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MOGUĆNOSTI I OGRANIČENJA KONZERVATIVNOG LEČENJA ENTEROKUTANIH FISTULA TANKOG CREVA

Uvod

Enterokutane fistule (EKF) predstavljaju ozbiljnu i potencijalno životno ugrožavajuću komplikaciju koja podrazumeva abnormalnu komunikaciju između gastrointestinalnog trakta i kože. U preko 85% slučajeva EKF nastaju kao posledica postoperativnih komplikacija, dok se u manjem broju slučajeva javljaju spontano, najčešće kod pacijenata sa inflamatornim bolestima creva, malignitetima, infekcijama ili nakon zračne terapije.

U okviru enterokutanih fistula razlikuju se one koje potiču iz tankog i iz debelog creva (kolokutane fistule). Ovaj rad se fokusira isključivo na fistule tankog creva, koje predstavljaju specifičan klinički i terapijski izazov zbog svoje kompleksnosti i često produženog i složenog toka lečenja.

Spontano zatvaranje EKF je moguće, ali relativno redak ishod, koji zavisi od više faktora, uključujući protok fistule, prisustvo infekcije, nutritivni status pacijenta i osnovnu bolest. Razumevanje mehanizama koji utiču na spontano zatvaranje i faktora koji usmeravaju tok lečenja ključno je za pravilan izbor terapijskog pristupa i izbegavanje nepotrebnih invazivnih intervencija.

Cilj ovog rada je narativni pregled aktuelne literature, sa fokusom na konzervativne terapijske strategije, faktore prognoze i ishode lečenja enterokutanih fistula tankog creva.

Materijali i metode: Ovaj rad predstavlja narativni pregled literature usmeren na konzervativno lečenje enterokutanih fistula tankog creva. Sistematska pretraga je sprovedena u bazama PubMed, Scopus, Web of Science i Cochrane Library, sa fokusom na radove objavljene u periodu od 2010. do 2025. godine. Za pretragu su korišćene ključne reči i fraze na engleskom jeziku: enterocutaneous fistula, conser-

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vative management, spontaneous closure, intestinal fistula. Pretraga je ograničena na radove na engleskom i srpskom jeziku.

Identifikovano je više desetina radova koji se bave različitim aspektima enterokutananih fistula, uključujući dijagnostiku, faktore prognoze, konzervativne terapijske pristupe i ishode lečenja. Većina uključenih studija obuhvatala je pacijente sa enterokutananim fistulama tankog creva, koji su ispitivani u kontekstu faktora poput protoka fistule, infekcije, nutritivnog statusa i prisustva komorbiditeta. Ukupan broj pacijenata iz relevantnih studija procenjuje se na nekoliko hiljada.

Uključene su studije koje su se fokusirale na konzervativni tretman kao osnovni ili početni modalitet lečenja, sa posebnim osvrtom na faktore koji utiču na spontano zatvaranje fistula. Isključene su studije koje obrađuju fistule debelog creva (kolokutane fistule) ili druge etiologije van fokusa rada.

Pregled i selekcija radova izvršeni su na osnovu naslova, apstrakta i punog teksta, a sintetizovani podaci su interpretirani deskriptivno, uz naglasak na identifikaciju ključnih principa konzervativnog lečenja, indikacija i ograničenja.

S obzirom na heterogenost studija i dizajn, koji varira od retrospektivnih serija slučajeva do meta-analiza, cilj rada je bio pružiti pregled aktuelnih saznanja i praktičnih smernica za vođenje pacijenata sa enterokutananim fistulama tankog creva.

Diskusija

Enterokutane fistule (EKF) predstavljaju ozbiljnu komplikaciju abdominalnih hirurških zahvata i patološku vezu između gastrointestinalnog trakta i kože. Njihova pojava značajno komplikuje tok lečenja pacijenata, povećava morbiditet i produžava hospitalizaciju (Härle i sar., 2024) [1]. Postoperativni uzrok je dominantan, sa oko 85% fistula koje nastaju usled dehiscencije anastomoze, infekcija ili nekroze okolnog tkiva, dok preostalih 15% obuhvata spontano nastale fistule koje su često povezane sa inflamatornim bolestima creva, malignitetima, traumama i zračenjem (Tang i sar., 2023; Rao i Reddy, 2025) [2, 3].

Stopa spontanog zatvaranja fistula varira značajno u literaturi, što odražava heterogenost pacijenata, različite protokole lečenja i selekciju slučajeva. Prosečne vrednosti spontanog zatvaranja kreću se između 15% i 30%, međutim, u određenim studijama su zabeleženi i značajno viši procenti, od 50% pa i do 70–79% u selektovanim populacijama sa optimalno sprovedenim konzervativnim tretmanom (Vărcuş i sar., 2022; Martinez i sar., 2008; Zhou i sar., 2024) [10, 9, 12]. Ove varijacije ukazuju na značaj precizne identifikacije pacijenata koji imaju veći potencijal za spontano zatvaranje, što je ključno za odabir terapijskog pristupa.

Konzervativni tretman EKF ima dvostruku funkciju – pokušaj postizanja spontanog zatvaranja fistule i istovremeno stabilizaciju pacijenta kao pripremu za

eventualnu hiruršku korekciju (Ali i sar., 2022; Deipolyi i Oklu, 2014) [4, 5]. Kontrola infekcije je jedan od najvažnijih faktora za uspeh lečenja. Prisutnost sepse, intraabdominalnih apscesa i peritonitisa značajno smanjuju šanse za spontano zatvaranje i povećavaju stopu komplikacija (Fischer i Bland, 2007; Liang i sar., 2023) [6, 7]. Selektivna antibiotska terapija i odgovarajuća drenaža su stoga neophodni, a kontinuirano praćenje kliničkog stanja i laboratorijskih parametara omogućava pravovremenu intervenciju.

Pored infekcije, mehanički i lokalni faktori imaju presudnu ulogu. Uklanjanje stranih tela, korekcija ishemije okolnog tkiva i smanjenje pritiska na fistulozni trakt omogućavaju regeneraciju i zaceljivanje. Zaštita kože oko fistule je od velike važnosti, jer iritacija crevnim sadržajem dovodi do maceracije, sekundarnih infekcija i komplikacija koje otežavaju lečenje (Härle i sar., 2024; Ali i sar., 2022) [1, 4].

U takvim situacijama koža oko fistule postaje crvena, vlažna i bolna, često sklona ulceracijama. Pravilna lokalna nega je stoga od suštinskog značaja. Preporučuje se pažljivo čišćenje i sušenje zahvaćenog područja, zatim primena zaštitnih barijernih sredstava kao što su kreme ili paste na bazi cink-oksida (npr. cink pasta), koje stvaraju mehaničku barijeru i ublažavaju iritaciju. U težim slučajevima mogu se koristiti specijalizovane obloge i barijerni filmovi, koji dodatno štite kožu i omogućavaju bolju toleranciju terapije.

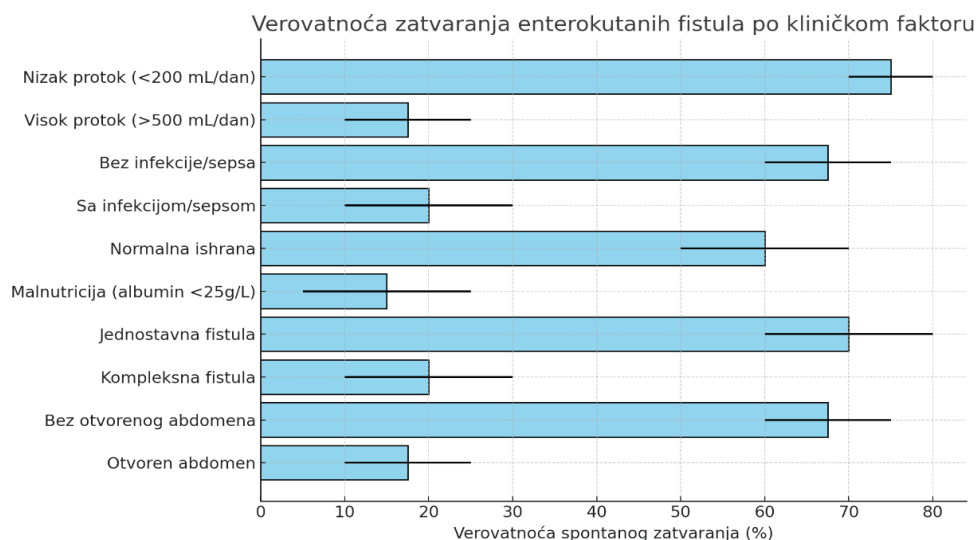
Nutritivni status pacijenta je možda i najvažniji faktor za uspeh konzervativnog tretmana. Hronični gubici tečnosti, proteina i elektrolita kroz fistulu brzo dovode do malnutricije, koja značajno usporava proces zarastanja (Lloyd i sar., 2006; Värčuš i sar., 2022) [14, 10]. Nizak nivo serumskog albumina (<25 g/L) predstavlja jak nezavisni faktor rizika za neuspeh lečenja i povećanu stopu komplikacija (Fischer i Bland, 2007) [6]. Prema smernicama, enteralna ishrana je poželjna kad god je moguća, jer podržava integritet crevne sluzokože i imuni odgovor, dok se kod fistula visokog protoka i kod pacijenata sa teškom kliničkom slikom koristi totalna parenteralna ishrana (TPN) (Tang i sar., 2023; Abubakar i sar., 2010) [2, 8]. Adekvatan nutritivni status uslov je za optimalan tok lečenja i smanjenje mortaliteta, što potvrđuju i metaanalize (Cheng i sar., 2023).

U molekularnom smislu, faktori kao što su VEGF i TGF- β igraju važnu ulogu u procesu angiogeneze i regeneracije tkiva, ali njihova efikasnost zavisi od opšteg stanja pacijenta i prisustva komorbiditeta (Ali i sar., 2022) [4]. Hronične inflamacije, maligniteti i prethodna zračenja smatraju se nepovoljnim faktorima za spontano zatvaranje (Rao i Reddy, 2025; Martinez i sar., 2008) [3, 9].

Među ključnim prognostičkim faktorima koji utiču na ishod konzervativnog lečenja EKF uočava se sledeće:

1. Protok fistule: Fistule sa protokom manjim od 200 mL/dan imaju značajno veće šanse za zatvaranje, dok visokoproduktivne fistule često zahtevaju hiruršku intervenciju (Fischer i Bland, 2007; Liang i sar., 2023) [6, 7].

2. Anatomska kompleksnost: Jednostruke fistule sa jednim kanalom imaju bolju prognozu u poređenju sa višekanalnim i kompleksnim fistulama (Härle i sar., 2024) [1].
3. Nutritivni status: Pored serumskog albumina, prisustvo sarkopenije i hipo-proteinemije povezani su sa lošim ishodima (Vărcaș i sar., 2022) [10].
4. Infekcija i sepsa: Aktivna infekcija i apscesi značajno smanjuju stopu zatvaranja (Tang i sar., 2023) [2].
5. Otvoren abdomen (open abdomen): Postoji negativan uticaj na zatvaranje fistula, sa značajno nižim šansama za uspeh (Fischer i Bland, 2007) [6].



Grafikon 1. Procenjeni opseg verovatnoće spontanog zatvaranja enterokutanih fistula konzervativnim tretmanom, u zavisnosti od ključnih kliničkih faktora. Vrednosti su sintetizovane na osnovu podataka iz više studija navedenih u diskusiji.

Farmakološki, upotreba analoga somatostatina, kao što je oktreotid, pokazuje korisne efekte u smanjenju protoka fistula, produženju vremena do zatvaranja i smanjenju trajanja hospitalizacije (Deipolyi i Oklu, 2014; Cheng i sar., 2023) [5]. Ipak, nije uočeno značajno poboljšanje u mortalitetu, što ukazuje da su ovi lekovi korisni kao dodatak, ali ne i zamena za sveobuhvatnu terapiju.

Terapijske metode, poput negativnog pritiska (NPWT) i primene fibrin-lepka (fibrin glue), pokazuju obećavajuće rezultate u selektovanim slučajevima, posebno kod fistula sa povoljnim karakteristikama (Zhou i sar., 2024) [12]. NPWT pomaže u održavanju suve i kontrolisane lokalne sredine, podstičući granulaciju i smanjujući rizik od sekundarnih infekcija (Cheng i sar., 2023) [5].

Značajan izazov kod konzervativnog tretmana predstavlja dugotrajnost procesa i potreba za kontinuiranim praćenjem. Tok lečenja može trajati nedeljama, čak i do nekoliko meseci, zahtevajući hospitalizaciju, prilagođavanje nutritivnog režima, ponovnu evaluaciju fistule i eventualnu pripremu za hiruršku intervenciju ukoliko spontano zatvaranje nije postignuto (Tang i sar., 2023; Vărcuş i sar., 2022) [2, 10]. Hirurška intervencija se preporučuje nakon što se postigne adekvatna nutritivna i infekcijska stabilizacija pacijenta, kako bi se smanjio rizik od recidiva i komplikacija (Owen i sar., 2013) [16].

Upravo zbog složenosti i heterogenosti kliničkih stanja, multidisciplinarni pristup, koji uključuje hirurge, nutricioniste, radiologe i specijaliste intenzivne nege, neophodan je za uspešno vođenje pacijenata sa EKF.

Zaključak

Enterokutane fistule tankog creva predstavljaju ozbiljan klinički izazov koji zahteva individualizovan i multidisciplinarn pristup. Iako većina pacijenata na kraju zahteva hirurško lečenje, konzervativna terapija ima nezamenljivu ulogu, kako u pokušaju spontanog zatvaranja tako i u pripremi pacijenta za bezbedniju i uspešniju operaciju. Ishod konzervativnog tretmana u velikoj meri zavisi od faktora kao što su protok i složenost fistule, prisustvo infekcije, nutritivni status i opšte zdravstveno stanje bolesnika. Pravilno sprovedena nutritivna podrška, kontrola infekcije, odgovarajuća lokalna nega i upotreba dodatnih terapijskih metoda (npr. somatostatin, NPWT, fibrinski lepak) mogu značajno poboljšati šanse za uspešan ishod.

Razumevanje patofiziologije i identifikacija prognostičkih faktora ključni su za pravovremenu odluku o nastavku konzervativnog lečenja ili upućivanju na operativni zahvat. Dalja istraživanja i standardizacija terapijskih protokola doprinela bi unapređenju kvaliteta lečenja i smanjenju mortaliteta kod pacijenata sa EKF.

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CONSERVATIVE MANAGEMENT OF SMALL BOWEL ENTEROCUTANEOUS FISTULAS: POSSIBILITIES AND LIMITATIONS

Introduction

Enterocutaneous fistulas (ECF) represent a serious and potentially life-threatening complication characterized by an abnormal communication between the gastrointestinal tract and the skin. In over 85% of cases, ECF occur as a result of postoperative complications, while spontaneous occurrence is less common, mostly seen in patients with inflammatory bowel diseases, malignancies, infections, or following radiation therapy. Among enterocutaneous fistulas, a distinction is made between those originating from the small intestine and those from the large intestine (colocutaneous fistulas). This paper focuses exclusively on small bowel fistulas, which represent a specific clinical and therapeutic challenge due to their complexity and often prolonged and complicated course of treatment. Spontaneous closure of ECF is possible but relatively rare, depending on several factors including fistula output, presence of infection, patient nutritional status, and underlying disease. Understanding the mechanisms influencing spontaneous closure and the factors guiding treatment course is crucial for appropriate therapeutic decision-making and avoiding unnecessary invasive interventions. The aim of this paper is a narrative review of current literature, focusing on conservative therapeutic strategies, prognostic factors, and treatment outcomes of small bowel enterocutaneous fistulas.

Materials and Methods

This paper presents a narrative literature review focused on the conservative treatment of small bowel enterocutaneous fistulas. A systematic search was conducted in

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the PubMed, Scopus, Web of Science, and Cochrane Library databases, concentrating on articles published between 2010 and 2025. The search utilized English keywords and phrases: enterocutaneous fistula, conservative management, spontaneous closure, intestinal fistula. The search was limited to articles in English and Serbian.

Several dozen articles addressing various aspects of enterocutaneous fistulas were identified, including diagnostics, prognostic factors, conservative therapeutic approaches, and treatment outcomes. Most included studies involved patients with small bowel enterocutaneous fistulas, examined in the context of factors such as fistula output, infection, nutritional status, and presence of comorbidities. The total number of patients in relevant studies is estimated to be in the several thousands. Studies focusing on conservative treatment as the primary or initial treatment modality were included, with particular attention to factors influencing spontaneous fistula closure. Studies addressing large bowel fistulas (colocutaneous fistulas) or other etiologies outside the scope of this paper were excluded.

Screening and selection of articles were performed based on titles, abstracts, and full texts. The synthesized data were interpreted descriptively, emphasizing identification of key principles of conservative treatment, indications, and limitations.

Given the heterogeneity of studies and designs ranging from retrospective case series to meta-analyses, the aim of this review was to provide an overview of current knowledge and practical guidance for managing patients with small bowel enterocutaneous fistulas.

Discussion

Enterocutaneous fistulas (ECF) represent a serious complication of abdominal surgical procedures and constitute a pathological connection between the gastrointestinal tract and the skin. Their occurrence significantly complicates patient management, increases morbidity, and prolongs hospitalization (Härle et al., 2024) [1]. The postoperative cause is dominant, with about 85% of fistulas arising due to anastomotic dehiscence, infections, or necrosis of surrounding tissue, while the remaining 15% include spontaneously occurring fistulas often associated with inflammatory bowel diseases, malignancies, trauma, and radiation (Tang et al., 2023; Rao and Reddy, 2025) [2,3]. The rate of spontaneous fistula closure varies significantly in the literature, reflecting patient heterogeneity, different treatment protocols, and case selection. Average rates of spontaneous closure range between 15% and 30%; however, some studies have reported significantly higher percentages, from 50% up to 70–79% in selected populations with optimally managed conservative treatment (Vărcuș et al., 2022; Martinez et al., 2008; Zhou et al., 2024) [10,9,12]. These variations highlight the importance of precisely identifying patients with a higher potential for spontaneous closure, which is crucial for selecting the therapeutic approach.

Conservative treatment of ECF serves a dual purpose—attempting spontaneous fistula closure and simultaneously stabilizing the patient in preparation for possible surgical correction (Ali et al., 2022; Deipolyi and Oklu, 2014) [4,5]. Infection control is one of the most important factors for treatment success. The presence of sepsis, intra-abdominal abscesses, and peritonitis significantly reduces the chances of spontaneous closure and increases complication rates (Fischer and Bland, 2007; Liang et al., 2023) [6,7]. Selective antibiotic therapy and appropriate drainage are therefore essential, with continuous monitoring of clinical status and laboratory parameters enabling timely intervention. Besides infection, mechanical and local factors play a crucial role. Removal of foreign bodies, correction of ischemia in surrounding tissue, and reduction of pressure on the fistulous tract enable regeneration and healing. Skin protection around the fistula is of great importance, as irritation from intestinal contents leads to maceration, secondary infections, and complications that hinder treatment (Härle et al., 2024; Ali et al., 2022) [1,4].

In such cases, the skin around the fistula becomes red, moist, and painful, often prone to ulcerations. Proper local care is therefore essential. Careful cleaning and drying of the affected area are recommended, followed by application of protective barrier agents such as zinc oxide-based creams or pastes (e.g., zinc paste), which create a mechanical barrier and soothe irritation. In more severe cases, specialized dressings and barrier films can be used to further protect the skin and improve therapy tolerance.

The patient's nutritional status is perhaps the most important factor for successful conservative treatment. Chronic losses of fluids, proteins, and electrolytes through the fistula rapidly lead to malnutrition, which significantly slows the healing process (Lloyd et al., 2006; Vărcuș et al., 2022) [14,10]. A low serum albumin level (<25 g/L) is a strong independent risk factor for treatment failure and increased complication rates (Fischer and Bland, 2007) [6]. According to guidelines, enteral nutrition is preferred whenever possible as it supports intestinal mucosal integrity and immune response, while total parenteral nutrition (TPN) is used in high-output fistulas and patients with severe clinical conditions (Tang et al., 2023; Abubakar et al., 2010) [2,8]. Adequate nutritional status is a prerequisite for optimal treatment course and reduced mortality, as confirmed by meta-analyses (Cheng et al., 2023).

At the molecular level, factors such as VEGF and TGF- β play important roles in angiogenesis and tissue regeneration, but their effectiveness depends on the patient's overall condition and presence of comorbidities (Ali et al., 2022) [4]. Chronic inflammation, malignancies, and previous radiation are considered unfavorable factors for spontaneous closure (Rao and Reddy, 2025; Martinez et al., 2008) [3,9].

Among the key prognostic factors influencing the outcome of conservative ECF treatment, the following stand out:

1. **Fistula output:** Fistulas with output less than 200 mL/day have significantly higher chances of closure, while high-output fistulas often require surgical intervention (Fischer and Bland, 2007; Liang et al., 2023) [6,7].
2. **Anatomical complexity:** Simple fistulas with a single tract have better prognosis compared to complex, multitract fistulas (Härle et al., 2024) [1].
3. **Nutritional status:** Besides serum albumin, presence of sarcopenia and hypo-proteinemia are associated with poor outcomes (Vărcuș et al., 2022) [10].
4. **Infection and sepsis:** Active infection and abscesses significantly reduce closure rates (Tang et al., 2023) [2].
5. **Open abdomen:** Has a negative impact on fistula closure with significantly lower success rates (Fischer and Bland, 2007) [6].

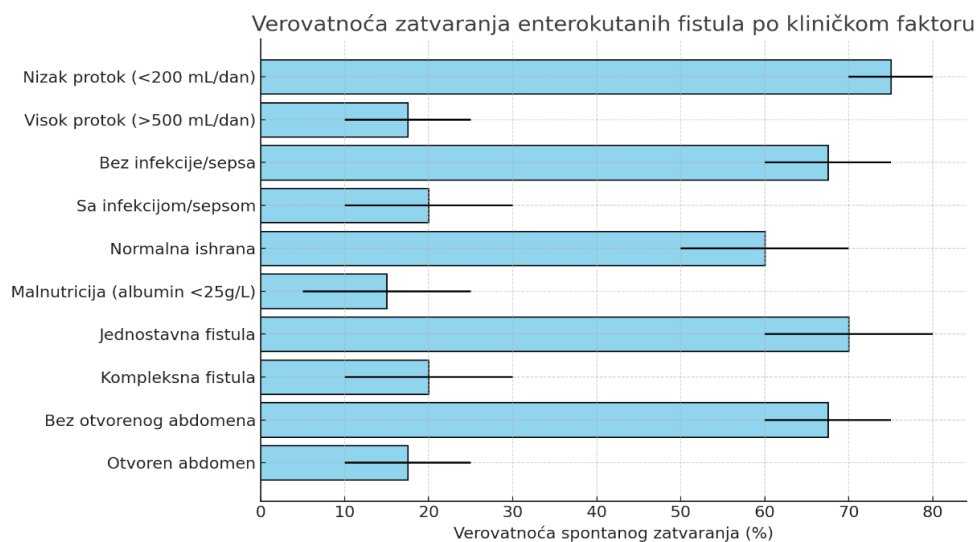


Chart 1. Estimated probability range of spontaneous closure of enterocutaneous fistulas with conservative treatment, depending on key clinical factors. Values synthesized from data in multiple studies cited in the discussion.

Pharmacologically, the use of somatostatin analogs such as octreotide shows beneficial effects in reducing fistula output, prolonging time to closure, and shortening hospital stay (Deipolyi and Oklu, 2014; Cheng et al., 2023) [5]. However, no significant improvement in mortality has been observed, indicating these drugs are useful adjuncts but not replacements for comprehensive therapy. Therapeutic methods such as negative pressure wound therapy (NPWT) and fibrin glue application show promising results in selected cases, especially in fistulas with favorable characteristics (Zhou et al., 2024) [12]. NPWT

helps maintain a dry and controlled local environment, promoting granulation and reducing the risk of secondary infections (Cheng et al., 2023) [5]. A significant challenge in conservative treatment is the prolonged process and need for continuous monitoring. The treatment course can last weeks to months, requiring hospitalization, nutritional regimen adjustments, fistula reassessment, and possible preparation for surgery if spontaneous closure is not achieved (Tang et al., 2023; Vărcuș et al., 2022) [2,10]. Surgical intervention is recommended after adequate nutritional and infectious stabilization to reduce the risk of recurrence and complications (Owen et al., 2013) [16].

Due to the complexity and heterogeneity of clinical conditions, a multidisciplinary approach involving surgeons, nutritionists, radiologists, and intensive care specialists is essential for successful management of patients with ECF.

Conclusion

Small bowel enterocutaneous fistulas represent a serious clinical challenge requiring an individualized and multidisciplinary approach. Although most patients ultimately require surgical treatment, conservative therapy plays an indispensable role both in attempting spontaneous closure and in preparing the patient for a safer and more successful operation. The outcome of conservative treatment largely depends on factors such as fistula output and complexity, presence of infection, nutritional status, and the patient's overall health condition. Properly implemented nutritional support, infection control, appropriate local care, and the use of adjunctive therapeutic methods (e.g., somatostatin, NPWT, fibrin glue) can significantly improve the chances of a successful outcome. Understanding the pathophysiology and identifying prognostic factors is crucial for timely decision-making regarding continuation of conservative management or referral for surgery. Further research and standardization of therapeutic protocols would contribute to improving treatment quality and reducing mortality in patients with ECF.

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