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Clinical and microbiological evaluation in patients with Fournier's gangrene

Ocena kliniczna i mikrobiologiczna u chorych na zgorzel Fourniera

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Abstract

Introduction: Necrotising fasciitis (Fournier's gangrene) is a bacterial inflammation of the subcutaneous tissues and skin, involving the urogenital area. The treatment is complex, with a high risk of systemic infection. A key aspect of treatment is antibiotic therapy. **Materials and methods:** The analysis involved 30 hospitalised patients with Fournier's gangrene. An attempt was made to determine the relationship between laboratory parameters, types of pathogens, patterns of antibiotic susceptibility/resistance, and treatment outcomes. **Results:** The average value of Fournier's Gangrene Severity Index (FGSI) was 4.37 ± 2.87. In the study group, a total of 18 (60%) patients had an infection caused by a single bacterial strain, while 12 (40%) had infections caused by multiple strains. The most commonly identified bacteria was *Escherichia coli* (53.33%) – 50% of monocultural infections and 58.33% of polyculture infections. The majority of bacteria were sensitive to piperacillin–tazobactam – 22 (73.33%) patients, clindamycin – 20 (66.66%) patients, and metronidazole – 18 (60%) patients. The highest percentage of antibiotic resistance was observed for cefuroxime – 19 (63.33%) patients, ciprofloxacin – 19 (63.33%) patients, and ceftriaxone – 17 (56.66%) patients. The average hospitalisation length was 30.03 ± 23.01 days. The overall mortality rate was 13.33% (n = 4). No correlation was found between the type of pathogen, hospitalisation length or mortality. No differences were observed in the results of laboratory parameters, FGSI, or length of hospitalisation in the analysed subgroups. **Conclusions:** Effective treatment of Fournier's gangrene requires performing a wound swab culture as quickly as possible and implementing a targeted antibiotic therapy. There is no single laboratory parameter that can predict treatment outcomes and patient prognosis. There are no differences in the clinical course and prognosis between multibacterial and monobacterial infections.

Keywords: *E. coli*, necrotising fasciitis, Fournier's gangrene, perineal infection

Streszczenie

Wprowadzenie: Martwicze zapalenie powięzi (zgorzel Fourniera) to bakteryjne zapalenie tkanek podskórnych i skóry obejmujące okolicę krocza i układu moczowo-płciowego. Leczenie choroby jest złożone i wieloetapowe, a ryzyko infekcji ogólnoustrojowej – wysokie. Kluczowy aspekt leczenia stanowi właściwa antybiotykoterapia. **Materiał i metody:** Analizie poddano przypadki 30 chorych hospitalizowanych z powodu zgorzeli Fourniera. Podjęto próbę stwierdzenia zależności między parametrami laboratoryjnymi, rodzajem patogenów, wzorcami wrażliwości/oporności na antybiotyki oraz wynikami leczenia. **Wyniki:** Średnia wartość Fournier's Gangrene Severity Index (FGSI) wyniosła 4,37 ± 2,87. W grupie badanej u 18 (60%) osób rozpoznano infekcję jednym szczepem bakterii, a u 12 (40%) – wieloma szczepami. Najczęściej identyfikowaną bakterią była *Escherichia coli*, obecna u 17 chorych (53,33% całej grupy) – 50% pacjentów z zakażeniami jednobakteryjnymi i 58,33% z zakażeniami wielobakteryjnymi. Większość bakterii była wrażliwa na piperacylinę–tazobaktam – 22 (73,33%) przypadki, klindamycynę – 20 (66,66%) i metronidazol – 18 (60%). Najwyższy stopień oporności na antybiotyki dotyczył cefuroksymu – 19 (63,33%) przypadków, ciprofloksacyny – 19 (63,33%) i ceftriaksonu – 17 (56,66%). Hospitalizacja trwała średnio 30,03 ± 23,01 dnia. Całkowita śmiertelność wyniosła 13,33% (n = 4). Nie stwierdzono korelacji między rodzajem patogenua długością hospitalizacji lub śmiertelnością. Między analizowanymi podgrupami nie zaobserwowano różnic w parametrach laboratoryjnych, FGSI ani długości hospitalizacji. **Wnioski:** Skuteczne leczenie zgorzeli Fourniera

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wymaga jak najszybszego wykonania posiewu z wymazu z rany i zastosowania celowanej antybiotykoterapii. Nie istnieje pojedynczy parametr laboratoryjny, który pozwoliłby określić rokowanie i przewidzieć wyniki leczenia. Między podgrupami chorych z zakażeniami wielo- i jednobakteryjnymi nie wykazano różnic w przebiegu klinicznym i rokowaniu.

Słowa kluczowe: *E. coli*, martwicze zapalenie powięzi, zgorzel Fourniera, bakteryjna infekcja krocza

INTRODUCTION

Fournier's gangrene (FG) is a devastating, aggressive, and necrotising infectious process that affects the perineum and genitourinary regions. The disease is considered a sub-category of necrotizing fasciitis due to its common aetiology and management methods[1]. The incidence of FG is estimated to be 1.6/100,000 males in the United States population, with a marked peak of 3.3/100,000 in the 50–79-year-old subpopulation[2].

The first symptoms typically include a painful swelling of the scrotum or perineum. It can be followed by fever and sepsis[1]. Physical examination shows necrotic areas of skin with additional oedema and erythema. Other symptoms occurring in more advanced cases include crepitus on palpation and a foul-smelling exudate. Fournier's gangrene can also be associated with epididymo-orchitis, perianal abscess, scrotal abscess, orchitis with abscess, epididymitis, scrotal phlegmon, gangrene of the scrotum and penis, orchitis with necrosis, inflammation of the skin and subcutaneous tissue of the penis, and gangrene of the scrotum, perineum, and buttocks[3].

The risk factors for FG occurrence and mortality rate include recent urological surgery, older age, alcoholism, renal failure, overweight or obesity, diabetes or malnutrition, and even specific drug intake[4,5]. The drugs that can contribute to FG are antidiabetic agents called sodium-glucose co-transporters type 2 (SGLT-2) inhibitors – flozins[6–8].

The most common microbiological aetiology of FG is a polymicrobial aerobic and anaerobic synergistic infection of the fascia and subcutaneous soft tissue. The most common Gram-positive bacteria are Group A *Streptococci* and *Staphylococcus aureus*, while the most prevalent Gram-negative bacteria are *Escherichia coli* and *Pseudomonas aeruginosa*. However, the microbiological evaluation shows mixed cultures in the majority of cases, and monoculture can also occur.

The treatment is often highly demanding due to the fact that the majority of patients quickly exhibit systemic infection symptoms, such as high fever and chills, while some may develop septic shock or organ failure[9]. Thus, quick and proper diagnosis and treatment are crucial for survival and complications rate. In almost 40% of cases, the treatment can be delayed due to vague and uncertain symptoms; thus, careful examination, particularly of obese patients, is needed. Imaging tests, such as computed tomography (CT) or magnetic resonance imaging (MRI), can also be helpful in defining pararectal involvement, although are not obligatory[1,10].

The treatment of FG should be interdisciplinary, and be a combination of surgical and urological interventions, antibiotic therapy, negative-pressure wound therapy (NPWT), hyperbaric oxygen therapy (HBOT), and plastic reconstructive procedures. First-line treatment is, of course, antibiotic therapy. The European guidelines advocate for immediate empiric parenteral antibiotic treatment after setting up the diagnosis[11]. The antibiotic combination should cover all probable causative microorganisms, assuming potential penetration of the inflammatory tissue. A suggested regimen could consist of a broad-spectrum penicillin or third-generation cephalosporin, gentamicin, and metronidazole or clindamycin. If possible, it should be refined as quickly as possible by guided microbiological culture antibiotic therapy. It is suggested that samples for bacterial cultures are taken before the first antibiotic administration if possible. The suggested regimens for antimicrobial therapy for FG of mixed or unknown microbiological aetiology are presented in Tab. 1[12].

Since FG is a rare disease, it is difficult to conduct prospective studies. However, in this study, a set of data from a large number of FG cases that occurred in the last five years was collected and analysed to determine the relationship between microbiology and the prognosis of FG. The study also aimed to identify the local pathogens associated with FG and their antibiotic sensitivity/resistance patterns based on bacterial culture. Additionally, the relationship between causative pathogens and mortality was investigated.

MATERIALS AND METHODS

In this retrospective study, we analysed data of 30 patients treated for FG from 2017 to 2022 in the Military Institute of Medicine – National Research Institute, Warsaw, Poland. The study group consisted of males only, with a mean age of 58 ± 15.37 years. Fournier's gangrene was diagnosed on a clinical basis, followed by microbiological confirmation of bacterial infection by wound tissue swab samples. Our study primarily aimed to identify pathogens associated with FG in the Polish population, and determine their antibiotic sensitivity/resistance patterns, the relationship between causative pathogens, prognostic factors, and mortality.

Laboratory assessment

The laboratory assessment was based on the following parameters: C-reactive protein (CRP), morphology: white

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Antimicrobial	Dosage
Piperacillin–tazobactam plus vancomycin	4.5 g every 6–8 h IV, 15 mg/kg every 12 h
Imipenem–cilastatin	1 g every 6–8 h IV
Meropenem	1 g every 8 h IV
Ertapenem	1 g once daily
Gentamicin	5 mg/kg daily
Cefotaxime plus metronidazole or clindamycin	2 g every 6 h IV, 500 mg every 6 h IV, 600–900 mg every 8 h IV
Cefotaxime plus fosfomycin plus metronidazole	2 g every 6 h IV, 5 g every 8 h IV, 500 mg every 6 h IV
IV – intravenous.	

Tab. 1. Suggested antimicrobial therapy regimens for FG of mixed microbiological aetiology

blood cells (WBC), haematocrit (HCT), blood platelets (PLT), sodium (Na), potassium (K), creatinine measured with CKD-EPI formula (creatinine – 2021), procalcitonin (PCT), international normalised ratio (INR) of PT (prothrombin time). Morphology was evaluated using the Sysmex Corporation XN-1000 automatic haematology analyser (Japan). Biochemistry was analysed using the Roche Diagnostics assays (Germany) and Hitachi High-Tech Corporation COBAS c503 PRO Automatic Analyzer (Japan).

Microbiological assessment

Samples for microbiological tests were taken from the gangrene wound. The collector was the attending physician, and the procedure was performed with maintaining aseptic rules. The microbiological assessment was performed at the Department of Medical Diagnostics of the Military Institute of Medicine, following the standard bacterial culture procedure. Pathogen types and antibiotic sensitivity or resistance patterns were assessed by experienced specialists with at least 10 years of professional experience.

Statistical analysis

Statistical analysis was performed using the IBM Statistical Package for the Social Sciences (IBM SPSS Statistics Corp.; Armonk, NY, USA) version 26 for Windows. Results with normal distribution were presented as means (*M*) and standard deviations (*SD*). Differences between groups were analysed using the *t*-Student test for independent means (two-tailed). A significance level of $p < 0.05$ was adopted.

RESULTS

Males admitted to the hospitals had primarily clinical assessment. In the first day of admission their mean systolic blood pressure was 115.84 ± 21.6 mm Hg, diastolic blood pressure was 70.84 ± 10.92 mm Hg, and hearth rate was 95.44 ± 27.89 per minute. The mean body temperature was 37.44 ± 1.29°C. The patients were assessed by the Fournier's Gangrene Severity Index score. The mean result was 4.37 ± 2.87 (range 1–12 points). Detailed biochemical and morphology parameters are presented in Tab. 2.

A Foley catheter was applied in 25 (83.33%) patients, and a suprapubic catheter in 12 (40%) individuals. Both urinary diversions was performed in 9 (30%) patients – in all these patients, a Foley catheter was followed by suprapubic cystostomy (after its removal). In the study group ($n = 30$), 18 (60%) individuals had monocultural infection, and in 12 (40%) polyculture infection was found. The most common microbiome involved in FG was *Escherichia coli*, which was found in 50% cases of monocultural infections ($n = 9$), and in 58.33% cases of polyculture infections ($n = 7$). The detailed distributions of bacterial cultures are presented in Fig. 1 and Tab. 3.

The microbiological evaluation showed that the majority of bacteria were sensitive to piperacillin–tazobactam ($n = 22$), clindamycin ($n = 20$), and metronidazole ($n = 18$). The highest rate of antibiotic resistance was for cefuroxime ($n = 19$), ciprofloxacin ($n = 19$), and ceftriaxone ($n = 17$). The most commonly used targeted antibiotic therapy included metronidazole, vancomycin, clindamycin, carbapenems, piperacillin, and tazobactam or linezolid, or their combinations. The mean length of hospital stay was 30.03 ± 23.01 days. The overall FG mortality rate was 13.33% ($n = 4$). The number of deaths in the two subgroups was equal (2 vs. 2). No correlation was noted between the type of pathogen and the length of hospital stay or mortality. Also, there were no differences in inflammation indicators (CRP, WBC, PCT) in the subgroups of patients infected with one culture of bacteria and those with polyculture infection ($p = 0.816$, $p = 0.483$, $p = 0.770$, respectively). The Fournier Gangrene Severity Index (FGSI) and length of hospitalisation did not differ statistically, either ($p = 0.566$, $p = 0.414$, respectively). The detailed parameters of both subgroups are presented in Tab. 4.

Parameter	Range	*M*	*SD*
CRP [mg/dL]	0–0.5	23.25	32.19
WBC [1,000/µL]	4.3–9.64	15.97	6.77
HCT [%]	40–51	33.52	6.69
PLT [1,000/µL]	160–350	280.55	129.84
Na [mmol/L]	136–145	135.89	6.02
K [mmol/L]	3.5–5.1	4.29	0.83
Crea [mg/dL]	0.7–1.2	1.61	1.18
GFR [mL/min/1.73 m^2]	>90	58.00	15.37
PCT [ng/mL]	<0.046	47.92	86.91
INR	0.8–1.2	1.42	0.55
CRP – C-reactive protein; **WBC** – white blood cells; **HCT** – haematocrit; **PLT** – blood platelets; **Na** – sodium; **K** – potassium; **Crea** – creatinine; **GFR** – glomerular filtration rate; **PCT** – procalcitonin; **INR** – international normalised ratio; ***M*** – mean; ***SD*** – standard deviation.			

Tab. 2. Results of morphology and biochemical parameters of the study group

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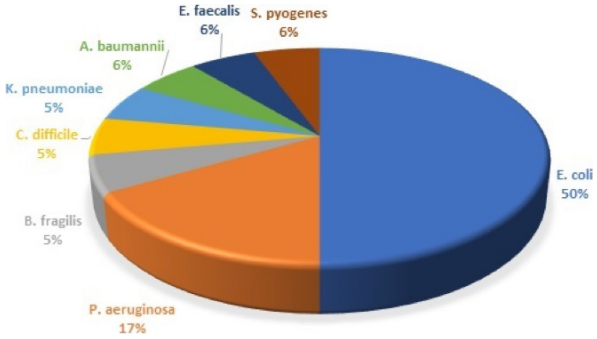


Fig. 1. Monocultures (n = *18) – bacterial distribution found in wound tissue*

Patient No.	Polycultures (*n* = 12)		
1	*Parabacteroides distasonis*	*Clostridium ramosum*	
2	*Escherichia coli*	*Streptococcus gallolyticus*	
3	*Escherichia coli*	*Streptococcus anginosus*	
4	*Acinetobacter baumannii*	*Staphylococcus aureus*	
5	*Proteus mirabilis*	*Enterococcus faecalis*	
6	*Enterococcus faecalis*	*Pseudomonas aeruginosa*	
7	*Escherichia coli*	*Enterococcus faecalis*	*Proteus mirabilis*
8	*Escherichia coli*	*Pseudomonas aeruginosa*	
9	*Escherichia coli*	*Bacteroides fragilis*	
10	*Escherichia coli*	*Enterococcus faecalis*	*Klebsiella pneumoniae*
11	*Escherichia coli*	*Enterococcus avium*	
12	*Klebsiella pneumoniae*	*Enterococcus faecalis*	

Tab. 3. Polycultures of bacteria found in wound tissues

Representative pictures of patients treated for FG are presented in the Figs. 2, 3.

DISCUSSION

We observed that the majority of FG cases were caused by monomicrobial infections, though the results were not statistically significant. The most common pathogen causing both monomicrobial and polymicrobial infections was *Escherichia coli*. These results are not surprising, as the pathogen is commonly found in the urinary tract, and many individuals, particularly elderly patients, are carriers of the bacteria[13,14]. Evaluation of antibiotic resistance showed that the bacteria were most commonly sensitive to piperacillin–tazobactam, clindamycin, and metronidazole, while the highest rates of antibiotic resistance were observed for cefuroxime, ciprofloxacin, and ceftriaxone. Following guidelines and antibiotic availability in the hospitals where the study was conducted, piperacillin–tazobactam or clindamycin were the most commonly chosen first-line empirical

Parameter	Monoculture (*n* = 18)		Polyculture (*n* = 12)		*p*
	M	*SD*	*M*	*SD*	
CRP [mg/dL]	245.35	392.57	215.35	189.27	0.816
WBC [1,000/μL]	15.51	6.99	16.62	6.40	0.483
PCT [ng/mL]	51.87	97.00	39.24	70.06	0.770
FGSI	4.11	2.42	4.75	3.39	0.566
L [days]	39.24	25.78	25.67	17.18	0.414

CRP – C-reactive protein; **WBC** – white blood cells; **PCT** – procalcitonin; **FGSI** – Fournier Gangrene Severity Index; **L** – hospitalisation length; ***M*** – mean; ***SD*** – standard deviation.

Tab. 4. Comparison of parameters in the subgroups with monoculture and polyculture infections

antibiotics. As for the second-line antibiotics, metronidazole or clindamycin were most frequently used. The mortality rate of patients in our study was 13.33%, i.e. slightly lower than that reported in most recent studies and analyses[15,16]. We did not find any factors that correlated with hospitalisation length, FGSI, or treatment outcomes.

As FG is a rare condition affecting the perineal and urogenital regions, and the clinical course of the disease is fulminant and varies among individuals, establishing accurate guidelines poses a significant challenge[17]. When managing patients with FG, extensive and repeated debridement of the gangrenous tissue is often necessary[18]. Several studies have shown that diabetes, old age, low blood pressure, high creatine kinase and lactate levels, abdominal involvement, haemoglobin level <10 g/dL, and a platelet count of less than 150×10^9/L are associated with poor outcomes in the perineum or genital area with gangrenous changes, though the data are not conclusive[19,20]. The data obtained in our study do not provide evidence suggesting that any single parameter significantly affects prognosis and treatment outcomes; however, the small group of patients may limit the generalisability of the findings.

Modern guidelines and recommendations emphasise the need for prompt initiation of treatment for FG with broad-spectrum antibiotics, followed by refinement based on culture and clinical response. It is important to note that the causative agents of the disease may vary by world region and study period. In a 2017 study by Yilmazlar et al., involving 50 patients from the Turkish population, the majority of FG cases were caused by monomicrobial infection – in 20% of patients and polymicrobial infection – in 76%. In the remaining cases, no bacteria were found. In the study, *Escherichia coli* was the most commonly identified microorganism (72%), followed by *Enterococcus* sp. (62%) and *Acinetobacter baumannii* (30%)[21]. A comparison of these findings with our study reveals differences in distribution; however, *Escherichia coli* remains the most common cause of infection. Despite antibiotic therapy, the mortality rate in the Turkish group was 26%. Bjurlin et al. demonstrated that the generally accepted and recommended empirical

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Fig. 2. Extensive necrosis of the scrotal and penile skin along with massive oedema of the surrounding subcutaneous tissue. Original material



Fig. 3. Condition after extensive resection of necrotic tissues in the perineal area. Original material

antibiotic therapy includes gentamicin, clindamycin, and ampicillin-sulbactam/3rd-generation cephalosporin. Some studies have suggested using metronidazole instead of clindamycin, as well as other aminoglycosides or fluoroquinolone-group antibiotics instead of gentamicin (which is also an aminoglycoside)[22]. In another study, by Castillejo Becerra et al., the authors confirmed that the majority of bacteria were sensitive to ampicillin-sulbactam, ceftriaxone, piperacillin–tazobactam, amikacin, and cefepime, while they were resistant to ampicillin, trimethoprim–sulfamethoxazole, levofloxacin, and clindamycin. Additionally, in their study, *Enterococcus faecalis* and *Streptococcus anginosus* were mostly resistant to vancomycin[23]. A retrospective comparative cohort study involving 168 patients found no significant differences in mortality between the patients on standard and prolonged parenteral antibiotic therapy (<10 days for 80 patients versus >10 days for 88 patients)[24]. The results demonstrated that shorter antibiotic courses in patients who achieved source control and initial antibiotic selection, excluding resistant organisms, did not lead to worse outcomes in FG. However, the most crucial aspect is that all studies have shown that antibiotic therapy for FG treatment should be adjusted based on culture and antibiogram results. Furthermore, empirical therapy should be modified according to changes in bacterial flora, taking into account regional trends.

One of the conditions predisposing individuals to the development of FG is diabetes[9,25]. Recently, there has been an increasing case of using drugs from the SGLT-2 receptor inhibitor group in the treatment of diabetes. These drugs, commonly known as flozins, apart from their hypoglycaemic effects, are drugs also demonstrating cardioprotective and nephroprotective effects. The mechanism of their action involves the induction of glucosuria, resulting in the most common adverse effects primarily related to urinary and genital tract infections[26]. In 2018, the U.S. Food and Drug Administration (FDA) reported 12 cases of FG in patients using SGLT-2 inhibitors between March 2013 and May 2018, adding it as an adverse effect[27]. It has been established that the use of these drugs increases the risk of FG[28]. Fadini et al. described 47 cases of FG among patients using SGLT-2 inhibitors during a similar time period as that analysed by the FDA[29]. Similarly, Bersoff-Matcha et al. reported 55 cases of FG in patients using SGLT-2 inhibitors between March 2013 and January 2019[28]. The exact pathophysiology of this phenomenon is not entirely clear, but it appears that induced glucosuria has an immunomodulatory effect and increases bacterial adhesion to the urothelium[30]. Glucosuria induced by SGLT-2 inhibitors creates an environment that promotes infections in the genital area, which can serve as a precursor to the development of FG. Therefore, it is important to be aware of the possible severe complications associated with the use of SGLT-2 inhibitors and exercise caution when prescribing this group of drugs to susceptible patients. If FG is suspected in a patient, immediate discontinuation of SGLT-2 inhibitor medications,

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along with antibiotic therapy and surgical intervention, if necessary, should be implemented.

Surprisingly, European guidelines do not recommend the use of adjunctive treatments for FG, except for methods required in the context of other clinical symptoms and the patient's condition[11]. However, a systematic review regarding wound closure techniques in the genitourinary area showed low-quality evidence (16 case series of patients with FG) recommending primary or secondary wound closure for scrotal defects using flaps, skin grafts, or extension outside the scrotum as possible additional treatments[31]. Another study, a randomised clinical trial from 2004, investigated the use of honey-soaked dressings in the treatment of FG[32]. In a relatively small group of 30 patients, 14 were treated with honey-soaked dressings, resulting in healthy granulation appearing in 4 patients within one week and in all patients within 3 weeks. The mortality rate in this group was 7.14%. On the other hand, in 16 patients treated with Edinburgh University's Solution of Lime (EUSOL) dressings, healthy granulation occurred within 4 weeks, and the mortality rate was 12.5%. The mean hospitalization length was 28 days in the honey-dressing group and 32 days in the EUSOL-dressing group. A 2005 systematic review analysed the use of HBOT, which involved intermittent inhalation of 100% oxygen at pressures exceeding atmospheric pressure, as an additional treatment to antibiotics. However, the results were inconsistent and inconclusive[33]. Nevertheless, a more recent study suggested a potential benefit of hyperbaric oxygen therapy. The study, conducted on a small group of 16 patients, compared to 12 cases of FG without the use of such therapy, demonstrated higher treatment effectiveness[34].

Based on our own experience, resulting from the care of patients with difficult-to-heal and extensive wounds (with FG referred from other centres in Poland where other treatment options have been exhausted), it can be concluded that hyperbaric therapy (HBOT) and NPWT may cause significant clinical improvement. The observations in our centre to date show that the use of the above-mentioned methods and cooperation of interdisciplinary teams consisting of urologists, surgeons and infectious diseases specialists brings the best treatment results.

One possible evaluation method for patients with FG is using scales, such as the Fournier's Gangrene Severity Index (FGSI)[35]. The scale is based on nine parameters, including body temperature, heart rate, respiratory rate, serum sodium levels, serum potassium levels, serum creatinine levels, haematocrit, white blood cell count, and bicarbonate levels. Each parameter is assigned a score of 0–4 points, resulting in a total score of 0 to 36. A score of <4 points is considered within the normal range, while an FGSI value of 9 has been associated with an estimated 75% probability of death[36]. Conversely, an FGSI score of ≤9 has been associated with a 78% probability of survival[36]. However, it should be noted that the scale is non-intuitive, and the thresholds have not been confirmed in population-wide studies. The results obtained in our study also failed to confirm its accuracy and usefulness. Nonetheless, this does not undermine the potential of using the scale in predicting treatment outcomes in patients with FG.

A prospective cohort study found that disease severity scores did predict outcomes but were not superior to scoring systems used for critical care evaluation[37]. Furthermore, the mortality rates for FG reported in previous studies were 10% (in 650 cases), 7.5% (in 1,641 cases), and 5% (in 9,249 cases)[38–40], which aligns with the results obtained in our study. All the studies listed above emphasise the need for prompt initiation of proper antibiotic group, which seems to be crucial for treatment outcomes. Moreover, due to the fact that the causative pathogens of FG are shifting and differ depending on the world's region, empirical antibiotic treatments for this disease should be modified accordingly, bearing in mind that the most common bacteria is *Escherichia coli*. Thus early empirical antibiotic therapy should target that bacteria, followed by accurate analysis of causative pathogens of FG due to the fact that this treatment is most important element in the management of the disease.

CONCLUSIONS

The key aspect is the management of FG is accurate diagnosis based on clinical symptoms, followed by rapid administration of broad-spectrum antibiotics. It should be noted that empirical antibiotic therapy should be preceded by taking a swab culture from the infected wound (before the first dose of antibiotics). Due to the increasing antibiotic resistance and variations in the types of bacteria causing FG depending on the region of the world, antibiotic therapy should be targeted at locally occurring pathogens. There are no definitive clinical or laboratory parameters that would predict treatment outcomes and prognosis. Infections with multiple types of bacteria do not significantly impact the quality of treatment or prognosis compared to the infections caused by a single pathogen.

STRENGTHS AND WEAKNESSES OF THE STUDY

The study was retrospective and relied on the analysis of available clinical and laboratory parameters. The small sample size limited statistical analysis. However, FG is a rare disease, and most studies available in the literature are based on similar or smaller study groups. Furthermore, previous analyses did not focus on determining the impact of mono- and polymicrobial infections, which makes this work original and valuable.

Statement of ethics

The study was qualified as noninterventional observation study. According to the Act of 6 September 2001 Pharmaceutical Law, the study was qualified as noninterventional observation study. It means that

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1) the treatment's products will be used in the way, which determines the marketing authorization; 2) qualification of patient to the group which uses a specific treatment's strategy does not result based on study protocol but it will be achieved according to current medical practice; 3) any additional diagnostic procedures and monitoring procedures will not be used against the patient. Moreover, the researchers did not transfer the personal data of observed patients to the organizer. Thus, this study did not require approval by Ethics Committee and registration in Central Register of Clinical Studies.

Conflict of interest

The authors declare no conflict of interest.

Data availability statement

All appropriate and significant data had been placed in the manuscript. Due to privacy and ethical reasons, some anonymised data can be presented after written request.

Author contributions

Original concept of study: AG, TZ. Collection, recording and/or compilation of data: AG, ŁM. Analysis and interpretation of data: AG, ADD, ŁM. Writing of manuscript: AG, ADD, ACD, AG, TZ. Critical review of manuscript: AG, ADD, AG, TZ. Final approval of manuscript: AG, TS, TZ.

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