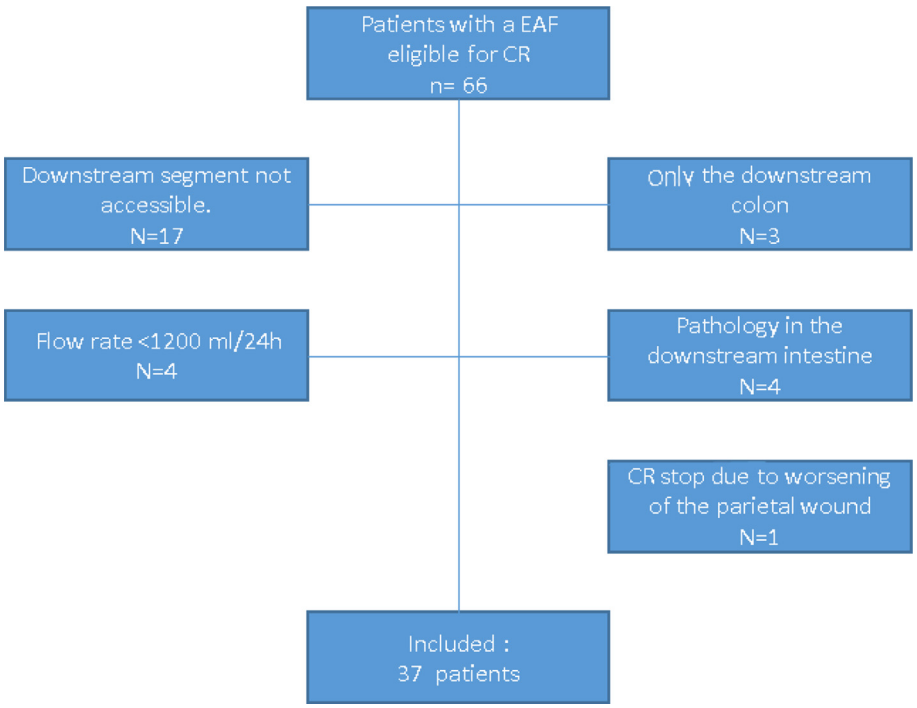

Fig. 1. Study flow chart.

Table 1
Patients' demographics and aetiology of entero-atmospheric fistulas (n = 37).

Male/female - n	26/11
Age - mean ± SD (range)	65.0 ± 12.3 (30–98)
Aetiology of small bowel resection – n (%)	
Cancer	6 (16)
Mechanical occlusion	12 (32)
Peritonitis	18 (49)
Trauma	1 (3)

Table 2
Surgical procedure and subsequent small bowel anatomy at admission.

Localization jejuno-parietal n (%)	29 (78)
Localization Ileo-parietal n (%)	8 (22)
Enterostomy like a loop stomy n (%)	29 (78)
Separated double end stomies n (%)	8 (22)
SB resection ≥30 cm – n (%)	12 (32)
Resection SB length (cm) (n = 12)[a]	58 ± 54
Afferent SB length (cm) (n = 21)[a]	66 ± 49
Afferent SB length <100 cm – n (%/21)	16 (76)
Efferent SB length (cm) (n = 28)[a]	133 ± 80
Total SB length (cm) (n = 20)[a]	224 ± 72
Total SB length <100 cm – n (%)	0 (0)
Downstream SB anatomy – n (%)	
Ileo-colon	23 (62)
Terminal ileostomy	8 (22)
Ileo-rectal anastomosis	1 (3)
Terminal colostomy	5 (14)

[a] Mean ± Standard Deviation. SB, small bowel.

of patients with plasma citrulline <20 μmol/l decreased from 10 (71%) to 3 (14%) (P < 0.00005) (n = 14) (Fig. 2).

3.4. Nutrition

At admission, 28 (76%) patients received PN (n = 25) or IV hydration without nutrients (n = 3). IVS are classified in Table 3 according to the ESPEN Clinical Classification [9].

The other 9 patients without IVS had a fistula flow rate of 1661 ± 495 ml/24 h. They displayed characteristics of IF2 and should have required nutritional IVS. Mean (±SD) energy and protein PN intakes were 23.9 ± 8.5 kcal/kg/day and 1.01 ± 0.39 g/kg/day respectively, in a mean volume of 2044 ± 917 ml/day.

During CR, mean energy and protein oral intakes were 22.4 ± 11 kcal/kg/day and 0.97 ± 0.43 g/kg/day, respectively. An additional enteral support was needed in 20 (59%) patients ("en Y" enteroclysis, n = 11; nasogastric tube, n = 7; gastrostomy, n = 1; jejunostomy, n = 2), for a complementary intake of nutrients and hydration or hydration alone (n = 1). The total mean amounts of energy and protein oral and enteral intakes were 31 ± 10.3 kcal/kg/day and 1.41 ± 0.47 g/kg/day. Parenteral nutrition was stopped in all patients, within a median (IQ25%-75%) of 3 (0–14) days after CR initiation. Two patients required an intravenous hydration IVS FE1 type without nutrients because of the of a high output terminal enterostomy at the end of the lower segment.

Therefore the median (IQ) time with saved PN was 78 (52–102) days per patient. The presumed cumulative number of days with saved PN was 2183 patients-days (or 6 patients-years).

3.5. Nutritional status

At admission, a majority of patients had one or several criteria of malnutrition (Table 4). Weight loss from usual weight was greater than 15% in 28% of patients, between 10% and 15% in 27%, between 5% and 10% in 15%. Overall, the weight did not change significantly during CR. However, when the BMI was initially less than 20, it increased by 2.4 ± 0.8 (p < 0.0003) and decreased by 2.0 ± 0.1 (P < 0.002) when it was initially greater than 30. Hypoalbuminemia <30 g/l was present in 23 patients (62%) before CR, in 23% during CR. However, the low albuminemia rate should be interpreted in relation to the CRP, which is higher at the beginning (45.5 ± 44.5 mg/l) than at the end (11.6 ± 11.7 mg/l, P < 0.00025). CR has been associated with improved nutritional status and an increase in NRI of 8.0 ± 10.0 (P < 0.0000007).

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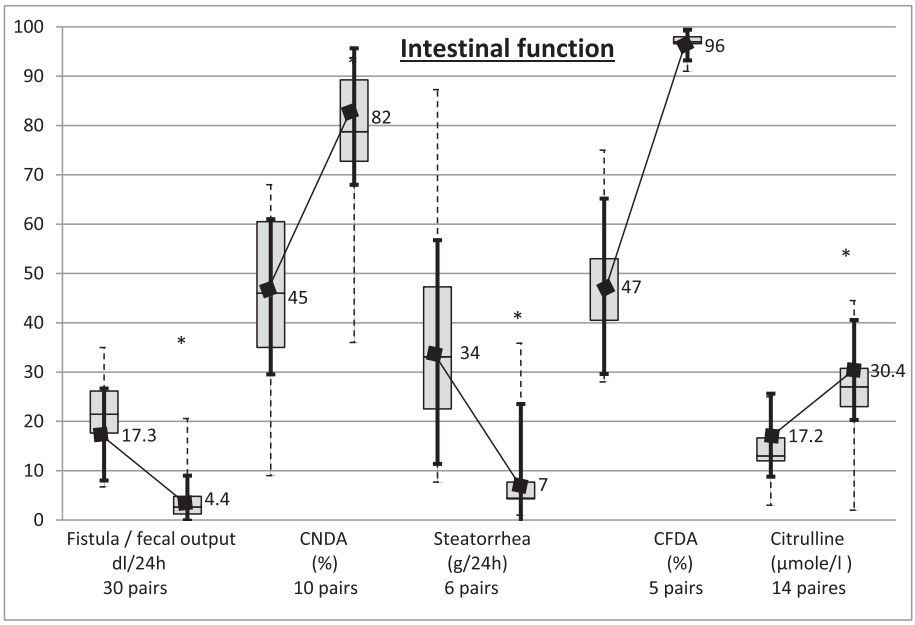

Fig. 2. Effects of chyme reinfusion (CR) on intestinal absorption measured before CR initiation (left boxes) and at discharge (right boxes). Fistular (before CR) and fecal outputs (during CR) are expressed as dl/24 h. Coefficient of nitrogen digestive absorption (CNDA) = (1-(intestinal nitrogen/nitrogen intake))*100. Coefficient of fat digestive absorption (CFDA) = (1-(intestinal lipids/lipid intake))*100. Values are presented as mean (square points), SD (vertical solid bars), quartile 2 and 3 (shaded squares), median (horizontal bar in the shaded squares), extremes (vertical dashed bars). n, number of patients measured twice: before CR and at discharge. ***P < 0.001.

Table 3
Repartition of patients according to the ESPEN clinical classification of intravenous support.

Volume of IVS (ml/day)	<1000	1001–2000	2001–3000	>3000
Type of IVS	1	2	3	4
FE: Fluids and electrolytes	2 (7)	1 (4)		
PN: Parenteral nutrition	3 (11)	12 (43)	4 (14)	6 (21)

IVS: Intravenous support. Results are expressed as n (%).

3.6. Plasma liver tests

Plasma liver tests were performed both before and during CR in 34/37 patients. At admission, 32 (94%) patients had one or several abnormal plasma liver tests (>2 N): ALAT (n = 10, 29%), ASAT (n = 2, 6%), AP (n = 17, 59%) and GGT (n = 22, 65%). With CR, the number of patients who had one or several plasma liver tests abnormalities decreased from 94 to 41% (P < 0.0001) (Fig. 3).

3.7. Evolution

Median delay (IQ 25–75%) between the surgery leading to EAF and admission in our centre was 39 (25–65) days. After admission CR was begun in a median delay of 9 (4–15) days and for a median duration of 89 (58–139) days. The date of end of CR corresponds to the date of the reconstructive surgery. Because of the complexity of wound care, only one patient could return home.

One patient closed the fistula without surgery. One patient died of lung metastases. The other 35 were operated on to restore intestinal continuity. The length of stay in surgery unit was 15 (11–21) days, known for 25 patients. The consequences of the surgery were simple in 20 patients. Complications were fistula recurrence (n = 7), death (n = 3) and other complications (n = 4). A patient has been lost to follow-up.

4. Discussion

The incidence of high throughput EAFs >1200 ml/d or IF2 due to EAFs is certainly less than $10/10^6$ inhabitants/year. EAF requires costly, complex care and prolonged hospitalization. Surgical restoration of continuity is rarely indicated within 6 months of its occurrence. PN is the reference treatment to compensate for intestinal failure, supported by a very abundant literature, protocoled for hospital and home care, covered by health insurance. In many countries, it is inaccessible for economic and dangerous reasons due to a lack of sufficient expertise in hospitals and at home [27].

CR is an enteral nutrition technique developed by Dr. Etienne Lévy in the 1970's [28]. It allows the use of the entire anatomically

Table 4
Evolution of nutritional status between admission (before CR initiation) and discharge (during CR).

Parameters	Before CR	After CR	P value
Weight loss (%)#	10.9 ± 8.4 (0–28)	9.7 ± 9.1 (20–42)	<0.001
Body mass index#	25.5 ± 6.7 (15.0–40.6)	26.1 ± 5.2 (19.3–37.8)	<0.001
Plasma albumin (g/l)#	28.4 ± 6.5 (11.4–44.0)	33.1 ± 5.1 (23.7–41.8)	<0.001
Plasma albumin <30 g/l	23 (62)	9 (24)	<0.001
NRI#	79.8 ± 11.7 (47–108)	88.1 ± 8.9 (70–106)	<0.001
NRI <83.5	22 (67)	10 (30)	
83.5 ≤ NRI≤97.5	9 (27)	19 (58)	<0.001
NRI >97.5	2 (6)	4 (12)	

Results are expressed as n (%), except# mean ± standard deviation (range). Nutritional risk index (NRI) is calculated as: 1.519*plasma Albumin +41.77* weight/usual weight. Malnutrition risk is classified by categories: severe (NRI<83.5), moderate 83.5 ≤ NRI≤97.5 and low (NRI>97.5).

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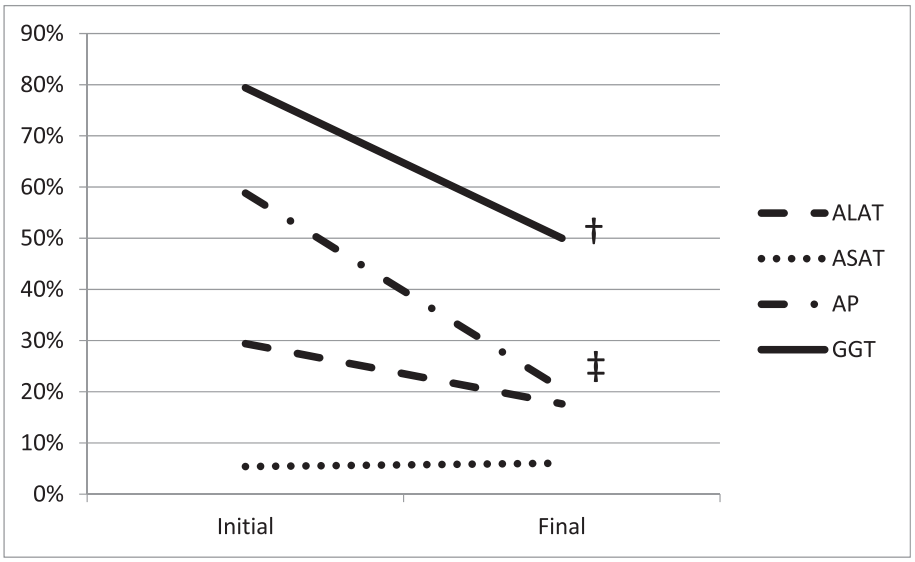

Fig. 3. Evolution of the percentage of patients with plasma liver tests abnormalities defined as higher than two times the normal values between admission (before CR initiation) and discharge (after CR initiation) (n = 34). †P < 0.02; ‡P < 0.001.

present intestine to benefit from all absorption functions and exocrine and endocrine secretions. There are very few publications on the subject [29], none of which compare CR methods with PN. CR is most often obtained by diverting existing equipment from its normal use, in a craft project that is not reproducible by other teams. To our knowledge, we are the only ones using pumps designed exclusively for CR (Enteromates).

After treatment in intensive care units and pending surgical restoration of continuity, patients with EAF are referred to tertiary centres in which multidisciplinary teams have expertise and validated care protocols. Hospitalizations are often long. In our digestive and nutritional rehabilitation unit, the medical team is composed of gastroenterologists, medical nutritionists and ultrasound radiologists. The surgical team specialized in small bowel surgery is accessible in a few minutes. The nurses have experience with stoma care. In our practice, any patient with high output EAF is a candidate for a CR, a priori, unless contraindicated or impossible. We note that most EAF can have a CR.

The output of an EAF is very variable in the nycthemeron, filling the pouch in a few minutes after meals and practically nil at night. A pump is necessary to replicate these physiological variations in flow, in the downstream intestinal segment, and anticipate the physiology of the intestine as it will be after the continuity restoration. However, CR is not sufficiently used because the lack of specific equipment [19].

In many publications, the chyme is collected in a container close to the patient, sometimes refrigerated, sieved, and then injected again with a syringe or enteral nutrition pump in the downstream segment. These disgusting manipulations and the smell of vomit discourage caregivers and many teams have abandoned CR after some experiments. Our method avoids any manual contact, odours, external microbial contamination and does not cause any volume deprivation. The fear of a microbial overgrowth in the chyme during its extracorporeal passage is theoretical: the outside temperature is lower than the body temperature and the time spent outside the body is brief. The concentration an average of bacteria in the reinfused fluid is low and don't justify to sterilize the stoma effluent before reinfusion [30]. Neither we nor the teams that performed CR reported any infectious diarrhea.

The pumps must be designed for CR and only be used for this purpose. The diversion of enteral nutrition pumps is inappropriate: the motors are not strong enough, the alarm systems are difficult to disengage and the tubes are too thin. A reinfusion pump must have a powerful motor and use 14 to 16 FR tubes, and be able to operate 24 h a day for several weeks. They must be portable, i.e. equipped with batteries, so that the patient can leave the room for several hours without interrupting CR or even returning home. The flow rate must be adjustable by an automated system or manually, at any time of the day and in the simplest possible way.

For the downstream tube, we use tubes without balloon. Foley's urinary catheters have a very small internal diameter compared to the external diameter. The distal orifice is often blocked if it has not been previously enlarged with scissors. The inflatable balloon up to 25 ml (diameter >4 cm) obstructs the small intestine to prevent reflux, but the downstream intestine may not tolerate high pressure. The excessive volume of the balloon in relation to the diameter of the small intestine can create ischemic lesions of the mucosa and then scar stenosis. Gastrostomy tubes inflated to a maximum of 5 ml are not occlusive and reduce reflux, the terminal orifice is in the axis of the tube, less susceptible to obstruction. The reflux of the reinfused chyme is natural during the first few days, until the effects of antidiarrheal drugs disappear and normal motor function of the downstream intestine is restored. The liquid that flows back into the bag is itself reinfused.

The stoma care requires a highly experienced nursing team. CR complicates the installation of the collector bag a little, but does not reduces its adhesion to the wall, perhaps on the contrary, due to the permanent vacuum provided by CR pump. The collection bag must be hermetically sealed. The air in the bag must only be the air swallowed by the patient. When there are several fistulas with four or six intestinal orifices and one or two intermediate intestinal segments, the intermediate segment is reinfused if it is long enough.

Nutrition has made a significant contribution to reducing mortality in EAF patients. Pureed feeding is not very greeding and patients may be discouraged. The role of the dietician is important, in conjunction with the cooks. A list of foods and recipes were developed, enriched by the experience of patients who had a CR at home. Oral feeding can be restarted as soon as possible, even if this increases the flow of the fistula. A complementary enteral nutrition improves the percentage of nutrients and energy absorbed in short bowel syndrome [31]. In our study, oral feeding alone was sufficient

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in 17 patients (46%). The other 20 received an enteral nutrition during the night, most often "en Y" in CR tube, when the ingesta was insufficient or in case of residual malabsorption. CR is usually immediately effective and reduces intestinal losses by one to several litres. It is necessary to proportionally reduce or stop the IVS to avoid accidents of volemic overload.

5. Discussion of the results

The measurement of CNDAs and CFDAs requires stool collection for three consecutive days and contemporary evaluation of ingesta. During the CR, it was only used in cases of diarrhea or suspicion of residual intestinal deficiency. The improvement in intestinal absorption, when measured, is dramatic. This is mainly due to the increase in active enterocyte mass as evidenced by the increase in citrulline [32]. Parenteral nutrition was stopped in all patients. This is one of the effects that all authors who practice CR have observed. Even if the downstream small intestine is short, CR improves intestinal functions. The ileal part of the small intestine is more adaptable than the jejunal part. The colon improves the digestive utilization [33–35]. CR restores the enterohepatic cycles of many nutrients and certain drugs and mainly that of bile salts, which reconstitutes their pool with a putative effect on the restoration of the ileocyte production of FX19, a messenger that inhibits the hepatic hypersecretion of bile salts [36]. CR stimulates the secretions of entero-hormones from ileocolic L-cells (GLP1, GLP2, PYY …) which have an effect on motor skills, trophicity, absorption capacities of the upstream gastrointestinal tract.

The improvement in nutritional status is particularly marked in initially malnourished patients. A low preoperative albumin concentration (<25 g/L) is related to increased postoperative mortality [11]. Disruptions of liver enzymes are almost constant and, like other authors [23], the improvement of abnormalities or their disappearance is observed in most patients. Improving liver function can help to restore protein anabolism and optimize nutritional status.

Reducing PN requirements is observed by all authors. IVS are stopped in 90% of patients, with variable delays or at a lower level in the clinical classification of the ESPEN. In our series, none of the 25 (89%) patients had PN-IVS during CR and only 2 had FE1-IVS. In 2013, in England, in patients with IF2, the monthly cost of IVS has been estimated at between 5000 and 10,000€ [37]. PN is only routinely and safely practiced in hospitals and at home in rich countries. CR is much cheaper. There is a strong expectation of validated practical CR solutions in developing countries where, Nagar writes "parenteral feeding is not only expensive and difficult to maintain, but in our experience, most patients develop severe sepsis within 3 weeks of their insertion" [38]. In Coetzee's work [27], 18 had septicemia episodes related to central lines in the control group of 22 patients. In the absence of a PN control group, cost savings cannot be measured. Closure of high output EAF is exceptional but reducing fistula flow is possible. Adding a complement of enteral nutrition in the downstream bowel can reduce IVS needs [17,18]. Had IVS needs not decreased, the theoretical maximum number of IVS days saved by the CR would have been 2183 days, time from IVS weaning to corrective surgery. We have estimated the daily cost of CR at 34.8€/day/patient in our unit. In 2000, Pichard et al. measured the cost of PN in hospital at 100€/day/patient [39].

CR anticipates postoperative complications of digestive continuity restoration that can be treated or prevented. This is an important quality advantage. In some patients, the surgical strategy to restore continuity has been modified (stenosis, fistula) or rehabilitation has been undertaken (anal incontinence).

6. Conclusion

CR is a logical, inexpensive and safe treatment that restores intestinal function in patients with high output EAF. The improvement of the nutritional state, the correction of liver test abnormalities, the complete weaning or the drastic reduction of IVS requirements, thus complications of the central venous line, are observed by all authors. The ESPEN and ASPEN working groups recommend that CR be attempted whenever possible. Due to the lack of suitable equipment, CR is very rarely used and the multiple methods described are not easily reproducible and require discouraging manipulations. There is a great demand for equipment specifically designed for CR.

Statement of authorship

Study concept: Layec, Picot.
Acquisition, analysis, or interpretation of data: all authors.
Drafting of the manuscript: Layec, Picot.
Critical revision of the manuscript: all authors.
Statistical analysis: Picot.

Conflicts of Interest

None for any of the authors.

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