Practical Review of Necrotizing Fasciitis: Principles and Evidence-based Management

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Summary: Necrotizing fasciitis is a severe, life-threatening soft tissue infection that presents as a surgical emergency. It is characterized by a rapid progression of inflammation leading to extensive tissue necrosis and destruction. Nonetheless, the diagnosis might be missed or delayed due to variable and nonspecific clinical presentation, contributing to high mortality rates. Therefore, early diagnosis and prompt, aggressive medical and surgical treatment are paramount. In this review, we highlight the defining characteristics, pathophysiology, diagnostic modalities, current principles of treatment, and evolving management strategies of necrotizing fasciitis. *(Plast Reconstr Surg Glob Open 2024; 12:e5533; doi: 10.1097/GOX.0000000000005533; Published online 19 January 2024.)*

INTRODUCTION

Necrotizing fasciitis (NF) is a rapidly progressing soft tissue infection that aggressively spreads along fascial layers and subcutaneous tissues.[1–3] Common sites of infection include the extremities, abdomen, and perineum. NF can be idiopathic or secondary (after trauma, chronic wounds, or skin abrasions).[4,5] Diagnosis can often be challenging and is primarily diagnosed based on clinical presentation. NF has a mortality rate of 8.7%–76%, underscoring the need for timely and accurate diagnosis and prompt medical and surgical treatment.[3] This practical review will focus on the basic tenets of NF, including classification, comorbidities related to NF, clinical presentation and diagnosis, and nonsurgical and surgical management principles.

CLASSIFICATION

NF is classified as types I–IV (Table 1).[6–12] Type I, the most common, is the polymicrobial type, accounting for 70%–90% of all NF cases.[6] To qualify under this NF type, pathogenic bacteria need to consist of at least two microorganisms. On the other hand, type II NF is a monomicrobial infection commonly attributed to beta-hemolytic Streptococcus A (GAS or *S. pyogenes*).[7,8] Less commonly *Staphylococcus aureus* (*S. aureus*), including the

methicillin-resistant *S. aureus* (MRSA) (10%–30% incidence), can be the causative pathogen. MRSA increases the level of complexity and may lead to toxic shock syndrome, resulting in a more unfavorable outcome.[9,10] The most common pathogens isolated in type III NF infection are *Clostridium* pathogens, *Vibrio* species, and gram-negative bacteria.[8,12] Type IV infections consist of fungal infections, most commonly *Candida* species and zygomycetes.[11]

COMORBIDITIES

The most common comorbidity associated with NF is diabetes mellitus, which has not been directly associated with increased mortality.[13–15] Other commonly associated comorbidities encompass the conditions causing immunosuppression or chronic illnesses characterized by immune dysfunction, such as IV drug use, alcohol use, congestive heart failure, chronic kidney disease, and Addison disease.[16–20] Moreover, in these patients, progression to severe sepsis is more likely.[21–24]

DIAGNOSIS

Clinical Signs and Symptoms

The diagnosis of NF can often be challenging during its early stages, as it usually presents with a classic triad of nonspecific signs: swelling, severe pain, and erythema.[25] However, a prominent finding for NF is significant pain out of proportion to physical findings and beyond the involved skin because the infection spreads more quickly through fascia.[26–28] In addition to the classic triad, early symptoms include local warmth, skin sclerosis, induration, foul "dishwasher" discharge, fever, and diarrhea. Patients are critically ill if they present late, often with septic shock,

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multiple organ dysfunction syndrome, altered mental status, and extensive soft tissue necrosis.[9] More advanced findings include bullae and crepitus.[29] Even though NF can involve any body part, it most commonly affects the extremities, with an incidence of 36%–55%[9] (Fig. 1). Furthermore, it frequently affects the trunk (18%–64%) and the perineum (up to 36%).[30–34]

Diagnostic/Laboratory Tests

Certain laboratory tests assist in ruling out other alternative diagnoses. For instance, leukocytosis [white blood cells (WBC) > 20,000/L] is highly concerning for NF. Furthermore, elevated renal labs (BUN > 18 mg/dL and Cr > 1.2 mg/dL) are demonstrative for an acute renal injury, typically seen in NF patients. In addition, elevated creatinine kinase is common.[35] One study suggested that C-reactive protein (CRP) > 16 mg/dL or CK > 600 IU/L should initiate a more extensive workup for GAS NF.[36]

The risk of NF can also be obtained using laboratory index measures based on serum parameters, clinical presentation, and associated comorbidities (Table 2).[37–48] One such scoring tool is the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC), which classifies patients into risk categories with algorithms for diagnostic resources.[38–41] However, the diagnostic value of LRINEC decreases in patients with multiple comorbidities (due to weakened inflammatory response) and after some hospital interventions, such as blood transfusion.[42] Recently, the modified LRINEC score has been suggested, which adds liver disease and serum lactate levels to the equation while redefining the cut-off values for CRP, WBC, and Hgb. Another laboratory scoring test often used is Fournier

Takeaways

Question: Summarizing current data to provide practical insight into management of necrotizing fasciitis (NF) to guide plastic surgeons who might manage NF in their daily practice.

Findings: This study is a comprehensive practical review of various aspects of NF, including potential future therapies, its current classification, and management.

Meaning: NF is a clinical diagnosis and surgical emergency that usually requires serial debridement. Reconstruction options after debridement include skin grafting, flaps, and other various techniques based on the wound location and extent.

Gangrene Severity Index, which assists the clinician in determining the necessity of surgical debridement.[43–45] Laboratory and anamnestic risk indicator for necrotizing fasciitis and site other than the lower limb, immunosuppression, age <60 years, renal impairment, and inflammatory markers (SIARI) scores are newer tools that have been deemed useful.[47] Moreover, SIARI was shown to possess higher diagnostic ability than LRINEC score.[48] However, it is essential to note that emergent debridement must be undertaken regardless of the laboratory index scoring, especially in cases with a high clinical suspicion.[46]

Imaging

Imaging plays a critical role in diagnosing NF, especially in cases where the diagnosis is ambiguous. In cases of NF, X-ray imaging can demonstrate soft tissue gas (observed in 24.8%–55.0% of patients), strongly

Table 1. Classification of NF

Type	Common Locations	Infectious Profile	Common Microorganisms	Vulnerable Populations	Important Nuances
Type I (most common)	Perineum, trunk, groin, abdominal wall	Polymicrobial	≥1 anaerobic (nontypable streptococci and Enterobacteriaceae) + aerobic (Gram + or Gram –)	Mostly immunocompromised Patients Newborns (a complication of omphalitis)	Chronic illnesses/immunosuppression (diabetes mellitus, peripheral vascular disease, chronic renal failure, HIV, chronic cardiac/pulmonary disease) Recreational drug use (I.V. drug misuse, alcohol abuse) trauma (blunt/penetrating trauma, surgery, burns) Nutritional issues (obesity, malnutrition)
Type II (less common)	Extremities, head & neck	Monomicrobial	β-hemolytic group-A streptococcus *Staphylococcus aureus* Other streptococci	Mostly immunocompetent individuals with a history of recent trauma/operation	Toxic shock syndrome (30% of cases)
Type III (uncommon)	Extremities, trunk, perineum	Monomicrobial	*Vibrio* species (*Vibrio vulnificus* *Vibrio damsela* *Vibrio parahaemolyticus*) *Clostridium* species Gram-negative bacteria *Aeromonas hydrophila*	*Vibrio*: following minor injuries exposed to salt water *Clostridium*: Injury/Surgical wounds, drug addicts *Aeromonas*: Seafood consumption	Fulminant course Multiorgan failure, if untreated
Type IV (very rare)	Extremities, trunk, perineum	Fungal	*Candida* species Zygomycetes	Mostly after trauma/burns in immunocompetent individuals severely immunocompromised individuals	Aggressive especially in immunocompromised

Fig. 1. NF of the leg and foot. A-B, The wound before and after debridement, respectively. C-E, Stages of healing after skin grafting.

Table 2. Summary of Laboratory Indices Used to Facilitate Diagnosis of NF

Laboratory Index	Summary of Included Parameters	Parameters	Criteria
LRINEC	Six common serum parameters at the time of presentation	CRP total WBC count Hemoglobin serum Na Creatinine glucose	≥6 = higher risk of NF
MLRINEC	Six common serum parameters + liver disease at the time of presentation	CRP total WBC count Hemoglobin serum Na Creatinine glucose Lactate liver disease	≥12 = higher risk of NF
FGSI	Three vital signs + six serum markers	Temperature heart rate Respiration rate serum Na Serum K creatinine Hematocrit total WBC count Serum bicarbonate	9 = cut-off value for NF >9 = mortality likelihood of 75% ≤9 = survival likelihood of 78%
SIARI	Four comorbidities + three serum markers	Site of infection outside the lower limb History of immunosuppression Age ≤ 60 Creatinine Inflammatory markers (total WBC count CRP)	3 = cut-off value for NF 6–7 = moderate risk of NF ≥8 = high risk for NF
LARINF	Three comorbidities + three serum markers	Heart, liver, or renal insufficiency Immunosuppression (does not include diabetes) Obesity Procalcitonin CRP Hemoglobin	≥5 = higher risk of NF

suggestive of *Clostridium* species.[49,50] Computed tomography and magnetic resonance imaging (MRI) are more sensitive and specific compared with plain radiography, and can reveal the degree of tissue infection, inflammation, fascial edema, and gas formation.[51–53] Although MRI does have clinical utility, especially in equivocal cases of NF, it is important to note that MRI is cost-prohibitive for NF as a first diagnostic modality.[54] Moreover, it delays the limb-saving intervention, which should ideally be performed within 12 hours of admission.[3,55,56] Ultrasonography is also helpful and can assist in equivocal cases; ultrasonography can demonstrate hyperechoic foci with reverberation artifact and dirty shadowing at the site of infection,[57] which signifies subcutaneous gas. Although this imaging modality can be beneficial, its biggest limitation lies in the outcome dependence on the ultrasonography skillset of the operator.

PRINCIPLES OF MANAGEMENT

Surgical Treatment

The mainstay of treatment for NF consists of emergency surgical debridement of the infected tissue. Surgical management is especially indicated in NF with systemic inflammatory response syndrome or multiorgan failure,

associated with a mortality rate of 70%.[9,20] Moreover, surgery is mandatory for a patient experiencing severe pain with erythema, ecchymosis, blisters, or bullae.[58]

Surgery reduces bioburden by inhibiting the spread along the fascial planes.[59] To minimize the risk of scarring and promote better wound healing, incisions are initially made parallel to the Langer lines.[9] Incisions perpendicular with Langer lines can be made to keep the wound open and to allow further drainage and removal of necrotic tissue, except in cases of abdominal wall or retroperitoneal space involvement.[12,20,60] Close ongoing surveillance over surgical wounds and tissue viability is required for the next 24 hours. In complex cases, repeat surgical debridement can be beneficial as a "second-look operation."[9,61]

It is imperative to remove all nonviable or necrotic tissue,[62] as the timing and the extent of the first debridement are the most important determining factors in mitigating the mortality rate.[63] Delays in surgical debridement, necrosectomy, and fasciotomy (≥12 hours) may result in fulminant NF and higher mortality.[9] For example, Ecker et al found that when surgery was delayed 24 hours, the mortality rate increased ninefold.[62]

Negative Pressure Wound Therapy

Wounds with significant contamination and questionable tissue integrity have led surgeons to pursue the closure of tissue via delayed closure (87), including negative pressure wound therapy (NPWT).[64] Vacuum-assisted closure systems (VAC) have been shown to reduce edema, substantially increase blood flow, reduce wound size, and decrease bacterial colonization in managing various wounds.[65] Successful use of both black polyurethane[66–69] and silver[70,71] foam dressings in NF has been reported. Nonetheless, the authors did not provide the reasoning behind the preference for the specific sponge types.

Still, there is no consensus on the use of NPWT in NF.[72] Although some authors experienced anaerobic infection development and progressive worsening of the patient on NPWT, others reported better infection control, sufficient granulation tissue, and more pain relief and odor reduction.[72,73] Although direct application of NPWT/VAC on a debrided raw surface is hypothesized to increase the bleeding risk, such a complication was not recorded.[72–74] Misiakos et al also observed the facilitation of wound closure with VAC use.[3] The authors noted that despite being more expensive than gauze dressings, VAC did not reduce the hospital stay ($P = 0.2$). Therefore, they recommended limiting VAC application to more complex cases of NF (eg, NF with several comorbidities, large wounds).[3]

Coverage and Reconstruction

Reconstructive goals for the treatment of NF are reducing morbidity from the extensive tissue debridement and restoring functionality. After radical excision of necrotic, nonviable tissue, healing by delayed primary closure or secondary intention can be offered to cover small wounds.[75] For larger/complex wounds, the reconstructive options include skin grafting [split (STSG)- and full-thickness], acellular dermal matrix, tissue expansion, and (pedicled and free) flaps.[75,76]

STSGs are one of the simplest and most used reconstructive techniques.[75] Whallett et al reported successful skin grafting of upper (2) and lower (1) extremity wounds.[77] Similar results were observed by Lemsanni et al with wound preparation with NPWT and subsequent skin grafting.[78] The use of STSGs and full-thickness skin grafting for extremity wound reconstruction was also described by La Padula et al. In their case series, only one flap (dorsal metacarpal artery flap) was performed in a secondary procedure for interphalangeal joint resurfacing.[79] Positive outcomes of skin grafting and NPWT for lower extremity NF have also been reported.[80–82]

Flaps with/without skin grafting may be used for complex and extensive defects. The flap choice usually depends on the region and wound requirements. For instance, pedicled latissimus dorsi (LD) and transverse rectus abdominis muscle flaps are suitable and popular options for chest wound reconstruction. In cases of unresolved infection, absence of vascular supply, extensive local damage, and defect depth, free flaps are preferred.[75] Free LD, gastrocnemius, and soleus flaps are frequently used to cover extremity defects after debridement.[83] Overall, the reverse radial forearm flap is one of the widely performed flaps for upper extremity reconstruction.[83] Additionally, free and pedicled flaps are used to cover the upper extremity (radial forearm, LD, rectus abdominis, and pedicled groin flaps) and lower extremity (free gracilis, gastrocnemius, and soleus flaps) stumps after amputation.[83] These procedures are relatively common, as up to one-quarter of NF patients still undergo amputation.[78,79,84]

Perineum Defects (Fournier Defects)

Several options are available to allow for adequate healing of a patient with NF of the perineum (Fournier gangrene). Goals of care include protective coverage and function of gonadal tissue and acceptable cosmesis. Due to the high prevalence of significant comorbidities in the at-risk population, single-stage procedures are often preferred.[85]

The perineum presents reconstructive challenges given the proximity of fecal and urine contamination, and at times, the usage of fecal and urinary diversion methods may be used.[86] These techniques are performed particularly when gross sphincter involvement, more extensive wounds, severe incontinence, or patients in a severely immunocompromised state are present.[86]

Several options are available for closure: healing by secondary intention, loose soft tissue approximation, skin grafting, and flap coverage.[87] If the wound is noted to be small and confined, healing by secondary intention is often used.[85,88] Currently, there is no consensus regarding the best reconstruction method for a patient with Fournier gangrene. However, the algorithm by Chen et al can be used to guide the reconstruction of large defects. They recommend the use of the scrotal advancement flap (<50% of the scrotal surface) and pedicled anterolateral thigh (ALT) or pudendal thigh flap (>50% of the scrotal surface) for the reconstruction of the simple scrotal defects. For the complex defects involving the perineum, various flaps (pedicled ALT with/without vastus lateralis
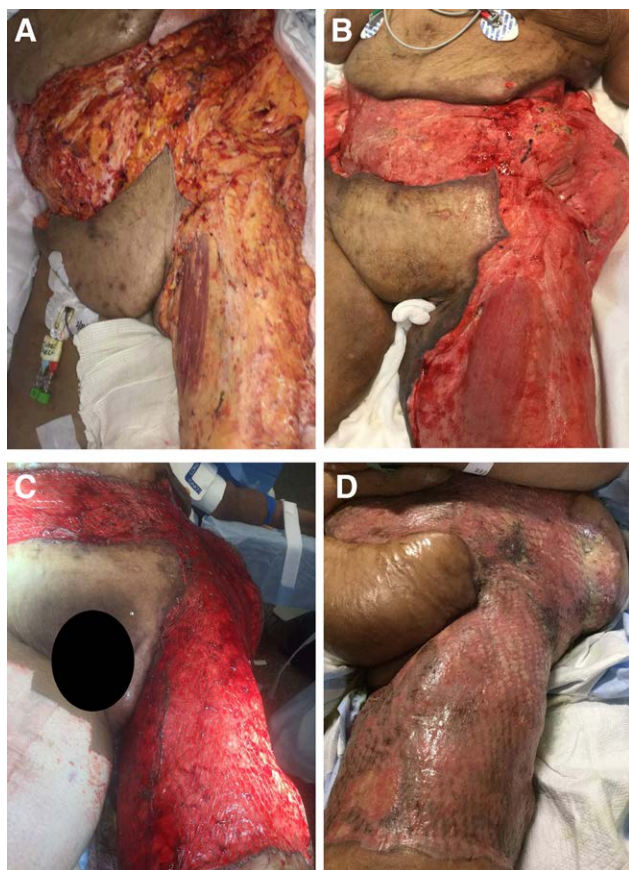
Fig. 2. Improvement of abdominal and thigh NF with treatment. A, Initial NF wound. B, Wound appearance after surgical debridement. C, Immediate postoperative appearance of the wound after skin graft application. D, Integration of the skin graft.

muscle, gracilis flap) with adjunctive VAC were suggested. If concomitant abdominal wall defect is present, STSG was recommended.[58] Using this algorithm, the authors successfully treated 31 patients with a 16% complication rate.

Compared with skin grafting, flap reconstruction provides more durable and robust repair with decreased complications and improved cosmesis.[8,89] The gracilis musculocutaneous flap is considered the workhorse flap for perineal reconstruction. However, other flaps, including local scrotal advancement, fasciocutaneous thigh, myocutaneous, and perforator flaps, have been used to repair NF perineal defects.[89,90] Nonetheless, skin grafting is frequently performed, as well. Studies have reported several advantages to skin grafting, such as short operative times, low morbidity rates, adequate functionality, and cosmesis.[91] Disadvantages include graft contraction and potential rejection secondary to shearing, infection, or hematoma formation.[8]

Abdominal Wall Reconstruction

NF can result in extensive full-thickness defects of the abdominal wall, constituting a reconstructive challenge[92] (Fig. 2). The primary goal of the reconstruction is to restore proper abdominal wall function and structure once an adequate necrosectomy is done. The long-term goals are to provide adequate skin closure, midline fascial closure, improved functionality, and good cosmesis.[92]

Currently, the reconstructive technique is chosen based on the type of abdominal defect.[93] Presence of the overlying skin bridge differentiates type I defects from type II defects.[94] Type I defects are typically repaired with a component separation. Component separation with a biologic mesh is an option if tension-free primary repair of fascia cannot be conducted after the wound is sufficiently granulated and infection is controlled.[12,95] Despite the infection risk, some authors have used synthetic mesh (Mersilene) to temporarily cover the abdominal defect until the infection is controlled.[96]

More complex constructive options are needed to repair type II defects. Autologous reconstruction has the advantage of avoiding the implantation of foreign mesh material, thereby reducing the risk of infection for the patient. Brafa et al[97] used an abdominoplastic technique with advancement flaps and umbilical preservation after two months of repeated debridements and VAC application. Two other patients treated in a similar fashion (abdominoplasty with upper abdominal flap mobilization) were discharged approximately 2 weeks later.[98] STSGs can be combined with local flaps for large wounds or used after the flap failure.[96,99] Rectus femoris myocutaneous flap is another option for coverage of a large anterior abdominal wall defect.[50] Free flaps (eg, tensor fasciae latae, ALT, LD, and gracilis) can be used to repair more extensive defects, and some may even provide motor functionality.[95,100] TFL can be preferred over ALT only in the absence of an adequate perforator, which would also allow sufficient mobilization.[86]

Antibiotic Management

Immediately upon clinical concern for NF, the patient should be made NPO and admitted to the ICU to enable aggressive resuscitation.[20,101] Broad-spectrum empiric antibiotics against gram-positive, gram-negative, and anaerobic organisms are recommended. A carbapenem (imipenem, meropenem, or ertapenem) or piperacillin–tazobactam plus vancomycin or daptomycin (good coverage against MRSA) plus clindamycin (for toxin-elaborating strains of GAS and *S. aureus*) are typically selected.[102,103] Antibiotics can be tailored based on the NF microbiological classification criteria (based on history, gram stain, and culture of the polymicrobial infection).[9] Antibiotic treatment for type 1 NF includes ampicillin/ampicillin–sulbactam combined with metronidazole or clindamycin.[15,20,31,33,34] Gram-negative coverage (eg, ampicillin–sulbactam, piperacillin–tazobactam, ticarcillin–clavulanate acid, third-generation or fourth-generation cephalosporins, or carbapenems) is critical for initial antibiotic therapy for patients previously hospitalized and/or on antibiotics.[9,104,105] In type 2 infections, *S. pyogenes* and S. aureus coverage is required; in most cases, first-generation or second-generation cephalosporins can be used. However, with MRSA, initial antibiotics should be replaced with vancomycin, or daptomycin and linezolid.[9,74,104–107] Some studies have advised adding
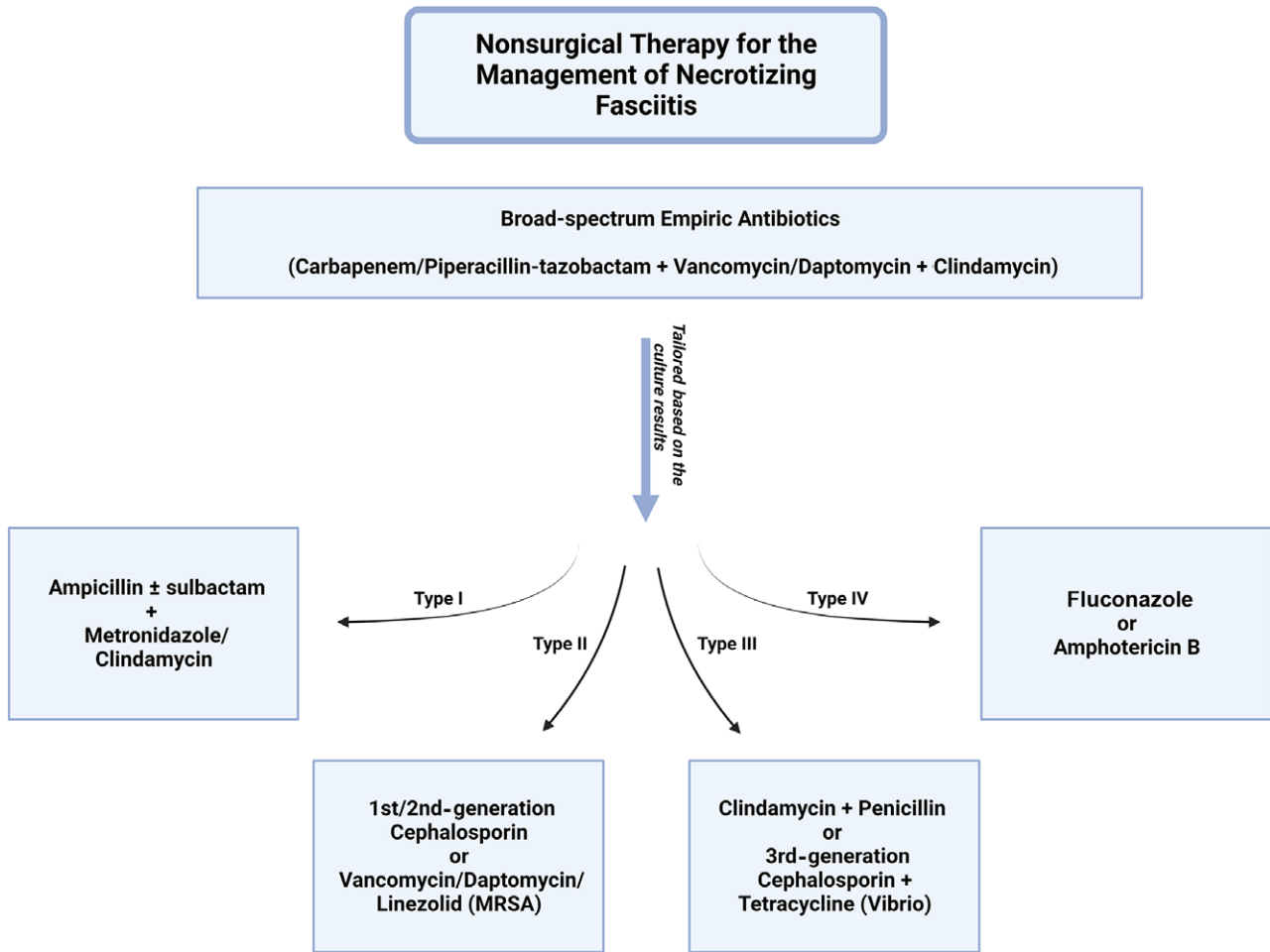
Fig. 3. Graphic description of antibiotic therapy in NF.

clindamycin to the antibiotic regimen when NF or myositis is present, as clindamycin's mechanism of action (inhibition of protein synthesis) makes it more efficacious than penicillin.[106,107] To adequately cover *Clostridium* species (type III NF), clindamycin and penicillin should be added to the antibiotic regimen.[9,74,104–107] For fungal infection seen with type IV NF disease, antifungal treatment, such as fluconazole or amphotericin B, should be initiated (Fig. 3).[9,104,105]

Antibiotic coverage should be continued for at least 5 days after resolving local and systemic signs and symptoms.[105] Eventually, empiric antibiotic therapy can be weaned depending on the results of blood, wound, and tissue cultures.[107] After source control, short (48 hours) antibiotic course is adequate.[108] Patients diagnosed with NF typically remain on antibiotic treatment for 4–6 weeks.[9]

Future Therapies

Hyperbaric oxygen (HBO) and Intravenous immunoglobulin (IVIG) have been suggested as adjunct treatments for NF. Research indicates that HBO improves patient survival while decreasing the number of surgical debridements and potentially the extent of reconstruction by inhibiting the systemic inflammatory response system and improving leukocyte activity.[78,109] Moreover, it can facilitate the transport of some antibiotics, such as aminoglycosides.[110] Risemann et al concluded that adjunct HBO therapy improved mortality from 66% to 23%.[86] Unfortunately, the study outcomes on HBO therapy in NF remain inconsistent, and further evaluation and more extensive studies are needed.

IVIG has been shown to be beneficial in patients with GAS NF that progressed into toxic shock syndrome.[74,111–113] Researchers have linked the efficacy of IVIG in NF to its ability to reduce a systemic inflammatory response by targeting the exotoxins.[114] IVIG has also shown some benefits in high-risk patients, including those with advanced age, bacteremia, and hypotension.[115] However, in a large-scale study of NF patients with shock, no benefit of adjunctive IVIG therapy was documented.[116] Therefore, IVIG's role in the management of NF is still debatable.

CONCLUSIONS

NF is a rapidly progressive and potentially life-threatening soft tissue infection, most commonly affecting the extremities. Clinical presentation is the key factor

for diagnosis, and a high level of clinical concern should prompt immediate medical intervention and aggressive surgical debridement to optimize patient survival. Initial treatment includes broad-spectrum antibiotics and aggressive debridement. Adjunctive NPWT can significantly improve postoperative wound outcomes. Finally, the patient may undergo reconstruction once the patient is medically stable, and patient's nutritional status and wound have been optimized. Although most patients benefit from skin grafting, local, pedicled, and free flaps; mesh; and acellular dermal matrix alone or in combination can be used based on the wound (eg, location, size) and patient (eg, comorbidities, adjacent injuries) characteristics. Timely diagnosis, early and extensive debridement, close postoperative surveillance, wound care, adequate wound closure, and management of complications are essential to improve patient outcomes.

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