Journal of Surgery
Chiaretti M, et al. J Surg 7: 1525
www.doi.org/10.29011/2575-9760.001525
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Case Report

Enterocutaneous Fistula Management and Clinical Nutrition in Sepsis of Abdominal Wall Incisional Hernia. Tips, Tricks and Literature Revision

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Citation: Chiaretti M, Mascolo P, Oricchio D, Frattaroli FM, Alunni Fegatelli D, et al. (2022) Enterocutaneous Fistula Management and Clinical Nutrition in Sepsis of Abdominal Wall Incisional Hernia. Tips, Tricks and Literature Revision. J Surg 7: 1525. DOI: 10.29011/2575-9760.001525

Received Date: 29 June, 2022; **Accepted Date:** 08 July, 2022; **Published Date:** 11 July, 2022

Abstract

Background: The Enterocutaneous Fistula (ECF) treatment requires a multidisciplinary approach and high costs, and shows critical morbidity and mortality rates. For these reasons, it is one of the most challenging problems in colorectal and incisional hernia surgery.

Methods: This article synopsizes the current classification systems' successful management and provides an in-depth review of septic source surgical control, Clinical Nutrition, Hyper Baric Oxygen Therapy (HBOT) and negative pressure (VAC), output quantity management, wound care, operative timeline, and considerations such as Inflammatory Bowel Disease (IBD), and Enteroatmospheric Fistula (EAF).

Result: We report a 71-year-old septic fistulated male with an incisional hernia, and chronic medullary dysplasia. This study compares our results with the literature. This case concerns a very complex and long-lasting clinical scenario because of erythropoietic and immunity systems default that led the patient to death. The use of negative pressure therapy to manage abdominal fistula is still controversial. Patients suffering from enterocutaneous fistula require adequate nutritional support to fight hypercatabolism due to the fistula's inflammation, fluids, proteins, and salts loss.

Conclusions: An aggressive multidisciplinary approach, including prosthesis explantation are needed. Clinical nutrition starts with TPN (Total Parenteral Nutrition) followed by EN (Enteral Nutrition) as soon as possible. Moreover, VAC and HBOT therapies are useful to treat this life-threatening condition.

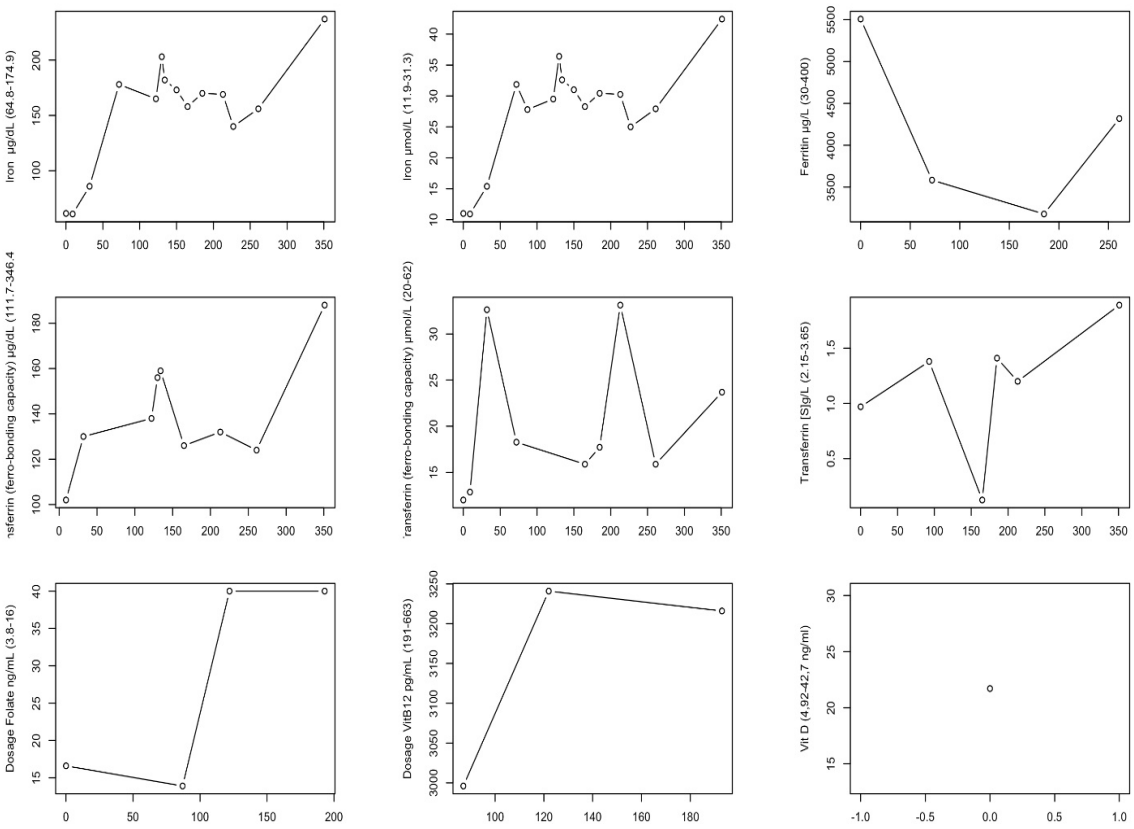
Keywords: Enterocutaneous fistula; Enteroatmospheric fistula; Prosthetic incisional hernia complications; Spontaneous fistula closure, EN, HEN, HPN

Introduction

The Enterocutaneous Fistula (ECF) is an unnatural connection between the gastrointestinal tract lumen and the skin, frequently associated with intra-abdominal abscesses. The Enteroatmospheric Fistula (EAF) is an unnatural connection between the gastrointestinal tract lumen and the wound [1]. It represents a fistula with an external opening in an open wound or directly exposed bowel [2,3]. The ECF represents a significant challenge for the General and Laparoscopic Surgeons for electrolyte, liquid, and protein loss and intestinal failure (IF), systemic sepsis, and Multi-Systems Organ Failure (MSOF) risk. There are many classification systems: 1) The output volume quantification is a prognostic data predicting the likelihood of closure and planning therapy type to follow [4-8]. Daily output could be high (more than 500 ml/day), moderate (200-500 ml/day), or low (less than 200 ml/day); 2) Etiologic classification distinguishes among spontaneous fistulation occurred (between 15 and 25%), and iatrogenic (75-85%). 3) The origin of fistula or location is a classification used for ECF and distinguishes in high/proximal, and low/distal, referred the Treitz angle along the gut: type I (esophageal, gastroduodenal, abdominal), type II (small bowel), type III (large bowel), and type IV (enteroatmospheric, regardless of origin) [5-8]. 4) The number of fistulas (single, multiple). 5) Based on clinical evolution, the ECF classification distinguishes three types of fistulation: Type 1 is self-limited, usually lasting around 28 days after the acute condition; Type 2 has a longer duration, and it is secondary to abdominal surgery and diagnosed in critical patients with multiple fistulas and metabolic instability that needs multidisciplinary and artificial nutritional support, prolonged recovery, long-lasting waiting for the spontaneous resolution of attempting surgery. Literature on ECFs' conservative treatment is successful only 33% [9,10]. Most of these patients' risk is progressing toward chronic and Type 3 diseases. The Type 3 consists of a chronic intestinal failure, which is a condition causing severe impairment of intestinal functions and needs long-term total parenteral nutrition at home to provide adequate nutritional support. The etiology of traumatic fistulation could be a gunshot, blade wound, iatrogenic anastomotic leak, and accidental injury for adhesiolysis. Spontaneous fistulae etiology could be the IBD (Inflammatory Bowel Disease), one of the most common causes, and foreign body (prosthesis implantation). Furthermore, other causes are inflammatory erosion, diverticular perforation in the diverticular disease, ulcerative cancer fistulation, appendicitis, and a radiotherapy treatment complication, and gut tuberculosis, or ischemia [6]. Moreover, intestinal infections such as typhus, actinomycosis, Klebsiella kpc, and resistant Gram-negative could be involved [11-13]. Furthermore, it can be either the evolution of a Type 2 ECF or the result of an IBD after multiple bowel resections. In this case, intestinal transplantation should be evaluated [14]. If Type 3 ECF is irreversible, it is necessary to train the patient and his/her family in home Total Parenteral Nutrition (HPN) management with help of home and community Nurses. If the disease is due to a benign condition, the survival average is 80% in adults and 90% in children [13]. These percentages drop with comorbidities [15]. The principles of ECF management are sepsis control, and patient's general and nutritional status improvement. Gastrointestinal anatomy should be precisely determined, and surgical closure postponed by at least six months if possible. Relaparotomy, viscerolysis, intestinal resection, and anastomosis are technically demanding procedures for the patient and supporting team, not so well emphasized in specialized literature. This challenge item we can face with a multidisciplinary and proven staff, including a nutritionist, infectious disease specialist, radiologist, and physiotherapist. Furthermore, hematologists (for clinical cases such as this one), enterostomal therapy nurses (ET nurse is a registered nurse RN, enterostomist), and abdominal surgeons are also needed. Moreover, family support is essential during the home step [16].

Frequently these patients are so impaired that they need to be transferred to a specialized center to treat bowel failure [13-18]. Nutritional disturbances in 50% to 90% of patients with ECF contribute significantly to overall morbidity and mortality [19,20]. "The challenge of caring for patients with ECF is not merely the management of the underlying conditions leading to ECF or the correct provision of appropriate nutrition (TPN or Enteral Nutrition NE) or both the prevention of complications, whether pulmonary thromboembolism (thrombosis of portal vein IF-associated to liver disease) or metabolic bone disease and central venous catheter-related bloodstream infection" [21]. This report looks at the role of the EN, "the multidisciplinary team, and novel therapies, including hormonal treatment" of ECF, but also surgical options [22]. "One of the most significant advances in the treatment of ECF was the development of TPN in the 1960s by Dudrik [23,24]. Although initial reports have shown a spontaneous fistula closure rate of up to 70% and mortality of 6% with intravenous feeding alone, these results are not replicated" [25,26]. In patients receiving nutritional support, the fistula closure rate is twice as likely to occur spontaneously [27,28]. For patients with long-lasting small bowel fistulas, additional copper, folic acid, and vitamin B12 may be useful, and trace minerals and vitamins A, D, E, and K, are needed [29]. Traditional surgical dogma based on early reports using overeating states that intestinal rest and TPN lead to a higher incidence of spontaneous closure of an ECF. The fundamental principle is the reduction of the gastrointestinal tract glands' secretions. Thereby, fistulas output reduction leads to faster healing [11]. The mean time for spontaneous closure of ECF in parenteral nutrition is 25-28 days (Type 1), although it can

take up to 12 weeks (Type 2) [9-11]. However, most of the studies in the literature involve heterogeneous patient populations. They are predominantly retrospective, making it difficult to compare the various studies and accurately predict the timing and rate of spontaneous closure [17]. The UK currently has two national bowel failure specialized units. Recent evidence suggests that these patients with bowel failure are managed better in regional units with a proven multidisciplinary team [18]. In Italy University Hospitals and, most important Regional Hospitals, bowel failure patients are hospitalized and managed in special units. In a limited resources hospital setting, it is important to consider the patient transfer to a regional center with expertise in ECF. Much controversy surrounds nearly every aspect of caring for these patients. The overall incidence of ECF is unknown [22,25]. The prevalence of case reports and case series is due to the scarcity of homogeneous patient populations and randomized clinical trials, making this situation unlikely to change soon. It is important to point out that ECF is associated with a significant risk of mortality, reported between 5% and 20%, with variability due to the heterogeneity of this cohort of patients. In addition to significant mortality rates, the morbidity associated with ECFs is excessive [30-32]. The cost to the National Health System and the psychological impact on the patient are difficult to quantify. However, data show a longer Intensive Care Unit (ICU) stay and higher hospital costs [33]. Literature emphasized TPN's role in the management of these patients. Bacteremia risk by CVC is high. The Enteral Nutrition (EN) treatment results are not well-known and popular among surgeons [22]. Insufficient evidence demonstrates that TPN is superior to EN in spontaneous closure rates. Concern that EN contributes to or worsens fistula production is probably unfounded [26]. EN has indeed demonstrated no infections and a lower rate of fistula formation in trauma patients well managed with an open abdomen [22,31]. For nutritional support in patients with ECF, EN should be the first choice unless there is a clear contraindication. Nutritional evaluation is assessed routinely by azoturia dosage, DEXA, and anthropometric measurements. Azoturia increases proportionally to muscular damage (sarcopenia). Azoturia excess is symptomatic of malnutrition because of a septic condition. For these reasons, artificial nutrition must be started or increased to contrast malnutrition by administering significant volumes of hydroelectrolytic solutions, colloids, albumin, amino acids, lipids, carbohydrates, vitamins, and trace elements. Albuminemia is a useful index in these patients with a prolonged half-life time of 3 weeks because of its size and FcRn-mediated recycling that prevents intracellular degradation, properties shared with IgG antibodies. On the other hand, transferrin, which has a serum half-life of 8 days, and promptly reports rapid changes, is used for evaluating these patients [23] (Graph 5A-I**)**. Decreased transferrin levels are associated with increased mortality and significantly lower rates of spontaneous fistula closure [32], indicating which patients will have a favorable outcome after surgical therapy [33] (Graph 5A-I**)**. This study compares our results with the specialized literature and gives tips and tricks employed in a long course of treatment in a heavily compromised patient. "This clinical case is reported in line with the Surgical CAse REport 2018 statement (SCARE)" [25]. In the present case report, we discuss multidisciplinary management and surgery, negative pressure therapy (VAC Therapy), and TPN, NE, and HNE in combination, with tips and tricks for the treatment of a patient with severe myelodysplasia and systemic and local septic disease, affected by chronic enterocutaneous fistula after surgery [34-39].



Graph 5: Study of the Iron Set-Up; A,B: Gradually decreasing sideremia for about 200 days until deterioration of erythropoiesis and resumption of blood transfusions. **C:** Gradually decreasing ferritin for about 180 days until deterioration of erythropoiesis and resumption of blood transfusions. **D-F:** Ferritin binding capacity gradually increasing for about 180 days until deterioration of erythropoiesis and resumption of blood transfusions. **G:** Fotale with a high compensatory dose. **H:** Vit B12 compensatory high dose.

Case Presentation

Seventy-one-old-years septic male patient, in 2005, January underwent a median xiphoid to pubis laparotomy for aneurysmectomy (a surgical procedure performed to repair a weak area in the Aorta, upper kidney arteries to bifurcation with common iliac arteries (aorto-peripheral bypass) and implantation of aorto-bifurcated Dacron woven prosthesis [22]. Moreover, the lower polar right kidney artery was reimplanted. In May 2005, the patient underwent a Rives operation. On 2005, August incisional abdominal hernia treatment is performed with prosthesis implantation. In 2006, February the patient underwent further reoperation because of the second recurrence treated with Gore-tex dual mash with holes mesh fixed with Prolene sutures repairing. Usually, the implantation of a foreign body, such as a surgical mesh, provokes an inflammatory response that delays the conversion of the third type (immature collagen) to the first type (mature collagen). Inflammation intensity (related to the mesh type and fixation method employed and possible wound infection) could significantly decrease the mechanical stability of the scar, causing inguinal hernia and incisional hernia formation [40]. In 2018 the patient was diagnosed with Myelodysplastic Syndrome (MDS) and treated with red blood cell transfusion every two wk. In May 2020, he was diagnosed with an extensive infection of the implanted prosthesis and was administered intravenous antibiotic therapy in a peripheral hospital. The patient was admitted on 2020 July 28th to the Emergency Department of the University Polyclinic Umberto I, the Sapienza University of Rome, for fever, chills, hot swelling at the touch, pain, bacteremia, and severe anemia. Anterior abdominal wall subfascial hematoma and extensive abscess collection were studied by ultrasound (US) localized around the implanted prosthesis and placement of drainage by interventional radiologists [21,41-43]. During the second week (wk), a radiologist performed a fistulography to highlight the course of the mesogastric fistula. Under local anesthesia, he applied a 12 Fr drainage under fluoroscopic guidance in the abscess. A sample for microbiological examination, followed by washing with saline solution, is performed. The procedure for a new

fluoroscopy check, and drainage repositioning by Seldinger (wired technique) and three washing with saline solution per day nurses performed. The small intestine CT scan localized an enterocutaneous jejunal fistulation at 90 cm forward Treitz's angle. Nasal, rectal, fistula ostomy, surgical wound swabs, urine cultures, blood cultures, and blood chemistry tests nurses performed. The hematologist knew this patient because he had been followed for myelodysplastic syndrome, for some years, in Outpatient Hematology Department. PLT 40,000 and low risk of evolution is the prognosis. Table 1 shows general conditions at the admittance. The wound's swab resulted in Enterococcus faecium. The CT scan with and without a contrast showed corpuscle collection with minimal blood component at the wall level in the mesogastric area, reduced in thickness but slightly increased in extension (anterior-posterior diameter: 51x67 mm, transverse diameter: 98x81, side diameter: 168x155 mm (Figures 8,9). Widespread adhesions among small loops and the inflamed peritoneum. The parietal peritoneum is fused with the posterior fascia of the rectus muscle. The nutritional state is severely impaired. The body weight is 49 Kg, height is 163 cm, and the Body Mass Index (BMI) 18.44 Kg/m^2 (underweight for the age, see Graph 8A,B). The hematologist recommended platelets infusion IV to maintain levels above 70,000/ml; steroids (20mg iv/day); and immunoglobulins (1g/Kg 48 hours before surgery) for surgery preparation. Infectious consultant recommendations include contact isolation notification for Enterococcus faecium and Vancomycin-resistant Enterococcus (VRE) for surgery preparation. Stop Teicoplanin and start with Linezolid 600 mg x 2 days, PLT monitoring because of Linezolid-related thrombocytopenia risk, and laboratory monitoring. The fourth wk after the patient's admission, the clinical picture is still septic, with a voluminous purulent collection. Three days after therapy, the patient complained of peaks up to 39.8°C under Linezolid due to Enterococcus faecium on the fistulous orifice that appeared in the abdominal region. Serial blood and urine cultures, organ functions, and chest x-ray were monitored. The therapy is changed with meropenem 1g x 4 and tigecycline 100 mg 1st dose and then 50mg daily. No allergies are known. Newly urine and blood cultures resulted positive for Escherichia coli and Pseudomonas aeruginosa. The infectious specialist replaced the current therapy with Carbapenem. Fever persistence, septic picture, and nasal swab positivity at Carbapenemase-Producing Enterobacteria (CPE) highlighted a Methicillin-Resistant Staphylococcus Aureus (MRSA) contamination. The C Reactive Protein (CRP), the Procalcitonin (PCT), and CPK are monitored. In the third week, a new drainage check with contrast shows a partial dimensional reduction of the collection, and drainage is replaced with a 12 Fr pigtail tube with the distal end in the residual cavity for frequent washing with saline solution (Fig 15). Cultures of the drainage fluid revealed Acinetobacter baumanii treated with a meropenem and daptomycin combination. The fever drops for the next four days, as well as CRP. PCT (<0.5 ng/mL), and leukopenia are registered. In the fourth wk after we found Enterococcus faecium VRE from wound secretions, negative blood cultures, Escherichia coli, and Pseudomonas aeruginosa in urine culture developed. The culture of the drainage fluid showed growth of Acinetobacter baumanii (sensitive only to colistin). The MRSA nasal swab resulted in negative. The rectal swab stated KPC colonization. Although five different combinations of specific antibiotics were tested, together with the consultants, we decided to remove the infected prosthesis because conservative therapy was not successful in controlling the septic source [44]. In the fifth wk, the patient underwent prosthetic explantation. The prosthesis was explanted in 2020, September 9th. The patient underwent a xiphoid to pubic laparotomy, isolation, and removal of the abscessed prosthesis and hematoma. The abscess cavities opened, the purulent material drained, and washed (Figures 1,2) with povidone solution diluted with saline solution. After revision of the hemostasis, the anterior fascia of the right abdominal rectus and left rectus muscles were sutured together on the midline that partially remains open in the central region. A VAC (Vacuum Assisted Closure Therapy) therapy sponge is applied. It is a drainage system with adhesive plastic sheets for applying the Negative-Pressure Wound Therapy (NPWT), also known as a VAC device and maintained for 72 hours because of the inflammation of the wall and tissues caused by the abscess [35,38,39]. Three days after, on September 12th, a relaparotomy is carried out. The retro-muscular space is prepared, cleaned, and closed without mesh application (Figure 3,4). The VAC device was applied newly. The patient was administered antibiotics, antifungals, albumin, and anticoagulant drugs during the postoperative course. We have monitored inflammation indexes (CRP and PCT) daily. Weekly evaluation of the nutritional status, urine and wound secretion cultures, and serial blood culture are taken by the Central Venous Catheter (CVC) and Peripheral Catheter (PVC). Every 72 hours, surgeons replaced the VAC sponge, stimulating wound granulation of the anterior abdominal wall wound for four wk. Because of the very slowness of the cicatrization process, after 8 wk patient was administered Hyper Baric Oxygen Therapy (HBOT) for 20 days [45,46]. The last HBOT application was in 2021, February 4th, without amazing results. TPN started on the second postoperative day until January 28th, when a nasal-jejunal 8Fr feeding tube, 120 cm in length (Figure 6,7,10,11,15), was positioned under fluoroscopy 20 cm over the Treitz angle. A slowly progressively weaning from TPN to EN was completed in thirty days, on February 22nd, rising to 3000 Kcal per day. EN infusion starts at five ml/h for the first 12 hours, with fistula output not exceeding 50-75 ml in the 24 hours. Otherwise, delivery remained for 24-36 hours at the reached infusive velocity. The output reduced the EN increased again by five ml/h, simultaneously reducing TPN by the same quantity. The

hydroelectrolytic imbalance is calculated by residents three times a week, and weekly serum nutrition markers (prealbumin, albumin, ferritin, transferrin and iron, and copper) adjust the HPN formula accordingly (Table 1, Graph 3A-I). Preoperative albumin value was 2.3 g/dL against 3.4 g / dL after surgery (normal values-nv 3.5-5.2 g/dL). Total blood proteins preoperative value was 4.5 g/dL increased to 5.5 g/dL (6.4-8.3 g/dL) at 12th post operative day (POD). The patient is discharged home on 187th POD [18] with blood chemistry values within the physiologic ranges and improved general condition and BMI (Table 1 and Graph 1-8). All this narration happened during the COVID pandemic with the patient hospitalized in strict isolation, in contact with the family only by telephone. The COVID swab was negative during hospitalization and re-checked every week until discharge. The first vaccine (Pfizer - BioNTech Covid-19 vaccine before discharge) was administered in a domestic regime with the active collaboration of the family and territorial health services [47]. Completion of weaning EN 3000 Cal a day on February 22nd 55.200 Kg, BMI 20.8 (Graph 8A,B), fistula output is 10 ml in 24 hours. Our team monitored him monthly with continuous improvement (Table 1 and Graph 8H, I ECF output and evacuation by enema, and spontaneously). Six months after surgery, the patient was in excellent clinical condition with negative inflammatory indices and weight gain, BMI 20.1 kg/m^2, h 163 cm, body weight 53.5 (for sex and age) with a significant improvement in his performance and general state incentive and physiotherapist. The EN administration velocity is set up at 50 ml/h. On 2021 March 15th, the patient was discharged at home, 240 days after, in good general condition body weight 56.500 Kg, and BMI 21.3 arising. On March 20th, the patient had 37.5°C, SpO_2 of 93%. The blood exams were normal, and the nasal-pharyngeal swab was negative for Sars-Cov2. Only four days after the Nasal-Jejunal feeding tube is blocked, the patient did not receive the EN for five days until the tube is unblocked with Coca-Cola washing with a 50 ml syringe (to obtain low pressure to prevent tube explosion and migration) (Figure 6,7,10,11,15). In this period, we can notice the fistula output decreasing. The blood metabolism and protein maintained standard levels, Hb was 8,3 g/dL, and neutrophils lightly increased. Gradually the EN restart on March 29th. In a month, the EN is increased progressively to 65 ml/h, and the fistula output is between 100 ml and 200 ml/daily. The weight of the patient increased to 57.700 Kg and BMI 21.7. Vital parameters remained regular, O2 Saturation 96-98%, medium temperature 36.5°C (Graph 1A,B,C,D). The patient evacuated every day, stimulated by an enema every other day to keep the intestine free downstream of the fistula. Evacuation the other day using enema washing stimulation to avoid obstruction over the fistula, and the stool volume increased. Sometimes the patient started to evacuate spontaneously. On May 7th, the patient's body weight at home increased to 62.1 Kg and BMI 23.4. Vital parameters remained normal, SpO_2 96-98%, medium temperature 36.5°C, proteins and iron, and the other regular blood exams. On July 12th, the patient's weight was long-lasting at 60 Kg and BMI 22.6 (Graph 8A,B), EN set at 80 ml/h, the fistula output was 66 ml/day, and fecal evacuation weight was about 100-200 gr. Blood exams showed anemia (Hb 6.8 g/dL). On July 23rd, the patient underwent a first blood transfusion and repeated transfusions on July 30th and August 13th because Hb was seven g/dL. The body weight and fistula output were changeless, and the other exams were regular. EN is set at 80 ml/h, and the weight increased to 62 Kg and BMI 23.3. On August 27th an important drop of fistula output (often under 50 ml/day) is observed. EN is increased by 20 ml/day to 100 ml/h. The patient's bodyweight increased to 64.600 Kg, BMI 24.2, and he often evacuated spontaneously. Blood exams showed anemia (Hb 7.2 g/dL), so he underwent a transfusion on August 30th, fever (37.9°C) because of cough and phlegm, SpO_2 95-97%. Because the fixation stitch anchoring the tube to the nasal sect was decubited, and the tube came out. Some days after by fluoroscopy procedure the tube was repositioned. The patient received hydration I.V. therapy. During this time, we observed a bodyweight loss of almost 2 kg. On September 7th patient underwent the nose-jejunal tube repositioning because closed. The patient had started enteral nutrition only during the day, turning off the machine at night and the tube wash out was not done. He drank a small cup of coffee a day, helpful in satisfying the patient and stimulating gut peristaltic, so he evacuated spontaneously daily. On September 10th, he underwent another transfusion. On November 2nd, we reported an encouraging reduction in fistula output (often under 10 ml/day). The EN was set to 65 ml/h because body weight increased to 66 Kg and BMI 24.8 with the risk of too much increasing, and hazardous for a third incisional hernia recurrence. The patient underwent blood sampling showing chronic anemia, so he did a weekly transfusion. The parameters of the patient were stable, SpO_2 96-98%, and no fever. On November 11th, we tried to reduce Octreotide administration because from the Alatri "S. Benedetto" Hospital Pharmacy, no more furniture available, so we scheduled only one injection per day. As a consequence, on November 12th increase in the fistula output (upper than 60-100 ml/day) is registered. The patient noticed the appearance of a hematoma near the enterocutaneous fistula on November 14th due to the contact with the ferrule, so he did medication with Amukine (hypochlorite sodium principle 0.05%, belonging to the category of antiseptics) and Ceftriaxone (in powder). Complete reabsorption of the hematoma and closure of the hole on November 19th. On December 4th, a second fistula appeared on the existing hematoma (Figure 5). A medication with Amukine and Ceftriaxone in powder is performed. On December 7th, the patient restarted the Octreotide therapy twice. A leak of a few of clotted blood and enteric output from the fistula on December 9th are observed. On December 15th, the patient underwent abdominal fistulography at the Radiology of

General Surgery Department of Umberto I Polyclinic. A new fistula near the oldest one is shown and discharged at home. On December 20th, the patient was moved to Alatri's Hospital because of a blood loss from the fistula. The abdominal CT scan showed a pseudoaneurysm of the Abdominal Aorta, and the patient was recovered to Polyclinic Umberto I. Four days later, he underwent endovascular pseudoaneurysm exclusion procedure, placing an endoprosthesis. On December 29th, he weighed 59.9 kg (BMI 22.5). The patient had a fistula output of 100 ml/day, a temperature of 36.4°C, and a saturation of 98%, and he was discharged on 2022 January 5th at home (Graph 1A,B,C,D). On January 13th, reduction of the fistula output (29 ml/day), general conditions satisfactory, the body temperature was 36.5°C, SpO^2 98%, bodyweight 58.500 kg (BMI 22), and evacuation every other day. On January 26th, the patient underwent a blood exam for anemia (Hb 5.6) and underwent two blood units and one platelets unit transfusion. On February 11th, a significant increase in fistula output was noticed (stable between 300 and 700 ml/day). The temperature was 36.5°C, SpO_2 96-98% body weight 55.800 Kg, BMI 21, and evacuation every other day. March 23rd increasing the fistula output (850 ml/day), body weight decreased to 52.700, BMI 19.8 (Graph 8A,B), and the hut closure for ten days. Then he alternated evacuations with enema and again closure of the hut. The temperature was 36.6°C, and SpO_2 was 90-93%. On April 16th, severe increase in the fistula output (1450 ml/day). On April 18th, the patient is moved to the Alatri Hospital, and on April 19th, the patient dead. The autopsy feedback was required.

HOME REGIME	2021, mar 15th discharged	2021, mar 24th	2021, apr, 16th	2021, may, 26th	2021, jun, 10th	2021, jun, 16th	2021, jul, 15th	2021, jul, 23rd	2021, jul, 27th	2021, aug, 12th	2021, aug, 27th	2021, sep, 16th	2021, sep, 24th	2021, oct, 14th	2021, oct, 28th	2021, dec, 1st	2021, dec, 22nd	2021, dec, 24th	2021, dec, 25th	2022, jan, 12th	2022, mar, 1st
Artificial Nutrition	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION	HOME ENTERAL NUTRITION
EN VITAL (1,5 Kcal/ml) PUMP SPEED ml/h	55	55	65	70	80	80	80	80	80	80	100	100	80	70	70	65	0	0	0	45	65
WATER ADMINISTRATION ml	1000	60	330	580	610	660	830	390	700	880	860	850	820	850	920	800	0	0	0	830	820
Transfusion and number of blood units								1 BLOOD SACK						1 BLOOD SACK			1 BLOOD SACK	2 BLOOD SACKS			2 BLOOD SACKS
MAX BODY TEMPERATURE °C	36	36.6	36.6	36.6	36.5	36.5	36.8	37.5	37	37.3	37.8	37.5	36.8	36.6	36.9	36.8	36	36.3	36.4	36.6	36.5
O2 SATURATION %	0	97	98	98	98	98	97	98	96	96	96	96	96	97	96	96	99	98	0	97	98
GR x10^12/L (4.3-5.90)	2.36	2.3	2.32	2.66	2.54	0	1.77	1.69	2	1.98	2	1.92	2.37	2.14	2.04	2.25	2.19	2.59	3.14	2.2	2.21
Hb g/dL (13.5-16.3)	8.5	8.3	8.9	10	9.8	0	7.3	6.8	7.7	7	7.2	6.2	7.5	6.9	6.7	7.1	6.6	8	9.6	6.7	6.3
Hct % (40-52)	26.4	25.4	25.5	31.3	31.7	0	21.5	19.4	21.4	20.1	21.1	19.3	23.8	21.1	19.8	20.4	20.3	21.9	26	20.1	19.5
MCV fL (80-96)	112	110	110	117	124	0	122	115	107	102	105	100	101	99	98	91	93	84.5	82.9	91	88
MCHC g/dL (32-36)	32.3	32.8	35	32	30.8	0	33.8	34.9	36.1	34.8	34	32.3	31.5	32.4	33.7	34.8	32.6	36.7	37.1	33.2	32.3
GB x10^9/L (4.4-11.30)	2.49	6.3	6.9	5.1	5.2	0	5.4	6.2	6.8	8.6	6.1	6.8	7.2	8.1	7.3	7.2	9.4	6.17	8.88	5.8	3.2
Neu# x10^9/L (1.8-7.70)	1.93	5.07	5.75	3.68	3.61	0	3.97	4.7	5.35	6.85	4.65	5.1	5.6	5.92	5.6	5.55	7.02	33	0	4.35	2.11
linfo# x10^9/L (1.0-4.80)	0.33	0.71	0.66	0.78	0.87	0	0.67	0.95	0.89	1.01	0.83	0.66	0.74	1.27	0.8	0.94	0	0.62	0	1.05	0.67
Neu % (40.9-68.1)	77.5	80.9	83.3	72.6	69.4	0	74.2	75.4	78.4	79.7	76.1	74.9	78.1	73.3	77	77.2	74.5	48.6	0	75.4	66.9
Linfo % (24.9-40.1)	13.4	11.3	9.5	15.4	16.7	0	12.6	15.2	13	11.8	13.6	9.7	10.3	15.7	10.9	13.1	12.1	10.1	0	18.2	21.3
Plt x10^9/L (150.000-450.000)	85	173	113	83	72	0	65	90	85	85	109	73	90	56	76	50	69	45	47	21	14
Reticulocytes % (0.5-2.5)	2.69	0	5.31	4.45	0	0	3.11	0	0	0	2.35	2.55	1.91	0.96	0	0.54	0	0	0	0.45	0
Total Proteins g/L (60-82)	56	62	68	70	69	69	72	0	0	0	71	68	0	71	0	72	82	0	68	68	63
Albumin g/L (35-55)	31	0	33.4	0	36.9	0	34.7	0	0	0	0	0	0	0	30.4	35.4	0	0	30	36.4	0
Albumin % (55.8-66.1)	0	48.1	47.9	50.9	49.7	48.1	47.2	0	0	0	43	39.2	0	44.6	0	41.7	0	0	0	0	60.6
ALFA 1 globulin % (2.9-4.9)	0	10.2	8.5	5.6	6	6.5	5,6	0	0	0	6.8	6.6	0	6.5	0	7.6	0	0	0	0	4.5
ALFA2 globulin % (7.1-11.8)	0	15.8	12.1	9.4	9.1	10.7	9.4	0	0	0	11.7	13.1	0	11.5	0	12.5	0	0	0	0	9
BETA 1 globulin % (4.7-7.2)	0	5.1	6	5	4.9	4.9	4.7	0	0	0	5.5	4.9	0	4.8	0	5	0	0	0	0	5.7
BETA 2 globulin % (3.2-6.5)	0	5.9	6.9	5.5	6.1	6.2	6.1	0	0	0	6.1	15.5	0	6.3	0	6.4	0	0	0	0	5.7
GAMMA globulin % (11.1-18.8)	0	14.9	18.6	23.6	24.2	23.6	27	0	0	0	26.9	20.7	0	26.3	0	26.8	0	0	0	0	14.5
Ratio A/G (1.1-2.4)	0	0.93	0.92	1.04	0.99	0.93	0.89	0	0	0	0.75	0.64	0	0.81	0	0.72	0	0	0	0	1.54
C-reactive Protein µg/L (100-6000)	61400	0	58020	0	0	40740	37520	0	0	0	0	0	0	0	0	0	68390	0	76900	0	0
erythrocyte sedimentation rate mm/h (0.00-25.00)	0	0	63	0	0	0	40	0	0	0	0	0	0	0	0	53	0	0	0	0	0
Iron **µg/dL** (64.8-174.9)	61.5	61	86	178	0	0	165	203	182	173	158	170	0	169	140	156	0	0	0	0	237
Iron **µmol/L** (11.9-31.3)	11.0	10.92	15.39	31.86	27.8	0	29.5	36.4	32.6	31	28.28	30.43	0	30.25	25	27.92	0	0	0	0	42.42
Ferritin µg/L (30-400)	5507	0	0	3584	0	0	0	0	0	0	0	3179	0	0	0	4319	0	0	0	0	0
Transferrin (ferro-bonding capacity) **µg/dL** (111.7-346.4)	0	102	130	0	0	0	138	156	159	0	126	0	0	132	0	124	0	0	0	0	188
Transferrin (ferro-bonding capacity) µmol/L (20-62)	12	12.86	32.63	18.27	0	0	0	0	0	0	15.88	17.72	0	33.13	0	15.88	0	0	0	0	23.69
transferrin saturation (% 16-45)	48	0	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0
Transferrin [S] g/L (2.15-3.65)	0.97	0	0	0	0	1.38	0	0	0	0	0.126	1.41	0	1.2	0	0	0	0	0	0	1.89
Dosage Folate ng/mL (3.8-16)	16.6	0	0	0	13.9	0	40	0	0	0	0	0	40	0	0	0	0	0	0	0	0
Dosage VitB12 pg/mL (191-663)	>2000	0	0	0	2996	0	3241	0	0	0	0	0	3216	0	0	0	0	0	0	0	0
Vit D (4,92-42,7 ng/ml)	21.71	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INR (0.81-1.20)	0.91	0	0	0.96	0	0	0.93	0	0	0	0	0	0	1.03	1.01	0.98	1	1.06	1.03	0	0
PT % (70-120)	131	0	0	105.7	0	0	110	0	0	0	0	0	0	96.2	98.6	102.9	100	0	0	0	0
PT sec (11-16)	10.50	0	0	10.3	0	0	10.1	0	0	0	0	0	0	11	11	10.5	10.7	0	0	0	0
PTT sec (25-35)	34.3	0	0	0	0	0	25	0	0	0	0	0	0	27.6	27.9	29.6	26.6	0	0	0	20.8
PTT ratio (0.80-1.30)	1.14	0	0	0	0	0	0.89	0	0	0	0	0	0	0.99	1	1.06	0.95	0.99	0.95	0	0.74
Fibrinogen	4.05	0	0	481	0	0	535	0	0	0	0	0	0	0	589	532	612	545	497	0	184
ATIII		0	0	108	0	0	0	0	0	0	0	0	0	0	0	0	0	0	103	0	138

GOT/AST U/L (9-45)	17	15	0	27	20	0	30	0	0	0	28	19	0	28	20	27	31	31	33	29	23
GPT/ALT U/L (10-40)	31	0	0	37	26	0	0	0	0	0	41	22	0	0	29	38	45	42	47	57	95
GGT U/L (8-61)	25	26	0	50	45	0	74	0	0	0	33	40	0	58	36	44	39	0	44	0	102
alkaline phosphatase U/L (40-129)	51	0	0	0	0	0	0	0	0	0	67	70	0	0	76	82	0	0	81	89	60
Bild mg/dL (<0.20)	0.22	0.12	0	0.21	0.23	0	0	0	0	0	0.2	0.16	0	0.19	0.18	0.22	0.15	0	0.34	0.17	0.13
BilT mg/dL (0.3-1.20)	0.43	0.23	0	0.45	0.57	0	0	0	0	0	0.46	0.35	0	0.45	0.4	0.53	0.38	0	0.63	0.36	0.29
LDH (135-225)	162	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	160	139	0	0
WEIGHT kg	56.5	56.8	56.5	59.1	60.4	60.8	60.3	59.4	58.5	62	62.6	66.7	65.1	63.1	64.5	64.2	0	0	0	58.4	56.5
Body Mass Index **BMI**	21.3	21.4	21.3	22.2	22.7	22.9	22.7	22.4	22	23.3	23.6	25.1	24.5	23.7	24.3	24.2	0	0	0	22	21.3
Glycemia **mg/dL** (70.30-100.90)	140.5	0	0	147	135	0	0	0	0	0	0	0	0	0	216	124	205	84	101	176	186
Glycemia **mmol**/L (3.9-5.6)	7.8	0	0	8.16	7.49	0	0	0	0	0	0	0	0	0	11.99	6.89	11.38	4.66	5.61	9.77	10.32
Urea **mmol/L** 1,7-8,3	6.3	9.28	0	10.16	20	0	27.49	0	0	0	0	0	25	23.56	19.28	9.19	26.78	11.43	12.14	0	25.35
Urea **mg/dL** (10.20-49.8)	17.7	26	0	61	56	0	77	0	0	0	0	0	70	66	54	55	75	32	34	0	71
Creatinine mg/dL (0.7-1.20-100.90)	0.47	0.38	0.46	0.44	0.45	0	0.5	0	0	0	0	0	0	0.48	0.5	0.46	0.67	0.8	0.8	0.59	0.51
canalization status (fistula-output in ml/24h)	0	70	195	61	66	46	61	70	105	141	25	62	85	3	115	143	0	0	0	43	100
ENEMA 1 (YES) 0 (NO)	0	1	0	0	1	1	0	0	1	0	1	0	1	1	1	0	0	0	0	0	0
Evacuations weight (gr)	0	0	0	0	200	100	300	0	300	0	500	0	500	100	200	200	0	0	0	0	200

Table 1: Hematochemical parameters, vital parameters, anthropometric parameters, intesine and fistulas output.

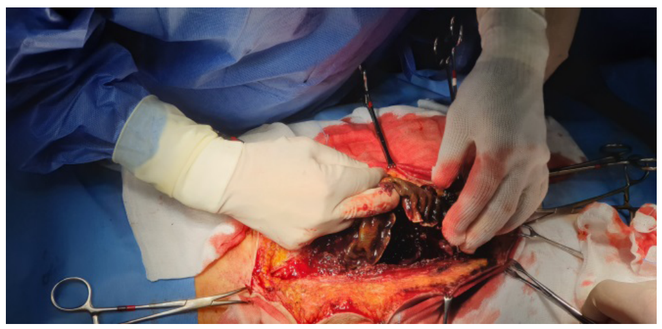


Figure 1: Removal of the upper prosthetic hematoma and then removal of the prosthesis Gore dual mesh with holes Adhesive part, under purulent accumulation.

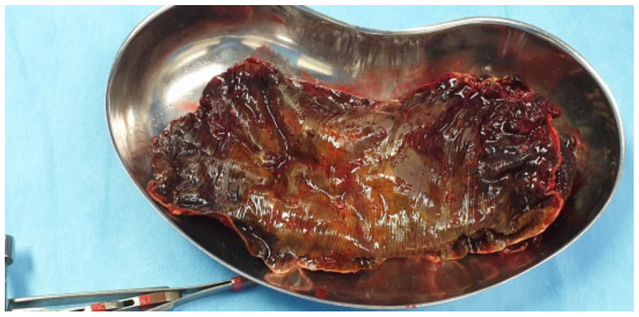


Figure 2: The removed shrinked Gore dual mesh prosthesis.

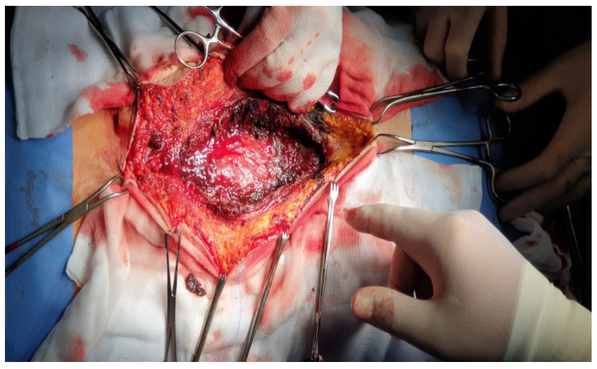


Figure 3: Loops emerging under the posterior fascia are showed.

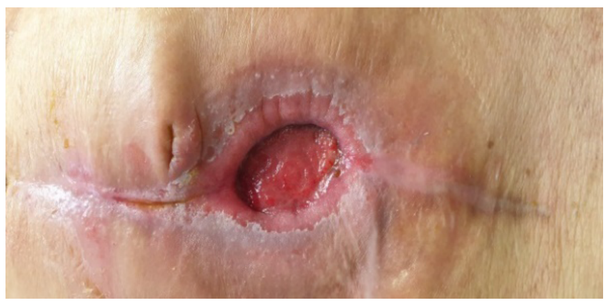


Figure 4: Wound in the post-operative period before ECF formation.

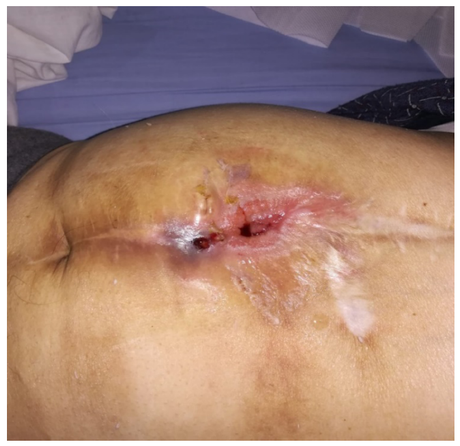


Figure 5: Wound with two ECF

Figure 6: The patient with the EN and TPN pumps and bags during weaning.

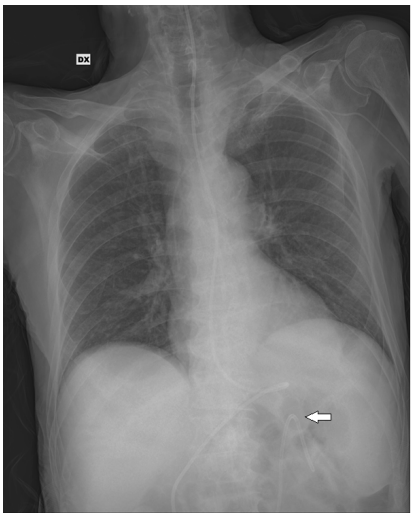


Figure 7: X ray abdomen ap, the white arrow indicates the Treitz's angle.

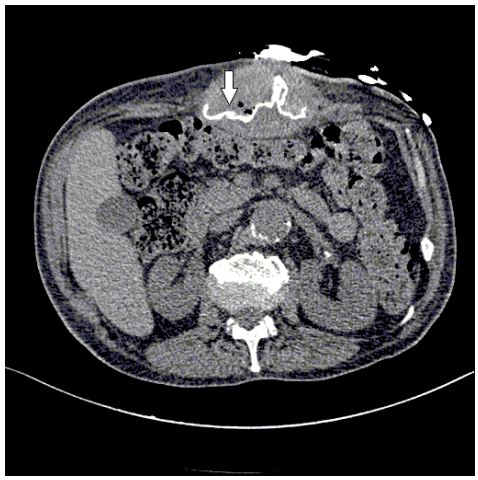


Figure 8: TC the white arrow indicates the shrinked prosthesis in to the abscess.

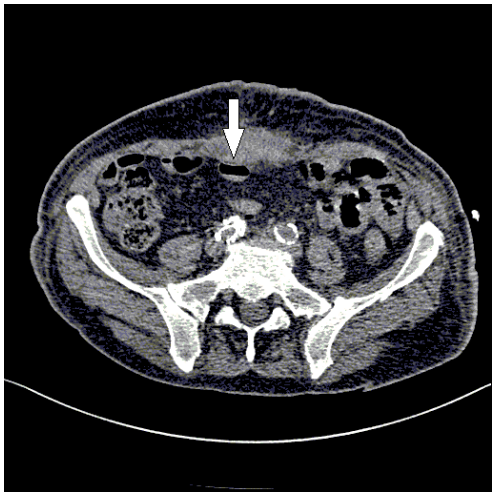


Figure 9: TC the white arrow indicates the ileal loop adherence to the parietal peritoneum.

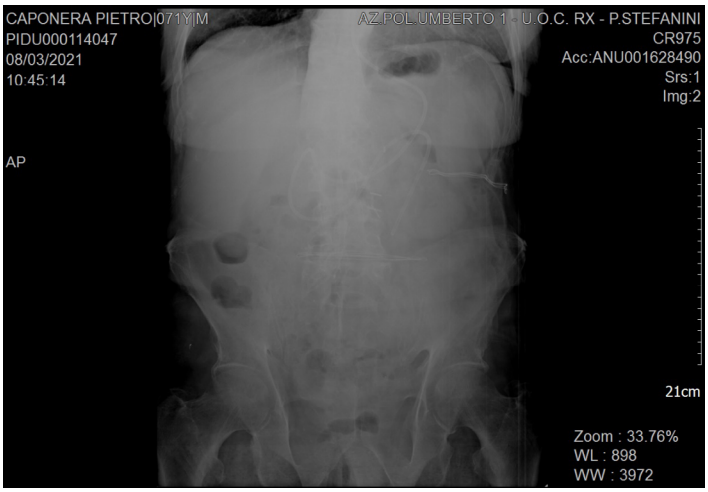
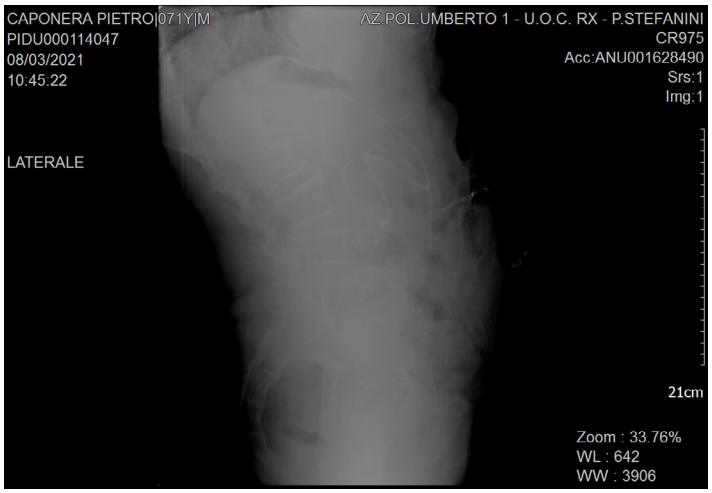
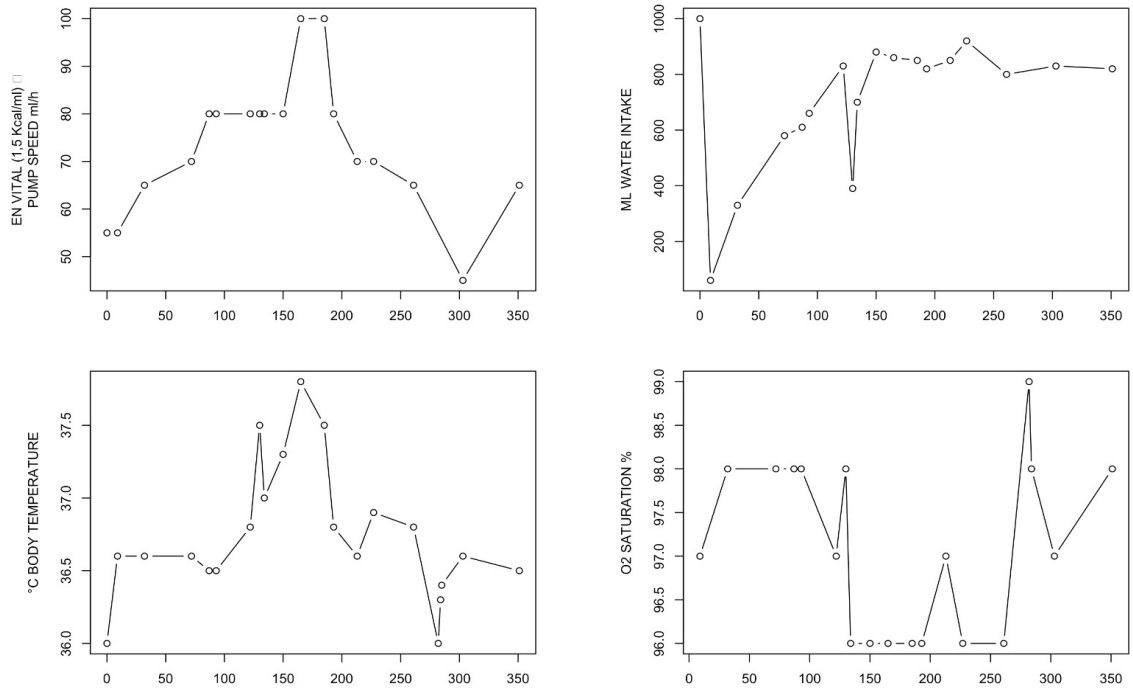


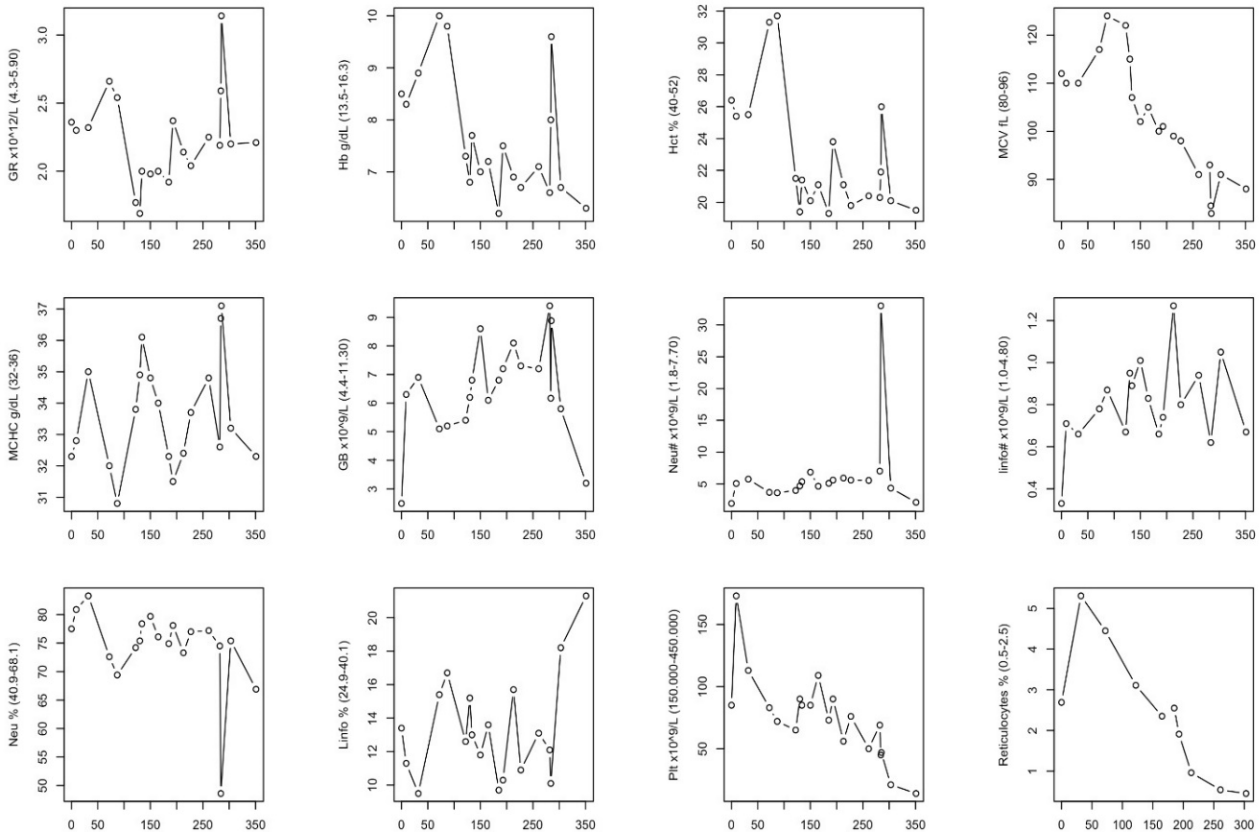
Figure 10: X ray abdomen anterior-posterior showes the tube tip over Treitz's angle



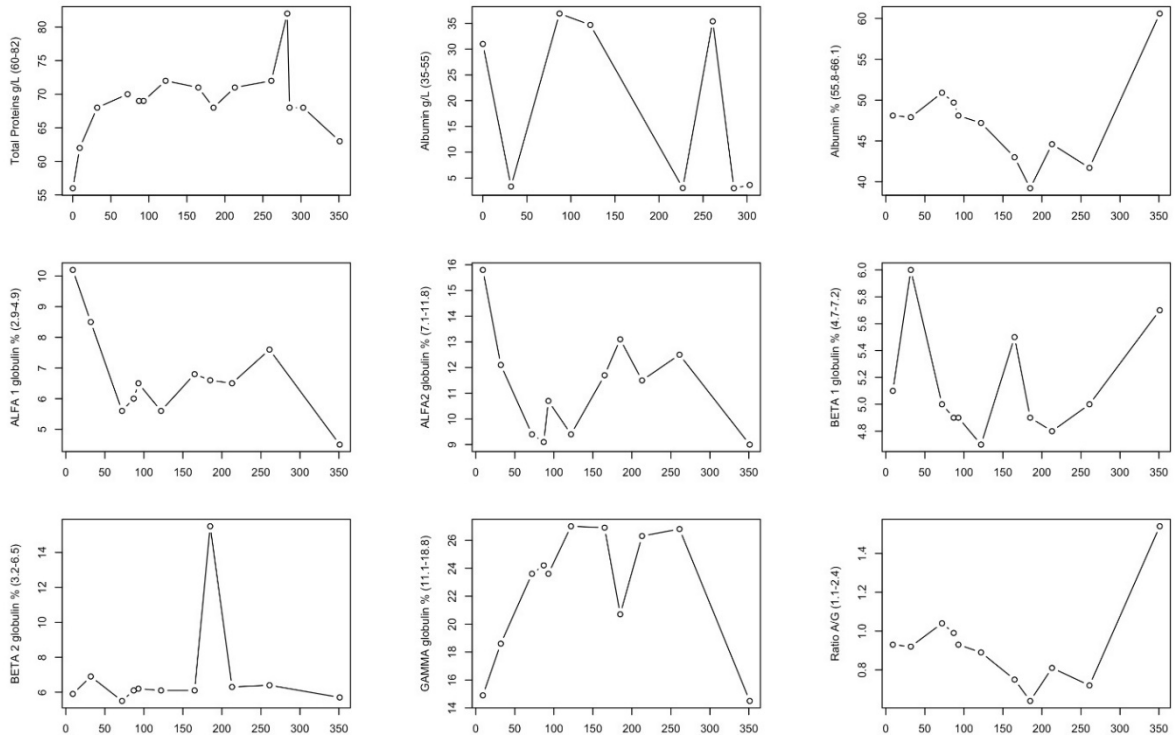
Figures 11. X ray abdomen lateral image showes the tube in to the jejunum.



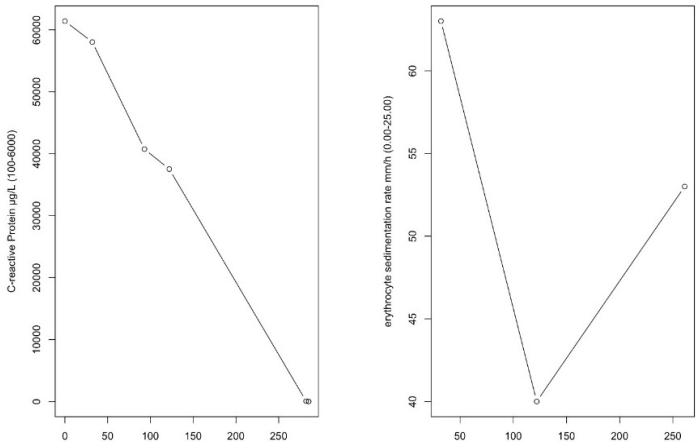
Graph 1: Study of Vital Parameters, Infusion Rate, Enteral Nutrition and Water. A: The first graph represents the infusion rate of the pump with solution for EN called Vital 1.5 Kcal/ml and it is observed that at discharge the patient was taking 55 ml/h, with a slow and progressive increase in the infusion rate before 20 ml/h then of 10 ml/h of 20 and a stabilized period at 80 ml/h which lasted about 2 months. Increasing infusion velocity up to 100 ml/h for about a month. Due to the increase in body weight and the increased risk of hernia, we then reduced the speed to 70 ml/h. The drop in the infusion rate was a consequence of technical errors that caused the nasal-jejunal tube to be obstructed, which was replaced three times under fluoroscopy (Figure 6,7,10,11,15). **B:** The second graph represents the amount of water that was administered both to hydrate the patient and to wash the tube. **C:** The patient had practically no fever because he was severely immunosuppressed but there were episodes of bronchitis. **D:** Saturation was always fair and in the phases of bronchitis oxygen therapy was administered half an hour every 3 hours.



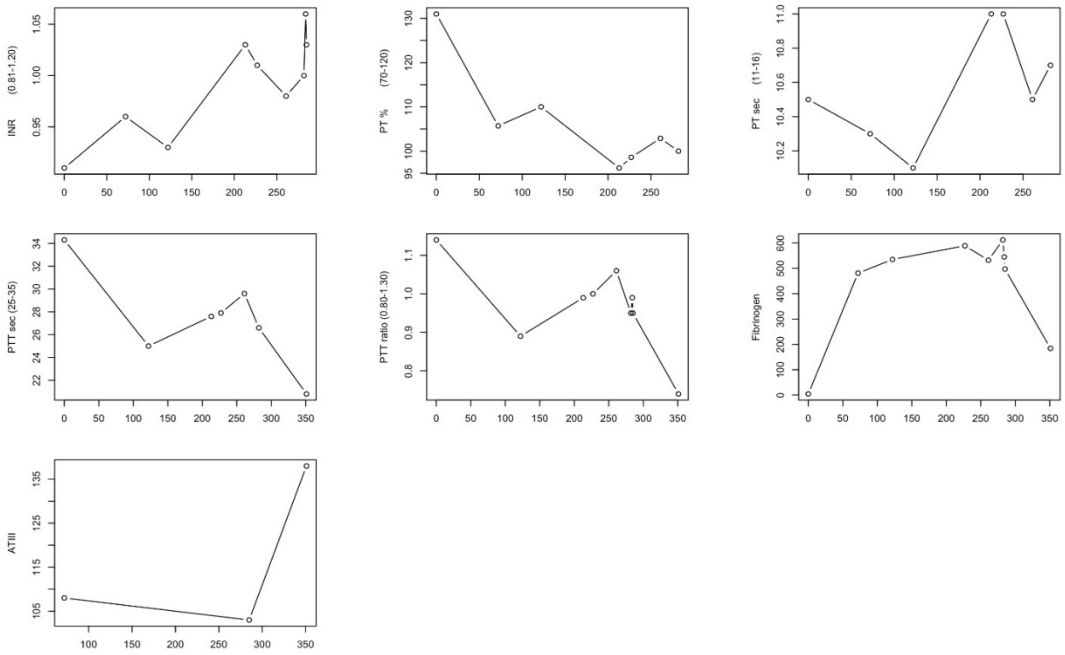
Graph 2: Study of Myelopoietic Function. A: Trend of red blood cells in the first 200 days without blood transfusions. **B:** Trend of hemoglobinemia in the first 200 days without blood transfusions. **C:** Hematocrit trend in the first 200 days without blood transfusions, the progressive decay of erythropoiesis is observed. **D:** Trend of the corpuscular volume in the first 200 days without blood transfusions, a progressive reduction of the corpuscular volume is observed after the first 200 days. **E:** Average hemoglobin content sustained with Vit B12 and cyanocobalamin, blood transfusions were performed after the first 200 days. **F:** The progressive recovery of leukopoiesis is observed but the number is still low. **G:** Neutrophilia is not observed until terminal episodes of bronchitis. **H:** The recivery iof leukopoiesis is observed but the number is still low. **I:** Percent neutrophils, mild neutropholia is observed up to terminal septic episodes with a drop in neutrophil production. **L:** Lymphocytes in percentage, lymphopenia is observed. **M:** Platelet production which remains stable enough for about 200 days of treatment and is subsequently reduced. **N:** reticulocytes production a clear growth phase is observed for the first two months of treatment followed by a slow progressive decline, which however was discrete for the first 200 days.



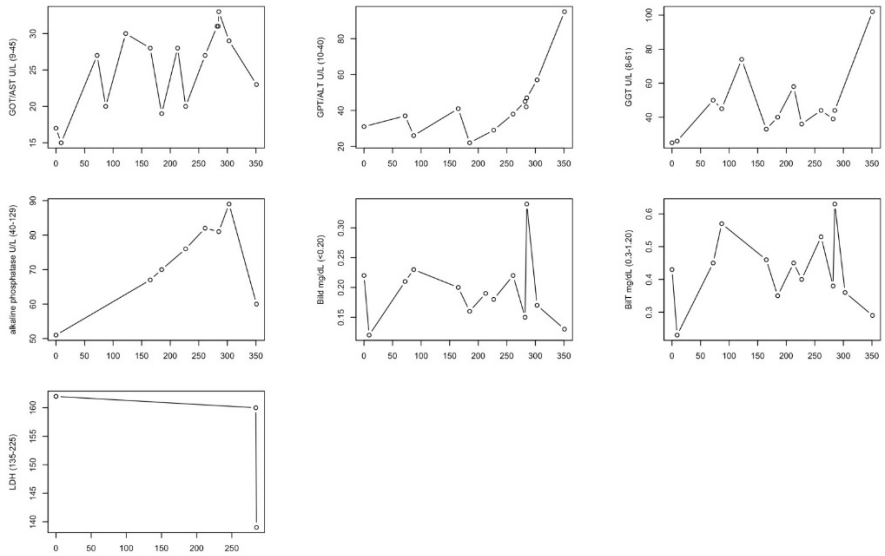
Graph 3: Protein Structure Study. A: Total protidemia, constant growth up to the septic episode and the decrease for MOSF. **B:** Progressive increase in albumin production with falls caused by the interruption of treatment for technical reasons in home care and slow recovery. **C:** Stability of the correct percentage of albumin for over 150 days of treatment. **D:** Fall of Alpha 1 proteins. **E:** Fall of Alpha 2 proteins. **F:** Fall of Beta 1 proteins. **G:** Fall of Beta 2 1 proteins. **H:** Production trend of Gammaglobulin 2 production with recovery of immune function. **I:** Ratio Albumina/Globuline.



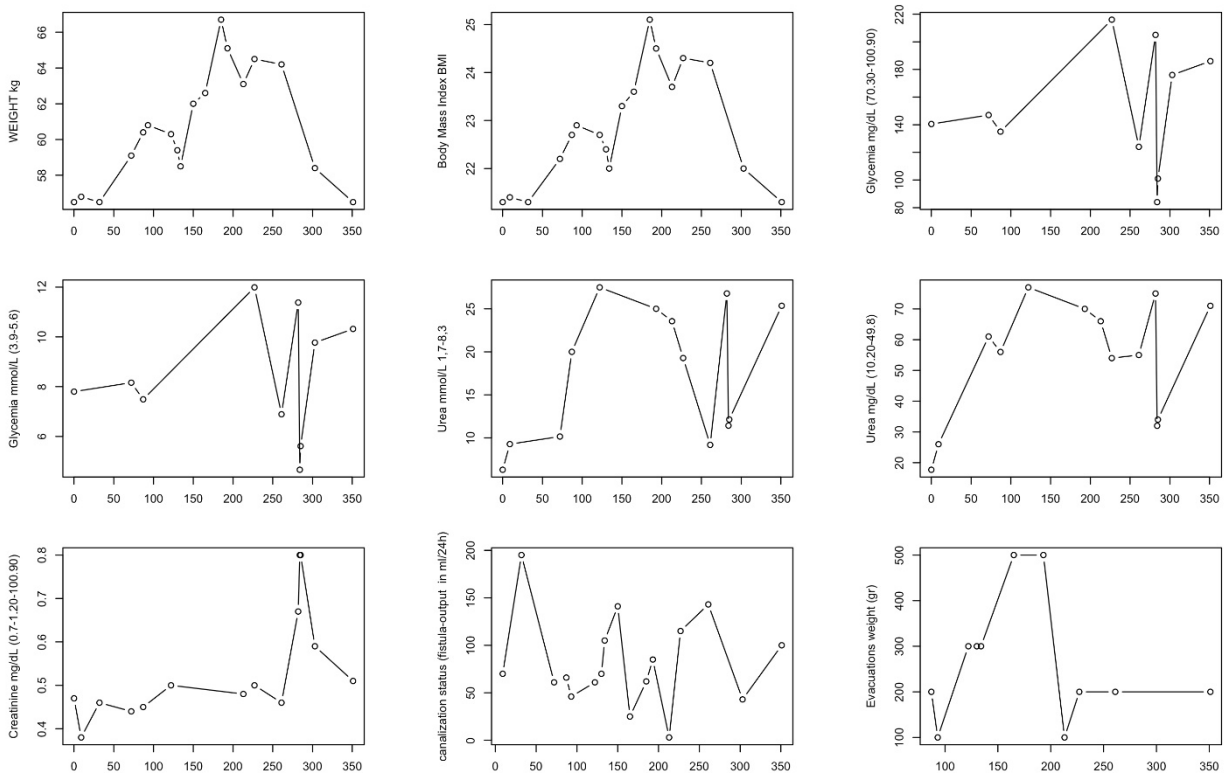
Graph 4: Study of the Set of Inflammation Parameters. A: Progressive fall of the C Reactive Protein. **B:** Progressive fall of the ESR for about 120 days followed by increasing due to the deterioration of erythropoietic function.



Graph 6: Study of Coagulation: A: INR slight progressive increase but always within the limits. **B-E** PT, PTT slight progressive decrease but always within the limits. **F:** Gradually increasing fibrinogen for about 200 days followed by an inflammatory increase with deterioration of erythropoiesis and septic state.



Graph 7: Study of the Liver Function. A: GOT/AST always within the limits. **B:** GPT/ALT always within the limits for 200 days then general and metabolic state impairment even at low dosages of nutritional support. **C:** GGT always within the limits for 200 days then general and metabolic state impairment even at low dosages of nutritional support. **D:** FALK slow progressive increase then general and metabolic state impairment even at low dosages of nutritional support. **E:** BILD always within the limits for 200 days then general and metabolic state impairment even at low dosages of nutritional support. **F:** BILT always within the limits both at high regimes and at low dosages of nutritional support. **G:** LDH always within the limits.



Graph 8: Study of the Metabolic Structure, Body Weight and BMI, Fistula Output and Canalization. A,B BODY WEIGHT/ BMI: Progressive increase for 200 days of treatment, reduction and stabilization up to the 270th day of treatment, progressive fall due to compromise from septic picture and decay of erythropoietic function. **C,D:** GLYCEMIA within the norm even at high doses up to the 200th day of treatment, then cortisone treatment to support erythropoiesis resulted in discrete hyperglycemia compensated by rapid insulin ad by the 250th septic event. **E, F** AZOTEMIA progressive increase in production due to reconstitution of the muscle component ad recovery of the patient's mobility with compensation of sarcopenia. BIOIMPEDENZIOMETRY was not performed because a delicate patient and hitherto negative for molecular swabs were not exposed to COVID risk. **F:** BILT always within the limits both at high regimes and at low dosages of nutritional support. **Graph 8G** Creatinine always within the limits. **H,I:** ECF **output** and **evacuation by enema, and spontaneously**. The output of the fistula is related to the state of the bowel canalization downstream of the fistula which we evaluated by having the patient weigh before and after spontaneous evacuation, in grams. We kept the downstream tract of the fistula free of fecal material by having a one-liter water and olive oil enema performed every other day.

Discussion

Management Discussion

Tigecycline starts at 100 mg at first administration, then 50 mg twice daily IV, followed with ceftazidime/avibactam (Zavicefta) 2.5g every 8 hours IV. Even if this combination cannot lead to a local and systemic infection healing, it was used as a bridge therapy that, together with contaminated prosthesis removal, and collection drainage, furnishes helpful protection. Ongoing antibiotic therapy, the blood chemistry, the blood cultures, and the wound, nasal, and rectal cultures were monitored weekly. Moreover, Acinetobacter baumanii is cultured from the drainage fluid. The specialist chooses Meropenem and Daptomycin to face rectal colonization by Klebsiella pneumoniae carbapenemase (KPC) (resistant to Carbapenem). Negative blood cultures [21]. The patient underwent three central venous catheters (CVC) infections, bacteremia, and right subclavian vein thrombosis occurred. Then, a polyurethane PICC (Peripherally Inserted Central Catheters both alcohol and iodine compatible, full range of catheter sizes from 1.9F to 6F and available in single, dual, and triple lumen) is placed. The chronic inflammation provoked ileal adherence to the parietal peritoneum of the abdominal wall. Eight days after surgery, biliary liquid output from the wound is observed.

Martha Quinn and collaborators identified 286 ECFs cases in 278 patients with a mean age of 64 years (20-96 years) [2]. In total, 112 (39.1%) fistulas developed following emergency surgery, 89 (31.1%) after elective surgery (as our patient), and the rest 85 (29.7%) were received from district hospitals. In total, 246 (86.0%) ECF fistulized after surgery (as our patient), 11 (3.8%) ECF after endoscopic procedures, 29 (10.1%) spontaneously, and 87 (30,1%) recovered after surgical resection [2]. All patients received TPN. Forty-seven (16.4%) patients died from sepsis/Multiple System Organ Failure (MSOF). 154 (53.8%) resolved with conservative treatment, and 46 (16.1%) died before fistula healing or surgery. 214 (74.8%) proximal to the duodenal-jejunal flexure ECF closed spontaneously without surgery, compared with 101 patients (35.4%) with distal disease ($p = 0.001$). Nineteen patients with distal disease underwent the initial operation, and 51 underwent definitive surgery. In-hospital mortality was 19.1% (53/278), with postoperative mortality at 30 days after definitive surgery being 9.8% (5/51) [2]. Mortality incidence remains high and is associated with systemic sepsis. Proximal ECF are more likely to close spontaneously. Distal ECF does not close spontaneously, and the treatment is often prolonged and complex, requiring a dedicated nutritional support team (as our patient). In this series, the spontaneous fistula closure was more common in upper gastrointestinal tract fistulas. Patients who recovered between fistula formation and definitive surgery and were not discharged home show higher mortality risks because of nutritional and immune system impairment [2]. ECFs are a challenging clinical scenario and still represent a life-threatening disease that heavily affects patients' quality of life. Numerous approaches are employed, but a therapeutic protocol has not yet been established. Moreover, the topic is still animatedly debated in General Surgery and Proctology meetings. The ECF treatment can be divided into 4 phases: sepsis control, nutritional management, effluent management, and skin protection [26]. Patients can experience many symptoms, from a small, localized abscess at the fistulation site to life-threatening septic shock. We paid immediate attention to addressing systemic and local sepsis treatment. The first action is to obtain the access to the circulatory system through Central Vein Catheterization (CVC). The septic source is identified by imaging, blood, and swab samples assessment. The IV hydroelectrolytic administration to balance the buffer system and rehydrate the patient starts. Then, IV broad-spectrum antibiotic therapy starts. The adjustment of the therapy is accomplished once identified bacterial flora types are done [48] (as our patient). If an intra-abdominal abscess is suspected, it must be localize, and drained by interventional radiology (IR) for source control [1,3,15,17,18,42,43]. IR (Interventional Radiology) is fundamental in more than 10% of patients presenting to peripheral centers [17]. The availability of this asset is one reason to transfer these patients to a Regional General Hospital. The IR procedure allows the removal of the abscess by placing drainage into the collection so that we can evacuate and sample the content (with microbiological tests) of the septic source. The procedure is performed under local anesthesia under the guidance of a CT scan (Figure 1). The IR prevents either delaying or re-entry of the patient into the operating room. Earning time improves general patient conditions and lowers both surgery and anesthesiologist risks. The CT scan following controls allows gastrointestinal tract anatomic study and a precise determination of ECF location along the gut. Patients often show a wound infection several ws after surgery or biliary drainage. When a cutaneous abscess makes suspect a hidden enteric fistula, an incision should be made that allows proper drainage, skincare, and set up a pouch. Commonly, after initial purulent drainage, enteric content follows. The nutritional state is assessed to evaluate nutritional needs. Patients who complain of ECF need adequate nutritional support to face their hypercatabolic state, fluid loss, and inflammatory state. The use of negative pressure (VAC therapy) is controversial as there is no clear evidence in the literature. Some studies report an increased incidence of fistulation (as in this case). In contrast, others claim the opposite. VAC sponge is not recommended if it lies in tight contact with the gut due to the risk of perforation (Figures 9,12,13). The VAC sponge placed on the wall near the intestinal loop weakens the intestinal structure and the rubbing and granulation of the scar tissue fistulizes the gut [8, 22,24,35,38,39,49,50] (as our patient). The literature on VAC use in open abdomen management show significant limitations due to the heterogeneity of the patients enrolled in the variety of technologies evaluated (craft versus commercially available systems) and at different pressure values, and modes (continuous or intermittent) [8,22,24,35,38,39,49,50]. The VAC is helpful for abdominal decompression in anasarca and abdominal compartmental syndrome [2,51]. Qualified professionals can recognize the possible complications in these patients, such as intestinal fistulas, perforations, hemorrhages, infections, and incisional hernias. Taking oral nutrition the patient can never take sufficient quantity and quality nutrition to cope with his catabolism. Additionally, oral feeding increases fistula production, which causes skin irritation. The National Institute for Health and Curative Excellence (NICE) recommends the use of Somatostatin [52,53] and advanced medication with the use of VAC for a short time [2,8,22,24,35,38,39]. Somatostatin is a natural hormone produced mainly by the delta cells of the pancreas. Adding somatostatin analogs is controversial and relatively expensive. Although somatostatin analogs reduce fistula production, they do not increase the closure rate [52]. According to other authors, Somatostatin and its analogs have an inhibitory effect on digestion by reducing enteric secretions, suppressing gastrointestinal hormones, decreasing gastric emptying rate, and splanchnic vasoconstriction [11, 52,53]. Somatostatin can promote spontaneous fistula closure. Due to Somatostatin's short half-life (1-2 minutes), a continuous IV infusion is required. Long-acting, costless analogs have been developed, such as Octreotide (with a

half-life of 113 minutes), which is currently widely used in treating ECFs. It allows intermittent subcutaneous administration [50,54,55]. When Octreotide and TPN have a synergistic effect on the reduction of gastrointestinal effluent quantity, an improvement in fistula closure rates is clearly observed [52-55] (as in this case). Better treatment is to start with TPN to reduce output, then weaning with EN (weaning in hospital), oral supplementation if needed (at home), and slowly and progressive oral feeding with selected foods and supplements. The gut absorbs EN wholly because enteral solutions could have elementary o semi-elementary structures without fibers and no residual. Twenty small gut cm could be enough to ensure feeding. Patients can be discharged home if the output remains low and skincare is adequate. If EN, for whatever reason, is not tolerated, intravenous supplementation is crucial to maintain fluid balance and nutrition. It is possible to discharge home under Home Parenteral Nutrition (HPN) with appropriate family and structural facilities for HPN management support [2,15]. Adult HPN patients admitted to the National Referral Center (UK) under the well-organized care experienced team, in close collaboration with home nurses, even a delicate process, such as patient education, can successfully take place at home. Reduced hospitalization and improved psychosocial well-being of both patients and family resulted [15]. In Italy, any ASL (Azienda Sanitaria Locale: Local Health System) has a Home Nutrition Management and Assistance Center (CAD). A national contract with commercial companies manages the Scottish National Clinical Network [56]. Quinn's work reports on three HEN patients [2]. Two of them failed and had a TPN period before surgery. Three other patients received TPN before surgery. One patient constantly administered intravenous fluids and electrolytes at home. Twelve patients were discharged with HPN until judged ready for surgery. HPN complications are reported in 5, including eight nutritional-line and CVC infections in 4 patients, a higher rate than observed in patients under HEN (0.84 per 1000 days, unpublished data on 2015). One patient had two hospitalizations for dehydration, and one had venous thrombosis and a line infection. In our clinic experience, the hospitalized patient underwent three nutritional-line infections and had venous thrombosis associated with the line infection because of bacteremia for the infected prosthesis. Oral foods have a complex structure with a high residue. Stools are acidic due to enzymatic content and bacterial fermentation, and this stool, if it touches the skin around the stoma, causes erosion and irritation, which makes it difficult ostomy set up, and pain and discomfort for the patient. Each time the patient moves, the bag detaches, and the feces smear the skin, worsening the skin irritation. In Quinn's experimentation, the median time interval between fistulation and definitive surgery in this group was nine months (3-36 months) with 108 mean TPN days (30-1095 days). In this group, no patients died after surgery [2]. Nineteen patients who were physically or mentally unable to manage HPN could not be discharged home for the period after ECF fistula appearance and surgical treatment. All patients underwent hospital TPN before definitive surgery. The median time interval between fistulation and surgery in this group lasted seven months (4-23 months) with a mean of 108 days (19-690) of TPN. Four patients died after surgery. The difference in mortality between these two groups of patients with acute ECF episodes was significant (Fisher's exact test $p = 0.02$). [2,56]. Therefore, hydroelectrolytic and acid-base daily balance assessments are mandatory. ECF treatment has been revolutionized with the advent of TPN [50]. The TPN has been the standard therapy for many years, although, nowadays, several studies have shown that EN may be feasible, easier, and more effective in preventing systemic infection complications [57]. For these reasons, after seven months, our staff decided to apply a nasal-jejunal tube (Figure 6,7,10,11) and slowly progressive weaning with EN. Treatment with TPN shows mortality of 19.1% (53/278) and postoperative mortality at 30 days after definitive surgery of 9.8% (5/51). Mortality has a tight relationship with sepsis, and even if EN is harmless but not widespread, oral feeding is the most popular [2]. Investigations have shown that both Somatostatin and Octreotide are effective in fistula output volume reduction, with some reports of a reduction of 70% in production after the first day of treatment [11,54,50,51]. The efficacy of this therapy is valued by three parameters: (A) fistula output volume, (B) time to closure, and (C) fistula closure rates [11,54,50,51]. Somatostatin/Octreotide treatment efficacy definitive evaluation in ECF is complex. In our experience (A) output volume of the fistula: 48 hours after the suspension of Octreotide, the output increased five times, and 48 hours after the resumption of administration, the output returned to 20 ml/day. A drug that reduces fistula output is helpful for patients with a high-flow output prognosis and improves the quality of life. Our staff experienced this phenomenon, also. (B) Time to close it is directly related to the length of stay, medical costs, and risk of complications. Although the literature is not unanimous on the benefits of Somatostatin/Octreotide on closure time, several controlled studies showed significant improvements [11,54,50,51]. (C) Fistula closure rates: most studies have shown that Somatostatin/Octreotide does not impact the closure rate in patients treated with Artificial Nutrition (AN) [54,50,51,56]. In ECF in patients with Crohn's disease, the timing of presentation of the ECF is significant. Patients with ECF who have not had surgery in the past are more likely to close the fistula upon initiation of biologic therapy than those with surgically treated fistula. For patients with ECF, the biological treatment must be balanced, avoiding immunosuppression risks, especially during TPN feeding. Crohn's disease patients' rate of ECF closure was studied with either 6-mercaptopurine or cyclosporine administration [58,59]. Additionally, there has been some interest in the use of infliximab, a primary monoclonal antibody (tumor necrosis factor-alpha, TNF-alpha) inhibitors, in patients with a Crohn's disease-related fistula [60,61]. Although most of the patients evaluated had

perianal fistulas, there are some encouraging preliminary results using infliximab in patients with ECF. These treatments are intended for an isolated patient population with Crohn's disease and not for postoperative fistulas, as sepsis would preclude their use. Some papers on ECF successfully treated with fibrin glue or absorbable plug (for anal fistulas) in colic fistula after an abdominal stab [11,53,42,62]. We also experienced this issue without success. These options are certainly of interest to surgeons seeking less invasive means of treating these patients; however, there is little evidence that these treatments are justified. While they do not add additional morbidity, cost remains a critical factor. The favorable prognostic factors for spontaneous fistula healing are an optimal nutritional state, serum albumin> 3 g/dL, the disappearance of inflammation, and infection healing. In cases of diverticular disease with fistula, low output, intestinal canalization is excellent. Unfavorable prognostic factors are excessive nitrogen output, and energy unbalance enlightened by a low blood-protein dosage (albumin and prealbumin, ferritin) for the nutritional status used. Furthermore, multiple fistulae, high flow rates, previous radiotherapy and surgery, and faulty canalization are unfavorable prognostic factors [63,64]. The inflammatory state shows high erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels. We usually meet these patients for the first time in an outpatient setting. Given their constellation of problems, it is not uncommon for patients to request hospitalization [65]. For fistulas that do not close, surgery is indicated [51]. The operation must be carefully planned for surgery to treat an ECF (timing in surgery is a crucial factor). Sixteen % of fistulas recur after surgery, and postoperative mortality is between 10 and 20 % [17]. Particular attention should be given to the perioperative pain management plan, including epidural catheters, transverse abdominal blocks, and patient-controlled analgesia. Before embarking on the event of surgery, it is imperative to time the operation appropriately. A general consideration is to wait at least six months, which is associated with decreased mortality following the operation [51]. If spontaneous non-closure happens during the waiting period, the fistula's anatomical position with an angio-CT scan and a fistulography are carried out. If the arise hypothesis that the fistula is reachable, endoscopy could be used. The position helps estimate the mucosal absorption capacity upward fistula (as well as in our case). This information makes decide if postpone surgery and meanwhile to implement the EN. Once the infected prosthesis is removed, the intervention of the general surgeon and the plastic surgeon is helpful for the appropriate reconstruction of the abdominal wall [8]. When the fistula is accessible endoscopically, non-surgical techniques, such as over-the-scope clips, can be attempted [26]. If intraoperative endoscopy is required, the patient lies in a lithotomic position. These devices are not adequate for treating chronic ECF but are reasonably practical for treating acute postoperative fistulas, if attainable. When dealing with small fistulas, superficial, distal, and low production, if the prognostic factors are all favorable, a primary closure with sutures, and different types of glue (fibrin glue and cyanoacrylate glue) could be attempted [2,10,17,20,66,67]. We also tried with fibrin glue, but the cork lasted only two days, and then spontaneously fell off. On the other hand, most studies have shown that Somatostatin and its analogs do not affect the effective closure rate in patients who have been given these drugs alongside conservative therapy [52-55]. While this may appear to be a failure of conservative therapy, it is more likely related to the nature of the individual fistula, such as its location or the presence of distal obstruction, foreign body, or malignant tumor. In addition to Somatostatin [52-55], Octreotide [54,55,51], glucagon [68], and calcitonin [68], there are other adjuvants used mainly or in combination with other therapies [55,68]. Proton pump inhibitors and H2 antagonist receptors proved gastric secretions reduction, so some researchers proposed their use to reduce ECF output [11,29,59]. It is well-known that proximal to the duodenal-jejunal flexure, ECF closes spontaneously without surgery [2]. These drugs neither reduce fistula production nor increase the rate of spontaneous fistula closure. Once the diagnosis of ECF is confirmed, a stepwise approach is required to ensure effective resolution of the fistula. After resuscitation and removal source of the infection, the next step is to ensure proper skin and wound care, a particularly challenging item considering the quality of the effluent and anatomical location of each particular fistula. Particularly with small bowel ECF, the effluent can be caustic to the surrounding skin [9,48]. It can be challenging to set up a bag to collect the enteric material produced by the fistula. The goal is to obtain an adequate bag adhesion to the skin, isolate the fistula, allow the peripheral tissue to granulate, and protect the surrounding healthy skin where the bag adheres (Figures 17,18). A customized collecting system or VAC therapy with fistula isolation may be required [4-6,34]. A multidisciplinary approach is essential, including an experienced wound/ostomy nurse in the team. Once the wound care issues are addressed, the next step in management is to classify the fistula as high or low and effluent production volume (High, moderate, low) [4-6,50]. As sed, a low-emission fistulas have a higher likelihood of spontaneous closure, and some patients with ECF will heal spontaneously with adequate nutritional support and wound care [6,44]. Several unfavorable factors can contribute to the persistence of fistulas, including obstruction or simple partial distal obstruction caused by fecal material, slowed transit, and intestinal malformation of the distal segment to the fistula location. Furthermore, unfavorable healing factors include residual prosthetic material (in the prosthetic implant site), previous exposure of the intestine to radiations, and still active infection. Moreover, IBD, epithelialization of the fistulous tract, and cancerization on chronically inflamed tissue. Is there a connection between intestinal contents (demonstrated by CT scan and fistulography), intestinal canalization (fistula output in ml), and the number of (1000 ml) enemas administered per week? In our opinion, there is a relationship, so we administered a 1-liter

enema every 48 hours to stimulate peristalsis and obtain complete colonic emptying. In our opinion, even if this is a troublesome procedure, enema favors the intestinal canalization, favoring intestinal fluids overcome the fistula orifice, and reducing its output, without any administration of steroids (as in our case) [66]. EN is little discussed but deserves more attention due to its low risks and numerous benefits if performed by expert hands. Twenty centimeters of ileus could be sufficient to allow the intake of nutrients in favorable conditions. If poorly conducted, EN can lead to increased fistula output if the higher volume overcomes the absorption capacity of the intestinal mucosa causing diarrhea that becomes a cause of dehydration and electrolyte imbalance. On the other hand, if the tube tip is less than 20 cm upstream, the fistula orifice EN could flow back, and Clinicians must compensate with hydroelectrolytic infusions IV. The nasal-duodenal or nasal-jejunal must be placed during hospitalization. If output increases significantly, anatomic or management cause understanding is needed. EN is continued at home after weaning from TPN with Enteral Nutrition in the hospital. The multidisciplinary team extends to patient homes, where home nurses can assist with TPN or EN administration. HPN includes scheduled monitoring of electrolytes values and serum nutrition markers and adjusting the HPN formula accordingly. Frequent measurements include prealbumin, albumin, ferritin, transferrin, iron, and copper [10] (Graph 5A-I). Graphs were performed with the statistical software R version 4.2.0.

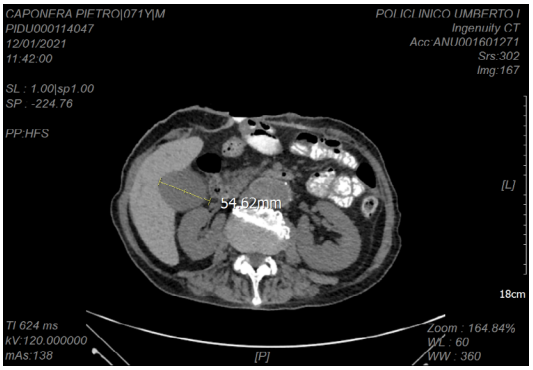


Figure 12: TC scan.

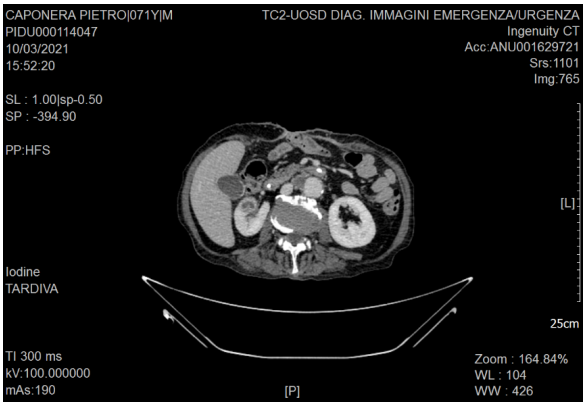


Figure 13: TC scan ECF.

Figure 14: Ostomy bag used for the collection of the ECF output.

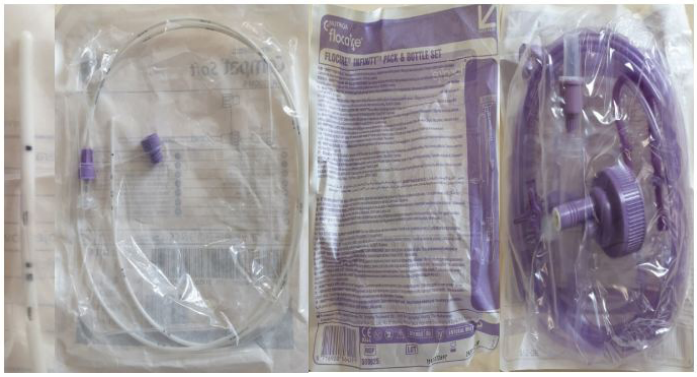


Figure 15: Jejunal-nose tube and nutritional line used for the EN administration.

Teduglutide Discussion

We attempted to propose the out-label use of Teduglutide to stimulate the growth of the mucosa to obtain the fistula closure. Teduglutide seems to improve mucosal growth and restore gastric emptying and secretion, reducing intestinal losses and promoting intestinal absorption. Moreover, Teduglutide is very expensive and is well-known for the high-risk enteric polyps' development from hypertrophy to dysplasia and then neoplasia degeneration risk. After careful clinical evaluation and discussion with relatives and the patient, the new therapy was approved but not authorized by Clinical Competent Authority even in out label use. Teduglutide is a 33-membered polypeptide and glucagon-like peptide-2 (GLP-2) analog used to treat short bowel syndrome. Commercial names are Gattex and Revestive, the CAS Number is 197922-42-2, and the Formula is C164H252N44O55S. Teduglutide is a novel glucagon-like-2 peptide analog, at the moment, used exclusively in the treatment of patients with short bowel syndrome because of its high costs and the high risk of enteral polyps' dysplasia and subsequently cancer degeneration risk. Short Bowel Syndrome (SBS) results from surgical repeated resection, extensive Digestive System vein/artery thrombosis, consequent gut resection, a congenital defect, or disease-associated absorption loss. TPN, a life-saving therapy in patients with SBS, intestinal failure, unable to compensate for their malabsorption, may survey by artificial nutrition. TPN has many inconveniences and life-threatening risks (e.g., catheter-related blood stream infections, central vein thrombosis, intestinal failure associated with liver disease). These possible complications may impair the quality of life of patients. Teduglutide treatment seems to maximize residual intestinal absorption, reduce the inconvenience of diarrhea, and prevent, reduce or eliminate the need for TPN (and its complications). Currently, evidence is limited, and treatments that improve the structural and functional integrity of the remaining intestine are needed. In a 3-wk, phase II balanced study, Teduglutide reduced diarrhea by around 700 g/day and fecal energy losses by around 0.8 MJ/day. "In two randomized, placebo-controlled, 24-week, phase III studies, similar findings were obtained evaluating the fluid composite effect, which is the sum of the beneficial effects of Teduglutide - reduction in the need for TPN, increase in urine production and reduction in oral fluid intake." [41]. Fluid composite effect reflects the increased intestinal fluid absorption (and the concomitant reduction in diarrhea). In studies of up to 24 weeks' duration, Teduglutide appears safe and well-tolerated. Teduglutide was associated with enhancing or restoring the structural and functional integrity of the remaining intestine with significant intestinotrophic and absorptive effects, facilitating a reduction in diarrhea and an equivalent reduction in the need for TPN.

Surgery Technic Discussion

The reoperation often requires a long time and several hours of adhesiolysis. Entering the abdomen is the most challenging part of the operation and is usually accessed at the apex of the xiphoid in virgin territory. To avoid accidental ureteral damages, "double pigtail" stents are advised. Adhesiolysis must be thorough to avoid fistulation. The anatomy of the intestine can be unclear, and it is essential to check the entire intestine to ensure proper anastomosis. Attempting to suture the fistula is not recommended, but resection of the segment containing the fistula with end-to-end or termino-lateral anastomosis is indicated [7,17]. The appropriate timing concept allows for softening of intra-peritoneal adhesions making adhesiolysis easier and thus improving the safety of the operation. The correct time is after inflammation and infection healing [50]. Twelve months later, the first surgery, reoperation, is carried out in two stages. The first step consists of adhesiolysis, intestinal resection (removal of the ECF), and anastomosis. The second step is cleaning and closing the abdominal wall. In our case, the fistula spontaneously formed a week after surgery for septic prosthesis removal. VAC application in the well-known area of adhesion of the ileal loops to the abdominal wall is another weak point. The wall was closed with a direct suture and left for secondary healing. The risk of Intestinal Failure (IF) and short bowel disease (SBD) is another issue to be considered when dealing with ECF. If the intestine is unable to absorb macronutrients (carbohydrates, proteins, and fats), micronutrients (vitamins, electrolytes, and minerals), and water because of high-flow fistula, TPN becomes mandatory integration [17]. A minor injury on the visceral peritoneum (accidentally produced) causes fistulation, and enteric fluid leaks through the surgical wound [17,69-75]. The Component Separation Technique (CST), initially described by Ramirez in 1990, involves the separation of the posterior rectus muscle sheath, the external oblique muscle, from the internal oblique muscle. In this way, it is possible to advance the muscular planes towards the midline of about 5 cm in the epigastric region. Up to 10 cm in the mesogastric region, 3 cm advancement in the hypogastric region, for each side, can be obtained, also. This procedure is

combined with mesh reinforcement and restores a dynamic and functional abdominal wall. There are several reports in the literature on the success of CST in the management of large ventral hernias, revealing hernia recurrence rates from 84-97.6% to 52%. It may sound intuitive, but it is worth saying that large ventral hernias are more likely to recur and have to employ bridging techniques with prostheses, even when using CST. Ideally, the CST is used to facilitate rapprochement of the rectus muscle to the midline with the support of a prosthetic mesh. Some defects are so extensive that bridging is still required even after component separation has been performed. Higher recurrence rates can be expected in these scenarios. A randomized comparison between CST and mesh closure in a patient with loop edema [17,76] out of Polytetrafluoroethylene Patches (PTFE) showed that wound complications were more frequent in the prosthetic group and that the 38% of cases required prosthetic removal due to infectious complications (as well in this case). It was reported that fibrin-based sealants reduce seroma and wound infection rates in patients undergoing CST or cyanoacrylate [17,77,78].

Discussion myelodysplastic syndrome

Myelodysplastic syndromes are blood disorders caused by damage to one of the stem cells line in the bone marrow. Stem cells fail to produce adequate amounts of functional blood stem cells, leading to a shortage of red blood cells, white blood cells, and platelets. In some cases, myelodysplastic syndromes develop into an aggressive tumor called acute myeloid leukemia. Patients with myelodysplastic syndromes (MDS) and diseases at low risk of developing acute leukemia are treated principally with the best supportive care that could improve their quality of life and functional performance. "Elderly patients commonly have multiple medical problems and use medications to deal with them. Elective and first-line treatment is predominantly the Synthetic Erythropoietin (EPO) (as in this case), which can help reduce the need for transfusions, but it is only effective in about 25% of patients treated. Particularly important for the elderly patient with MDS is the age-related decline in normal bone marrow function, including impaired responsiveness to stress factors such as infections (as in this case) or myelosuppressive treatments. Personalized care in this population can be carried out in synergy between geriatric, oncological, surgical, and nursing strategies "[43]. Erythropoietin is given as a subcutaneous injection, usually once (as in this case), up to 2 times per week. In the case of our patient, the association of EPO with pyridoxine and the administration of cyanocobalamin prompted erythropoiesis to recover progressively. Erythroblasts indicate improvement and red blood cell count and hematocrit recovery. In addition, normalization of iron and ferritin, a saturation of transferrin, suspension of erythropoietin administration, and red blood transfusions are interrupted (Graph 5A-I**)** . Our patient died of MSOF, leukopenia, anemia, thrombocytopenia, and a septic state [79] for a progressive MDS-related decline in normal bone marrow function.

SARS CoV-2 discussion

In response to the COVID pandemic, the National Health System has increased the availability of beds for COVID-19 patients, limiting assistance to non-deferrable emergencies and cancer cases. The ESMO guidelines (European Society For Medical Oncology) stratify the risk into three priority levels: high (the patient's condition is immediately life-threatening, clinically unstable, and the extent of the benefit justifies the intervention and the risk of contagion, and our patient was so); medium risk (the patient's situation is not critical but a delay beyond six weeks could have an impact on the overall outcome); low risk (https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/breast-cancer-in-the-covid-19-era). The guidelines of the Italy Ministry of Health are thought preventing the virus spread within the hospitals. In cases of surgical site infection is possible to hospitalize the patient even if the Covid infection risk is high. Surgical Site Infection (SSI) was described with specific Centers for Disease Control and Prevention criteria (National Health Institute Working Group for the Prevention and Control of COVID-19 Infections) [80]. On these bases, the patient was admitted to our ward on 2020 July 28th. A few SARS CoV-2 cases occurred among our residents, and staff during the hospitalization. The patient underwent weekly nasopharyngeal and oro-pharyngeal SARS CoV-2 swabs during hospitalization until discharge, constantly negative for the careful observation of the COVID protocol.

Discussion on the importance of the abdominal binder (synonym elastic girdle) with hole for ostomy bag

During major abdominal surgery, the patient undergoes a muscular fascia incision. The preparation of the ostomy also includes a division of the rear and anterior fascia. Obese, elderly, and predisposed patients could develop incisional or parastomal hernias because of reduced abdominal wall resistance. After surgery, the patient will no longer have the containment capacity he had. Moreover, any effort, even just getting out the bed, could lead to erniation. The containment track is of fundamental importance to prevent incisional hernia formation and improve quality of life. After surgery to close the abdominal cavity, sutures are performed. In the immediate postoperative period, intestinal motility, gaseous distension of loops, and contractions of the abdominal muscles can create a push from the inside outward that increases tension on the sutures, which can cause ischemia of musculature in the suture line. An elasticized girdle helps pressure distribution in the surgically treated area closed with sutures and all-over anterior abdomen wall. Elasticized girdle constant use produces an opposite force (from the outside to inwards), distributing the tension over a larger abdominal surface, avoiding sutures' stress. In this way, a reduction of pain and psychological satisfaction

improvement is obtained in patients with midline abdominal wound, even if againist dehiscence-risk protection is not proven [81]. Furthermore, the girdle minimizes movement of damaged layers, making the patient feel comfortable, improves circulation, and promotes edema and inflammation reduction, supporting healing [82]. Even though the expected benefit is the prevention of abdominal-wall complications, no data support this practice. Last, elasticized belt reduces the hematoma's outspreading. Finally, the girdle helps to make the bruises caused by the surgery go away sooner, reducing the risk of complications such as seromas and psychological distress. Due to the sparse evidence and poor quality of the literature, solid conclusions may be difficult to make, and procedure-specific, high-quality randomized clinical trials are warranted [83]. Individual fitting and improved information about when and how to use the girdle is helpful for patient comfort and optimal function. Adverse side effects from wearing a girdle were also studied [84-86]. The importance of both written and oral information is reminded. In our experience, the girdle could be uncomfortable during summer because of maintaining a high temperature on the wound during hospitalization.

Conclusion

ECF are very fragile patients, comparable to cancer patients, so we can understand how mortality from generalized sepsis remains high. First of all, these patients must be treated in specialized centers. Dependence on a multidisciplinary team to address wound care and nutritional optimization is critical to achieving the desired result. The multidisciplinary team extends to patient homes, where home nurses can assist with TPN administration. When conservative management fails and the patient shows septic symptoms, an aggressive multidisciplinary approach, including the surgical option (bowel resection), VAC Therapy, and HBOT, is needed to treat this life-threatening condition. It is essential to teach the relative or the person who assists the patient daily to use the aids and administer EN. HPN includes frequent monitoring of electrolyte values and serum nutrition markers and adjusting the HPN formula accordingly. Frequent measurements include prealbumin, albumin, ferritin, transferrin, iron, and copper [13] (Graph 5A-I**)**. The calories and protein intake with TPN were 1900 Kcal per day, calculated based on metabolic needs but only managed to balance the extreme increased in catabolism. The ECF fistula is a demanding and high-risk condition because it is debilitating in patients who are already problematic and often require a long preoperative metabolic preparation before attempting the surgical repair.

The treatment of ECF is challenging to deal with of the use of personnel, assets, and high costs for the National Health Service. About 75% of ECF are iatrogenic, so attention must be focused on improving surgical techniques. The rehabilitation process may require a second intervention months after, or in some cases, resolve spontaneously with medical therapy ad clinical observation. EN is more effective on intake, according to the fistula output. Our patient needed constant bowel stimulation, both through the use of enemas and glycerin suppositories. These patients undergo a condition of slow peristaltic motion. If not adequately treated, hypoperistalsis worsens fistula production, which could even become fatal. Fistulas proximal to duodenal-jejunal flexion are more likely to close spontaneously. If the fistula does not close spontaneously, the treatment is necessarily prolonged and managed by a multi-specialist team. The fact that the enema may or may not be helpful cannot be established with our data, as a general rule based on a case report, but in our experience, the enema was undoubtedly a helpful therapy. The fistula output values fluctuate throughout the period (highs and lows follow each other) while the evacuations increase in the first five months and then collapse and remain constant until the end of the study; therefore, we limit ourselves to these considerations. At home, the patient just weaned from TPN with NE. The Octreotide is undoubtedly helpful in reducing the output of the fistula by 80% in our experience. If we decided to feed the patient orally, the output would increase because of the fistula position and feed molecular structure, causing the patient's metabolic imbalance. If TPN treatment is resumed, we will expose the patient to sepsis, thrombosis, and embolism risks with a marked deterioration in the quality of life. We propose that those who produce case reports on the subject follow the same scheme to make papers comparable and carry out a Cochran survey for homogeneous groups to formulate guidelines and experimental clinical protocol.

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