

REPUBLIQUE DU CAMEROUN

Paix – Travail – Patrie

MINISTRE DE L'ENSEIGNEMENT

SUPERIEUR

L'UNIVERSITE DE YAOUNDE 1

FACULTE DE MEDECINE ET DES
SCIENCES BIOMEDICALES



REPUBLIC OF CAMEROON

Peace – Work – Fatherland

MINISTRY OF HIGHER EDUCATION

THE UNIVERSITY OF YAOUNDE I

FACULTY OF MEDICINE AND
BIOMEDICAL SCIENCES

DEPARTMENT OF SURGERY AND SPECIALTIES

Outcome and Prognostic Factors of Fracture – Related Infections in Yaoundé

Thesis submitted and defended publicly in partial fulfilment of the requirements for the award of MD degree by;

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Mat N° 17M010

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and traumatology*

Co-Supervisors

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2023 – 2024 Academic year

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Date of defense:...../...../2024

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2023 – 2024 Academic year

TABLE OF CONTENT

TABLE OF CONTENT	I
DEDICATION	III
ACKNOWLEDGEMENT	IV
THE ADMINISTRATIVE AND TEACHING STAFF OF THE FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES	VI
PHYSICIAN'S OATH	XIX
ABSTRACT	XX
RESUME.....	XXII
LIST OF TABLES	1
LIST OF FIGURES.....	2
LIST OF ABBREVIATIONS AND ACRONYMES	3
INTRODUCTION.....	5
LITERATURE REVIEW.....	11
1. OVERVIEW	12
1.1 Definition	12
1.2 Relevance.....	12
1.3 Recall	12
1.4 Epidemiology of FRI	21
1.5 Why do fractures get infected (Risk factors)	23
1.6 Pathogenesis.....	24
1.7 Classification.....	26
2. DIAGNOSIS OF FRI	30
2.1 Patients history and Clinical presentation.....	30
2.2 Work-up	30

2.3. Positive Diagnosis of FRI	31
3. MANAGEMENT OF FRI	33
3.1 Treatment Goal	33
3.2 Means and Methods	33
4. FOLLOW-UP	46
5. OUTCOME AND PROGNOSIS.....	47
6. PREVENTION	50
7. STATE OF THE ART	54
 METHODOLOGY.....	56
1. STUDY DESIGN	57
2. SITE OF STUDY	57
3. DURATION OF STUDY.....	57
4. STUDY POPULATION.....	57
a. Source population.....	57
b. Target population.....	57
c. Inclusion criteria.....	57
d. Exclusion criteria	57
5. SAMPLE SIZE ESTIMATION	58
6. MATERIAL.....	58
7. PROCEDURE	59
 RESULTS.....	61
DISCUSSION	87
CONCLUSION AND RECOMMENDATIONS	97
REFERENCES	101
APPENDIX	CII

DEDICATION

**This work is dedicated to my
beloved parents and the entire
SIME family**

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- To my dearest friends Sah Badaire, Ymele Natacha and to all my loved ones, for the support and all the advices. May the grant you more success.
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THE ADMINISTRATIVE AND TEACHING STAFF OF THE FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES

2023 - 2024 Academic Year

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PHYSICIAN'S OATH

Declaration of Geneva adopted by the Geneva Assembly of the World Medical Association in Geneva, Switzerland, September 1948 and amended by the 22nd World Medical Assembly, Sydney, Australia (August 1968)].

On admission to the medical profession;

I will solemnly pledge myself to consecrate my life to the service of humanity

I will give my teachers the respect and gratitude which is their due

I will practice my profession with conscience and dignity

The health of my patients will be my first consideration

I will respect secrets confided in me, even after the patient has died

I will maintain by all the means in my power the honour and noble traditions of the medical profession

My colleagues will be my brothers

I will not permit considerations of religion, nationality, race, party politics or social standing to intervene between my duty and my patient

I will maintain the utmost respect for human life from the time of conception, even under threat I will not use my medical knowledge contrary to the laws of humanity

I make these promises solemnly, freely and upon my honour

ABSTRACT

Background: Fracture-related infections (FRI) are a significant concern in the field of orthopedic and trauma surgery. The management of FRI described in western literature is basically surgical with is not always the case in our setting due to the high cost of surgery solely under the patients' responsibility, hence may alter their strict application and pose a challenge for healthcare professionals. While studies on FRI outcome and prognostic factors have been conducted in high-income countries, there is a lack of information in low and medium-income countries (LMICs) particularly in Cameroon. This gap in knowledge is concerning, as LMICs face unique challenges in terms of limited resources, socioeconomic factors and comorbidities there by justifying the interest of our study which had as main objective to determine what the outcome was and what were the factors affecting its prognosis.

Means and methods: We conducted a prospective cohort study on FRIs suspected, diagnosed and followed up between December 2022 and May 2024. Recruitment of participants was done at the different hospitals on real time in search of patients who have been diagnosed with FRI or present signs and symptoms in line with the diagnostic criteria of FRI. The patients were interrogated and their individual questionnaires filled. They were then followed up for a period of at least 3 months and re-evaluated.

Main outcome measures: The primary outcome measures were the recurrence of infection and bone union. Whereas the secondary outcome measures were functional evaluation using the Upper Extremity Functional scale and Lower Extremity Functional Scale and quality of life evaluation using the Short Form (SF) 12- score.

Results: A total of 104 patients with confirmed FRI were included in this study and followed up at least 3 months after treatment for FRI with a mean age of 40.46 years (SD 14.90). Seventy-six (73.08%) patients were. Thirty-five (33.65%) cases were managed by suppression therapy, 17 (16.35%) cases by Debridement Antibiotics and External fixation. Seventy-three (70.19%) participants were not treated according to the recommended guidelines. Fifty (48.08%) cases were treated successfully while 54 (51.92%) had a bad outcome. The recurrence rate of FRI was 38.46% and bone union was achieved at final evaluation in 62 (59.62%) participants. In multivariate analysis, the independent prognostic factors affecting the outcome of FRI were; smoking ($p=0.03$, OR= 0.87), type of fixation ($p= 0.04$, OR= 0.96), Cierny-mader classification;

Anatomic type ($p=0.04$, OR= 0.80), Physiologic host ($p= 0.02$, OR= 1.11), type of initial surgery ($p= 0.02$, OR= 0.78), delay of surgery ($p= 0.05$, OR= 0.61), delay of first wash ($p=0.00$, OR= 0.98), antibiotic duration ($p=0.00$, OR= 0.89), suppression therapy ($p=0.00$, OR=0.14), Masquelet technique ($p=0.04$, OR=1.15).

Conclusion: FRI is a serious complication that can occur after the surgical treatment for fractures. From the results of this study, we can say that the treatment of FRI in Yaoundé is not in line with the international guidelines. The outcome of FRI is not satisfactory with high rates of recurrence of infection and bone nonunion and the functional outcome was not satisfactory. The factors affecting the outcome of FRI were smoking, type of fixation, cierny-mader classification, type of initial surgery, delay of surgery and first debridement, antibiotic duration, suppression therapy and the induced membrane technique.

Key words: Fracture-related infections; outcome; prognostic factors;

RESUME

Introduction: Les infections liées à la fracture (FRI) posent un problème important en chirurgie orthopédique et traumatologique. La prise en charge des infections liées à la fracture décrite dans la littérature occidentale est essentiellement chirurgicale, alors que cela n'est pas toujours le cas dans notre contexte en raison du coût élevé de la chirurgie, qui est à la charge exclusive des patients, ce qui peut modifier leur application stricte et constituer un défi pour les professionnels de santé. Alors que des études sur les résultats et les facteurs pronostiques de la FRI ont été menées dans des pays à revenu élevé, il y a un manque d'informations dans les pays à revenu faible et moyen (PRFM), en particulier au Cameroun. Ce manque est préoccupant, car les PRFM sont confrontés à des difficultés en termes de ressources limitées, de facteurs socio-économiques et de comorbidités, ce qui justifie l'intérêt de notre étude, dont l'objectif principal était de déterminer le résultat et les facteurs qui influencent le pronostic.

Méthodologie: Nous avons mené une étude de cohorte prospective sur les FRI suspectées, diagnostiquées ou suivies entre décembre 2022 et mai 2024. Le repérage des patients s'est fait en temps réel dans les différents hôpitaux, à la recherche de malades ayant été diagnostiqué avec une FRI ou présentant des signes et des symptômes conformes aux critères diagnostiques de la FRI. Les patients ont été interrogés et les questionnaires remplis. Ils ont ensuite été suivis pendant une période d'au moins douze mois et réévalués.

Principaux critères d'évaluation: Les principaux critères d'évaluation étaient la récurrence de l'infection et la consolidation osseuse. Les critères d'appréciation secondaires étaient l'évaluation fonctionnelle à l'aide de l'échelle fonctionnelle respectivement des membres supérieurs et inférieurs, ainsi que l'évaluation de la qualité de vie à l'aide du score Short Form (SF) – 12.

Résultats: Au total, 104 patients souffrant d'une FRI confirmée ont été inclus dans cette étude et suivis au moins trois mois après le traitement, l'âge moyen étant de 40,46 ans (SD 14,90). Soixante-seize (73,08 %) patients étaient des hommes. Trente-cinq (33,65%) cas ont été traités par la thérapie de suppression et 17 (16,35%) cas ont été traités par débridement, antibiotiques et fixation externe. Soixante-treize (70,19 %) participants n'ont pas été traités selon les recommandations. Cinquante (48,08 %) participants ont été traités avec succès, tandis que 54 (51,92 %) patients ont eu un mauvais résultat. Le taux de récurrence de la FRI était de 38,46 % et

la consolidation osseuse était présent chez 62 (59,62 %) participants. Dans l'analyse multivariée, les facteurs pronostiques indépendants affectant l'issue de la FRI étaient les suivants ; le tabagisme ($p=0,03$, OR= 0,87), le type de fixation ($p= 0,04$, OR= 0,96), la classification de Cierny-Mader ; type anatomique ($p=0,04$, OR= 0,80), hôte physiologique ($p= 0,02$, OR= 1,11), le type de chirurgie initiale ($p= 0,02$, OR= 0,78), délai d'intervention ($p= 0,05$, OR= 0,61), délai du premier lavage ($p=0,00$, OR= 0,98), durée d'antibiothérapie ($p=0,00$, OR= 0,89), traitement suppressif ($p=0,00$, OR=0,14), technique de Masquelet ($p=0,04$, OR=1,15).

Conclusion: La FRI est une complication grave qui peut survenir après le traitement chirurgical des fractures. D'après les résultats de cette étude, nous pouvons dire que le traitement de la FRI à Yaoundé n'est pas conforme aux directives internationales. Le traitement de la FRI n'est pas satisfaisant, avec des taux élevés de récurrence de l'infection et de défaut de consolidation osseuse, et le résultat fonctionnel n'est pas satisfaisant. Les facteurs affectant le résultat du traitement de la FRI sont le tabagisme, le type de fixation, la classification de Cierny-Mader, le type de chirurgie initiale, le délai de la chirurgie et le délai du premier débridement, la durée de l'antibiothérapie, la thérapie de suppression et la technique de Masquelet.

Mots clés : Infections liées à la fracture, résultats du traitement, facteurs pronostics,

LIST OF TABLES

Table I : Proportion of fracture-related infections according to anatomical area	22
Table II : Most common microorganisms in fracture-related infection.....	26
Table III : Distribution of patients by study site.....	62
Table IV : Patients demographic of patients with a FRI.....	64
Table V : Delay of admission, fist wash and delay of antibiotic for FRI patients.....	67
Table VI : Location of infection.....	69
Table VII : Specimen collection.....	71
Table VIII : Culture results.....	71
Table IX : Bacteriological profile.....	72
Table X : Classification of FRI.....	73
Table XI : Treatment plan according to onset of infection.....	75
Table XII : Willenegger and roth classification of FRI according to management.....	75
Table XIII : Respect of international guidelines.....	76
Table XIV : Primary outcome of FRI.....	76
Table XV : Relationship between age, BMI, delay onset of infection and outcome.....	78
Table XVI : Relationship between gender, comorbidity and outcome.....	78
Table XVII : Relationship between clinical features and outcome.....	79
Table XVIII : Relationship between work-ups and outcome.....	80
Table XIX : Relationship between management and results of FRI.....	81
Table XX : Willenegger and Roth classification of FRI and outcome.....	81
Table XXI : Cierny-mader physiological host classification and outcome.....	82
Table XXII : Relationship between type of initial surgery, type of surgery and outcome.....	82
Table XXIII : Results of multivariate logistic regression identifying factors affecting the outcome of FRI.....	86

LIST OF FIGURES

Figure 1 : Structure of a long bone	14
Figure 2: Microscopic structure of bone	15
Figure 3 : Stages of bone healing.	18
Figure 4 : (a) Standard uniplanar external fixator. (b) Ring external fixator	20
Figure 5 : Hybrid external fixator	20
Figure 6 : Mechanisms of bone changes during bacterial infection in FRI	25
Figure 7 : Cierny-Mader classification	28
Figure 8 : FRI diagnostic criteria	32
Figure 9 : Algorithm describing the basic treatment principles for fracture-related infection	36
Figure 10 : Duration of antimicrobial therapy according to treatment strategy.....	43
Figure 11 : Descriptive flow chart of FRI	45
Figure 12 : Summary of FRI	53
Figure 13: age distribution	62
Figure 14: gender distribution of patients with FRI	63
Figure 15: Comorbidities of patients with FRI	65
Figure 16 : Repartition of patients with respect to circumstance of injury	65
Figure 17 : Fracture type of FRI.....	66
Figure 18 : Open fracture classification by Gustilo-anderson for FRI patients	66
Figure 19 : Initial management following fracture	68
Figure 20 : Onset of FRI.....	68
Figure 21 : Clinical signs of FRI	70
Figure 22 : Radiological signs of infection	70
Figure 23 : Treatment of FRI	74
Figure 24: Outcome of Fracture – Related Infection	77
Figure 25 : Relationship between BACH classification and outcome	83
Figure 26: Respect of international guidelines and outcome	84

LIST OF ABBREVIATIONS AND ACRONYMES

BS: Bone Scan

BMI: Body Mass Index

CHF: Chronic Heart Failure

CRP: C – Reactive Protein

CP: Computed Tomography

DAIR: Debridement Antibiotics Implant Retain

DAIEX: Debridement Antibiotics Implant Exchange

ESR: Erythrocyte Sedimentation Rate

FRI: Fracture Related Infection

FDG-PET: Fluorodeoxyglucose position emission

GNB: Gram Negative Bacteria

IAFF: Infection After Fracture Fixation

IV: Intra-venous

IRB: Institutional Review Board

LMIC: Low and Medium Income Countries

LEFS: Lower Extremity Functional Scale

LC: Leucocyte Count

MRI: Magnetic Imaging Resonance

MRSA: Methicillin resistant staphylococcus aureus

MSSA: Methicillin sensitive staphylococcus aureus

mRUST: modified Radiological Union Scale

OAI: Ostheosynthesis Associated Infection

PAD: Peripheral Arterial Disease

PJI: Prosthetic Joint Injury

POP: Perioperative Antibiotic Prophylaxis

PMNs: Polymorphonuclear neutrophils

QOLS: Quality Life Scale

SSI: Surgical Site Infection

UEFS: Upper Extremity Functional Scale

WBC: White Blood Cells

YCH: Yaoundé Central Hospital

YGH: Yaoundé General Hospital

INTRODUCTION

1 BACKGROUND

A fracture Related Infection (FRI) is an infection in the presence of a fracture or during treatment process for a fracture, and includes all infections with or without implant, which may involve any bone part (cortical, medullary and epiphysis) [1]. This includes early infection around fracture implants, infected non-unions, hematogenous infections arising after fracture healing and infections in fractures with no internal fixation [1]. FRI can have a devastating impact on a patient's quality of life with huge socioeconomic consequences[2]. They are often not only unable to participate in social activity due to their limited mobility and function but also encounter higher direct and indirect health care costs [2,3]. Moreover, recent studies show that FRI is a serious phenomenon, with a worldwide average incidence ranging from 1% (closed fractures) to over 30% (open fractures) [4]. In Northeast China (2021) the incidence of FRI was about 1.5% [5]. In Africa, the incidence is even higher: a study carried out in Cameroon found an incidence of 31.4% in open tibia fractures [6].

The FRI international Consensus Group published the initial definition and diagnostic criteria in 2018 and the term ‘fracture-related infection’ was adopted [1]. FRI call upon multidisciplinary management in addressing multiple facets including patient factors, fracture considerations of mechanical stability, biological viability, and pathogenicity of the infecting organism. Treatment is based on international recommendations developed in northern countries, but their application may encounter difficulties specific to Low and Medium Income Countries (LMIC) [7]. Indeed, the management of FRI according to these guidelines is essentially surgical, that is; DAIR (Debridement Antibiotics Implant Retention), DAIEX (Debridement Antibiotics Implant Exchange), Debridement Antibiotics Implant Removal, amputation etc [8]. In developing countries, the fact that these costly and often multiple therapeutic modalities are exclusively the patients' responsibility, limits their strict application [9,10]. Thus, the management of FRI in our context may be dictated by the prevailing situation, and so may differ from that described in literature. Outcome may therefore differ from what expected. An understanding of FRI clinical outcome, identifying prognostic factors specific to our setting empowers better-informed decision making, prognostication, and formulation of realistic treatment plans adapted to our context.

We proposed to conduct this study with objective to evaluate the results of FRI management in Yaoundé and also to identify the prognostic factors specific to our setting.

1.1 RESEARCH QUESTIONS

Primary;

1. What is the outcome and prognostic factors of Fracture related infections in Yaoundé

Secondary;

1. Does the treatment of fracture related infections in Yaoundé respects' international guidelines?
2. What is the result of the treatment of fracture related infections in Yaoundé
3. What are the prognostic factors of fracture related infections in Yaoundé

1.2 RESEARCH HYPOTHESIS

1. The treatment of FRI in Yaoundé does not respect international guidelines.
2. The outcome of FRI in Yaoundé is worse compared to that described in literature.
3. The outcome of FRI in Yaoundé depends on the severity of the lesions and the adequacy of proposed treatment to the international guidelines.

1.3 OBJECTIVES

1.3.1 General Objective

To improve on the treatment and prognosis of Fracture related infections in Yaoundé.

1.3.2 Specific Objectives

1. To describe the treatment of FRI in Yaoundé.
2. To analyse the adequacy of FRI treatment in Yaoundé with respect to international guidelines.
3. To evaluate the outcome of FRI treatment in Yaoundé.
4. To determine the factors predicting the outcome of FRI in Yaoundé.

1.4 OUTCOME MEASURES

1.5.1 Primary outcome measures

1. Bone union following the Modified Radiologic Union Score for Tibial fractures (mRUST) criteria [11]
2. Recurrence of infection

1.5.2 Secondary outcome measures

1. Functional evaluation using the LEFS (lower extremity functional scale) [12] or using the UEFS (Upper extremity functional sale) [13]
2. Quality of life evaluation using the Short Form (SF)- 12 score [14]

1.5 OPERATIONAL DEFINITIONS

- **Fractures:** A fracture is a breach in the structural continuity of the bone cortex, with a degree of injury to the surrounding soft tissues [15].
- **Fracture related infection:** is an infection in the presence of a fracture or during treatment process for a fracture, and includes all infections with or without implant, which may involve any bone part (cortical, medullary and epiphysis). In this study, diagnosis of FRI was based on the criteria from the consensus group [16].
- **DAIR:** debridement, antibiotics and implant retention (DAIR) is the treatment of choice for acute postoperative and acute hematogenous periprosthetic joint infection (PJI) and FRI [17].
- **DAExFix:** debridement, antibiotics and external fixation is the treatment method adopted for the management of pre-operative FRI in open fractures. This treatment method is not defined in the literature of FRI but was rather coined in the course of this study to suit the clinical profile [17].
- **Suppressive therapy:** this consist of the administration of antibiotics alongside regular wound dressing with the aim of eradicating a localized infection, especially in cases where debridement cannot be done due to the age of the biofilm (chronic infection) in the presence of an internal fixator [18].
- **Consolidation:** fracture consolidation refers to the process by which a fractured bone heals through a dynamic interplay of biological processes to restore original anatomic structure and mechanical function of the bone [16].
- **Non-union:** non-union of bone is the body's inability to heal a fracture. That is, a fracture that persists for a minimum of nine months without signs of healing for three months [17].
- **Delayed union:** it is generally defined as a failure to reach bony union by 6 months post-injury. This also includes fractures that are taking longer than expected to heal.
- **Sinus:** discharging, blind-ended track that extends from the surface of the skin to an underlying abscess/cavity.
- **Fistula:** it is an abnormal communication between the bone/implant with the surrounding through a musculo-cutaneous orifice [16].
- **Osteosynthesis:** it is a type of reconstructive surgery aimed at stabilizing and joining the ends of a broken bone after a fracture, an osteotomy, or a non-union from a previous fracture. Bone fragments are stabilized by using mechanical devices [19].
- **Ideal soft tissue coverage:** can be defined as well vascularized, space filling, preferably sensate, epithelialized tissue that is soft, not fibrotic, robust and stable, covering bone and

metal implants with optimal function and cosmetic appearance [18].

- **Good outcome:** disappearance of initial clinical signs and symptoms of FRI and bone union at reevaluation.
- **Bad outcome:** Persistence / recurrence of clinical signs and symptoms of FRI and/or bone non-union at reevaluation.

LITERATURE REVIEW

1. OVERVIEW

1.1 Definition

A fracture Related Infection (FRI) is an infection in the presence of a fracture or during treatment for a fracture, and includes all infections with or without implant, which may involve any bone part (cortical, medullary and epiphysis) [1].

1.2 Relevance

Fracture-related infection (FRI) is a serious complication related to orthopedic trauma, with a high risk of devastating outcomes for the patients both from an infectious disease and a surgical point of view. The principles of treatments (diagnostic sampling, excision of dead tissue, stabilization, dead-space management, soft tissue cover and anti-microbial therapy) are well established [20], but the effectiveness of how each of these principles is delivered, the results of these principles and what factors affected these results has not been widely investigated especially in Low and medium income countries. This is a major deficiency in the literature, as it makes clinical decision making more difficult when deciding on how to deliver these principles for individual patients.

1.3 Recall

1.3.1 BONE ANATOMY

The skeleton can be divided into two subgroups, the axial skeleton and the appendicular skeleton.

The axial skeleton consists of the bones of the skull (cranium), vertebral column, ribs, and sternum, whereas the appendicular skeleton consists of the bones of the upper and lower limbs.

Bone is a calcified, living, connective tissue that forms the majority of the skeleton.

There are two types of bone, compact and spongy (trabecular or cancellous). Compact bone is dense bone that forms the outer shell of all bones and surrounds spongy bone. Spongy bone consists of spicules of bone enclosing cavities containing blood-forming cells (marrow) [21]. A long bone has two parts: the diaphysis and the epiphysis. The diaphysis is the tubular shaft that runs between the proximal and distal ends of the bone. The hollow region in the diaphysis is called the medullary cavity, which is filled with yellow marrow. The wider section at each end of the bone is called the epiphysis, which is filled with spongy bone. Red marrow fills the spaces in the spongy

bone. Each epiphysis meets the diaphysis at the metaphysis, the narrow area that contains the epiphyseal plate (growth plate), and a layer of hyaline (transparent) cartilage in a growing bone. When the bone stops growing in early adulthood (approximately 18–21 years), the cartilage is replaced by osseous tissue and the epiphyseal plate becomes an epiphyseal line [22].

The medullary cavity has a delicate membranous lining called the endosteum, where bone growth, repair, and remodeling occur. The outer surface of the bone is covered with a fibrous membrane called the periosteum [22].

The periosteum is a peripheral membrane, easily detached from the bone in children. It varies in thickness, and becomes thinner in adults. The periosteum plays an important role in fracture healing. It also acts as a wall between the bone and the soft tissues, for example, by slowing down the spread of certain pathological processes from the bone to the soft tissues

Bone consists mainly of the bone matrix and three major cell types;

- Osteocytes; which are found in cavities (lacunae) between bone matrix layers (lamellae), with cytoplasmic processes extending into small canaliculi
- Osteoblasts; which synthesize the organic components of the matrix. Deposition of the inorganic components of bone also depends on viable osteoblasts.
- Osteoclasts; which are multinucleated, giant cells involved in the resorption and remodeling of bone tissue [23] .

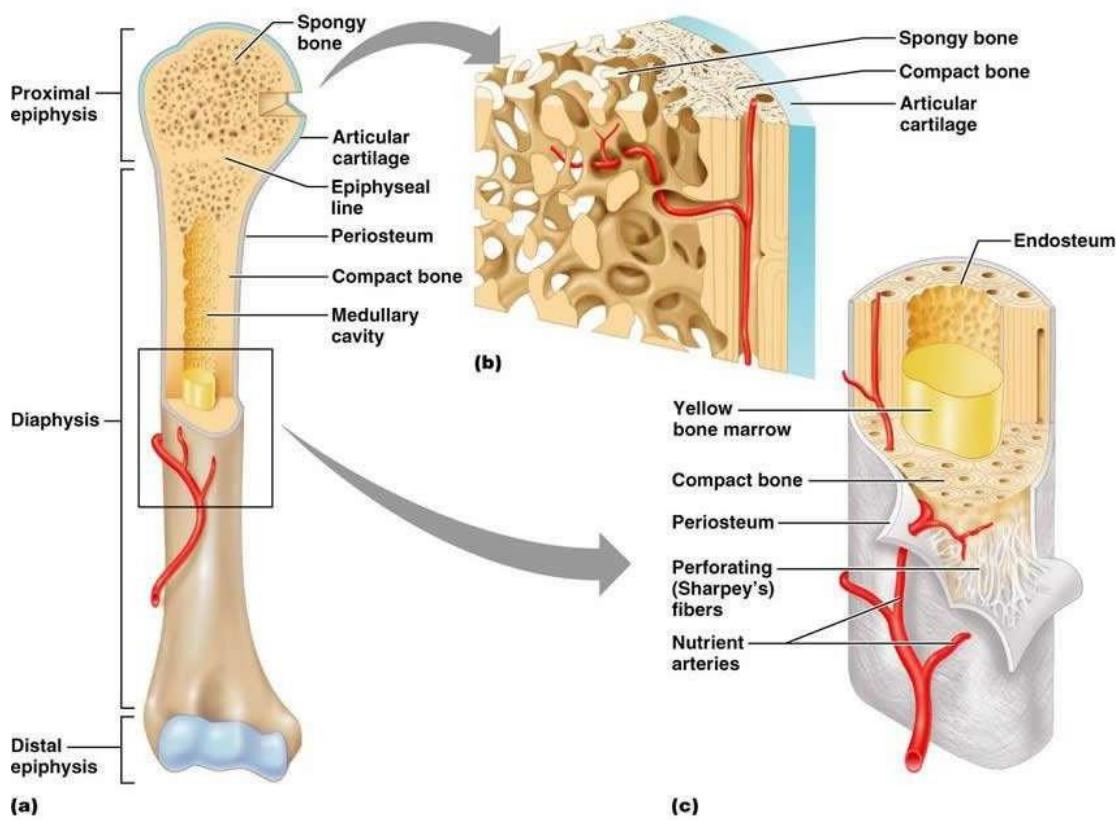


Figure 1 : Structure of a long bone

a- A long bone b- Cross section of the epiphysis c- Cross section of the diaphysis

(Source Medical Encyclopedia)

Most bone in adults, compact or cancellous, is organized as lamellar bone, characterized by multiple layers or lamellae of calcified matrix, each 3-7 μm thick. The lamellae are organized either parallel to each other or concentrically around a central canal. In each lamella, type I collagen fibers are aligned in parallel, with the pitch of the fibers' orientation shifted orthogonally (by about 90 degrees) in successive lamellae. An osteon (or Haversian system) refers to the complex of concentric lamellae surrounding a small central canal that contains blood vessels, nerves, loose connective tissue, and endosteum. Between successive lamellae are lacunae, each with one osteocyte, interconnected by canaliculi containing the cells' dendritic processes [23].

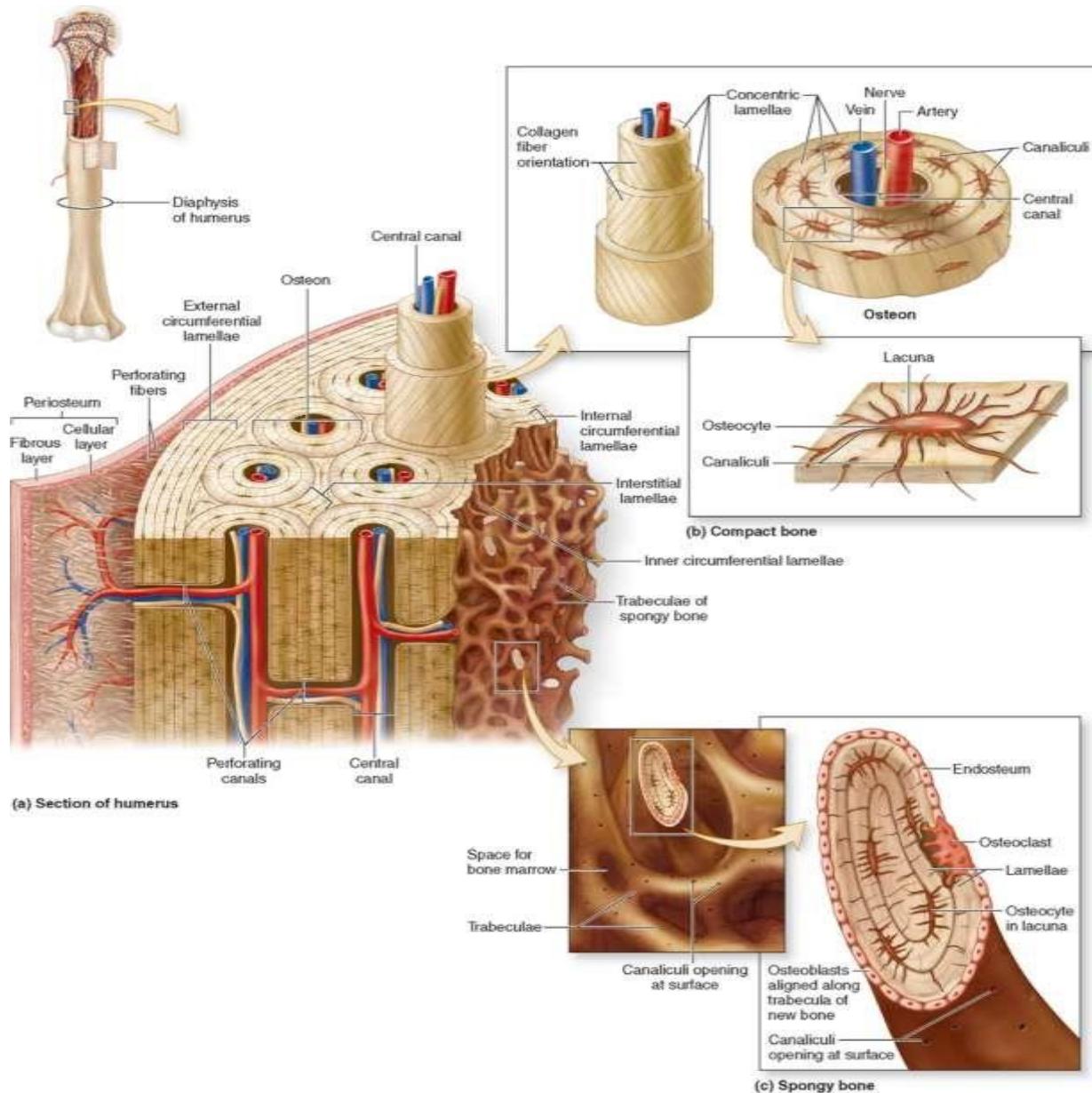


Figure 2: Microscopic structure of bone

a- section of the diaphysis showing the different bone structures b-an osteon in a compact bone c-Spongy bone showing trabeculae

(Source: Junqueira's Basic Histology. 13e ed. McGraw-Hill Medical)

1.3.2 BONE PHYSIOLOGY

1.3.2.1 Bone growth and remodeling

Bone remodeling is defined as the local removal and subsequent replacement of bone. Remodeling is structurally important for eliminating old bone and bone that has suffered accumulated micro damage. It also allows the body to change the shape or composition of bones to respond to different stresses on the bones.

Remodeling is regulated by both local factors and systemic factors. Systemic factors include vitamin D, Parathyroid hormone (PTH) and calcitonin. Local factors include low-density lipoprotein receptor-related protein 5 (LRP5), bone morphogenetic protein (BMP), transforming growth factor (TGF)-beta, and mechanical strain (according to Wolf law)[24].

In a general sense, the process is initiated when bone lining cells retract, exposing the matrix underneath to osteoclasts. Osteoclasts then resorb bone in the resorption or Howship pits. Once this step is completed, osteoblasts fill in along the resorption pit and replace the resorbed bone with osteoid. Osteoblasts then either are incorporated to form osteocytes or become quiescent bone lining cells. The osteoid is later mineralized. The absorption phase takes 2-4 weeks, the formation phase 4-6 months [25].

The osteoblast serves as an intermediary in this process, receiving systemic signals and then releasing M-CSF and RANKL that help initiate the process of resorption by stimulating the precursor cells to become osteoclasts. At the same time, the osteoblast can also release osteoprotegerin (OPG), which is a competitive inhibitor of RANKL, and thereby decrease osteoclastic activity. It is therefore the osteoblast that regulates much of the process [25].

The signals that drive osteoblasts to release factors to activate osteoclasts do not cause them to start bone formation. Instead, factors released from the extracellular matrix itself, including TGF-beta (migration), insulin-like growth factors (IGFs), and BMPs, cause the osteoblast to form new osteoid [25].

Normal uncoupling occurs in selected instances; bone growth in childhood is the most notable example where formation exceeds resorption. Resorption eventually equals formation and homeostasis is achieved; however, in adulthood and old age, resorption exceeds formation and the bones become osteoporotic. The need for tight regulation of serum calcium outweighs the importance of coupling, and the body will allow uncoupled absorption to release calcium if it is needed. Pathologic uncoupling occurs in osteoporosis, osteopetrosis, tumors, Paget disease, and other conditions [24].

1.3.2.2 Bone Fracture Repair

Bone Fracture healing: is an intricate and fluent regenerative process that aims at restoring the damaged bone to its pre-injury state and cellular composition [26]. A fracture is a breach in the structural continuity of the bone cortex, with a degree of injury to the surrounding soft tissues.

Fracture healing starts with **an anabolic phase** where there is recruitment and differentiation of stem cells with subsequent increases in the skeletal and vascular tissue volume. A cartilaginous callus forms at the fracture site, whereas at the periphery of this callus, the periosteum swells, and the primary bone formation starts. Simultaneously with cartilaginous callus formation, the cells involved in angiogenesis are recruited and differentiated in the nearby muscle mass. With further progression of chondrocyte differentiation, the extracellular matrix is mineralized, and the chondrocytes undergo apoptosis. This is followed by a **catabolic phase** where cartilage resorption ensues, resulting in tissue and callus volume reduction [27].

There are two main modes of bone healing: **Primary bone healing** is determined by an absolutely stable structure with a mechanical load of less than 2%. This is intramembranous bone healing that occurs through Haversian remodeling. The other type is **secondary bone healing**, which occurs with non-rigid fixation methods such as braces, external fixators, bridging pattern plates, intramedullary nails, etc. These fixings allow for mechanical loads of 2-10%. It occurs through endochondral bone healing. Bone healing may involve a combination of primary and secondary processes based on the stability of the entire structure. Following the fracture, secondary healing begins, which consists of four steps [28]:

1. Hematoma formation
2. Granulation tissue formation
3. Bony callus formation
4. Bone remodeling

However, there is considerable overlap between these stages. Principle cells and their secretions are involved in the healing process, in which the mesenchymal stem cells play a pivotal role. They are delivered mainly by two major sources; periosteum and endosteum. Others involved include inflammatory cells, endothelial cells, fibroblasts, osteoblasts, and osteoclasts [28] . These steps are summarized in figure 3 below

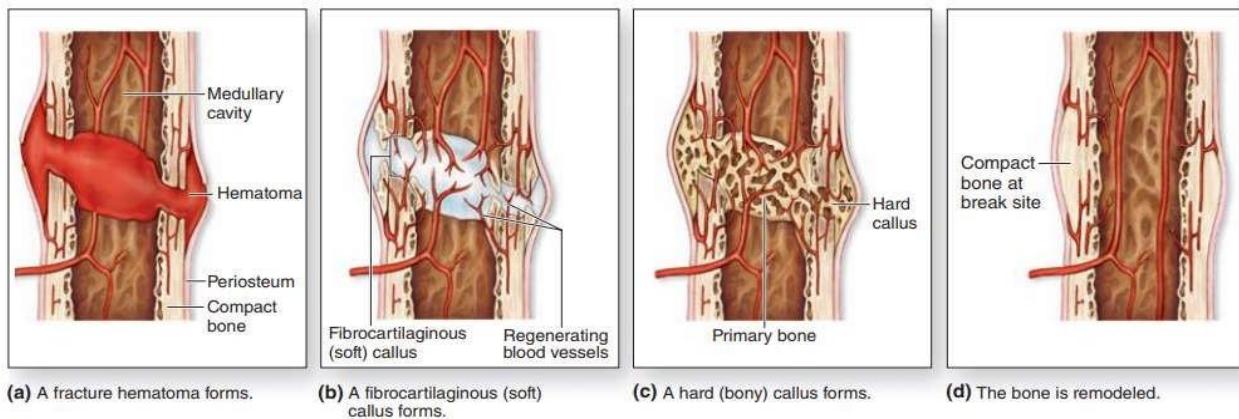


Figure 3 : Stages of bone healing.

(Source: Junqueira's Basic Histology. 13e ed. McGraw-Hill Medical)

1.3.3. FRACTURE FIXATION

The basic goal of fracture fixation is to stabilize the fractured bone, to enable fast healing of the injured bone, and to return early mobility and full function of the injured extremity. Fractures can be treated conservatively or with external and internal fixation. Conservative fracture treatment consists of closed reduction to restore the bone alignment. Subsequent stabilization is then achieved with traction or external splinting by slings, splints, or casts. Braces are used to limit range of motion of a joint. External fixators provide fracture fixation based on the principle of splinting. There are three basic types of external fixators: standard uniplanar fixator, ring fixator, and hybrid fixator. The numerous devices used for internal fixation are roughly divided into a few major categories: wires, pins and screws, plates, and intramedullary nails or rods. Staples and clamps are also used occasionally for osteotomy or fracture fixation. Autogenous bone grafts, allografts, and bone graft substitutes are frequently used for the treatment of bone defects of various causes. For infected fractures as well as for treatment of bone infections, antibiotic beads are frequently used [29]

1.3.3.1 Conservative Fracture treatment

Conservative treatment of a fracture consists of closed reduction to restore the alignment and subsequent stabilization. Conservative treatment is achieved by traction or by external splinting. Traction devices are temporarily applied along the long axis of the bone. They align the bone fragments and provide some stability. Traction devices work only when the fragments are still

connected to some soft tissues. Skeletal traction entails the insertion of either a Kirschner (K) wire or Steinman pin through the bone [30].

External slings, splints, and casts are made mainly of plaster of Paris, synthetic casting material, plastic, or metal. They can be used for the temporary immobilization of the injured extremity or for definitive fracture treatment. They may be used in combination with internal fixation to provide additional support [30].

1.3.3.2 External Fixation

External fixators provide fracture fixation based on the principle of splinting. They are the only system that allows the surgeon to control the flexibility of the fixation. External fixators are the standard in treating open fractures with substantial soft-tissue injuries that require vascular procedures, fasciotomy, soft-tissue flaps, or multiple debridement, to avoid additional damage to an already compromised limb. The other indications for the application of an external fixator are polytrauma; fractures in children to avoid pin fixation through the growth plate; temporary joint bridging before later open reduction internal fixation (ORIF); and arthrodesis of the ankle, elbow, or knee. In these latter cases, external fixators are especially indicated in acute or chronic infections, in limb-lengthening procedures, and occasionally after corrective osteotomies.

External fixators are made of pins or wires (Schanz screws, Steinman pins, Kirschner wires) that are placed percutaneously into the bone above and below the fracture site. These pins or wires are connected by various clamps to external fixation rods (stainless steel or carbon fiber rods). There are three basic types of external fixators: standard pin fixator, ring fixator, and hybrid fixator [29].

Figure 4a below shows a standard uniplanar external fixator radiograph of the wrist. The device was placed to treat a comminuted distal radius fracture, with pins in the second metacarpal and radial shaft. An ulnar styloid fracture is also present. Figure 4b shows a ring external fixator radiograph (Ilizarov) that transfixes a healing proximal tibial fracture [31].



Figure 4 : (a) Standard uniplanar external fixator. (b) Ring external fixator [31]

The figure below shows a Hybrid external fixator radiograph of the left leg in a patient who sustained gunshot injury to the leg. The device was placed to treat severely comminuted open proximal tibial and fibular fractures.

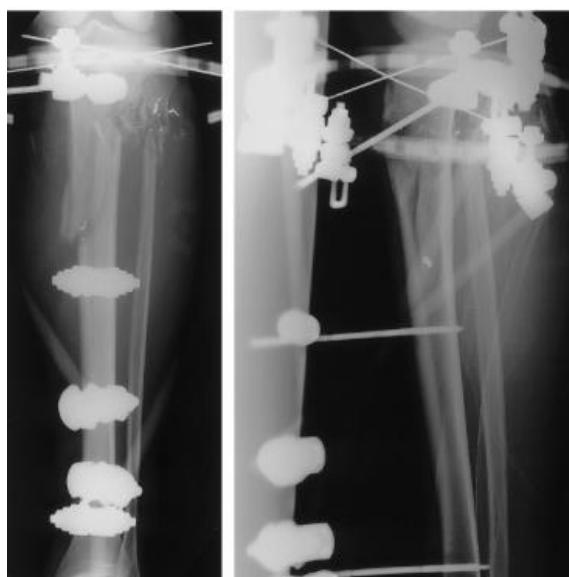


Figure 5 : Hybrid external fixator [31]

1.3.3.3 Internal Fixation

Since the late 1950s, open reduction and internal fixation (ORIF) has been used to restore bone anatomy and enable early mobilization and to overcome the limitations encountered when fractures are treated with skeletal traction or cast immobilization (1,2,5,6). The main goal of internal fixation is the achievement of prompt and, if possible, full function of the injured limb, with rapid rehabilitation of the patient. Numerous devices are available for internal fixation. These devices can be roughly divided into a few major categories: wires, pins and screws, plates, and intramedullary nails or rods. Staples and clamps are also used occasionally for osteotomy or fracture fixation [32].

. Epidemiology of FRI

The prevalence of FRI increased by 0.28 from 8.4 cases per 100,000 inhabitants to 10.7 cases per 100,000 inhabitants between 2008 and 2018 as revealed by a study conducted in Germany. The proportion of fractures resulting in FRI increased from 1.05 to 1.23% [33]. Gender distribution was equal. Patients aged 60–69 years and 70–79 years comprised the largest proportion with 20.2% and 20.7%, respectively, whereby prevalence increased with age group [33].

Another study carried out in Europe and Asia on FRI revealed the patient population to be predominantly male (69.5%). More than half of the patients (59.9%) had previously (within the 3 years prior to their inclusion in the current study) undergone orthopedic treatment related to the bone infection with a median number of treatments of 2.0 (range = 1.0-20.0). The origin of infection was fracture fixation for open or closed fracture (53.8%), prosthetic joint infection (PJI) (29.5%), or osteomyelitis (16.8%) [28]. Aside from *S. aureus* infection (MSSA or MRSA), 15.8% of patients had infections involving additional organisms[34] . The median time from onset of infection symptoms until baseline hospitalization was 14 days. Urgent (within 1 day) hospital admission was required in 43.5% and emergency (same day) admission in 21.6% and 60% of the patients had already had some orthopedic treatment related to infection prior to recruitment. The remaining patients (34.9%) were admitted semi-electively. Only three patients (1.0%) received an ambulatory treatment. The median time between admission and surgery was one day. The mean duration of hospital stay was 29.9 days (SD = 31.9), ranging from one to 247 days[34] . Treating surgeons recorded the cure rate at 1, 6, and 12 months as 4.5%, 36.8% and 62.1%, respectively. At one year, 63.6% of FRIs, 21.2% of PJI's and 15.3% cases of osteomyelitis were described as cured [34].

A prospective study conducted in Ghana between 2000 and 2005 on 194 patients treated for closed fractures revealed the cumulative incidence of wound infection after internal fixation was

3.3% which demonstrates that the incidence of wound infection following internal fixation is comparable with hospitals in a temperate climate in industrialized countries [35].

A study conducted in Cameroon between 2016 and 2017 on post-traumatic osteomyelitis including 31 patients revealed; the modal age range was 21-50 years (67.8%) and the sex ratio 1.8:4. The commonest bones affected were the tibia (48.5%) and femur (32.3%). Predisposing factors identified included open fractures (76%), delay surgical debridement (83.3%), presence of prosthesis (58%) and surgical wound infections (23%) [36]. Another study conducted in Cameroon between July 2015 and December 2020 on Open Tibia Fractures including 105 patients showed that 33 patients presented with FRI (31.4%)[37] .

The table below shows the proportion of infection following treatment for fractures relative to the fracture location, country and the year of study. We can see that higher proportions of infection was recorded in tibial fractures (shaft, plafond, plateau)[38] .

Table I : Proportion of fracture-related infections according to anatomical area [38]

Fracture location	Country/ year	Fixation technique	Nº of Patient	Nº of infections	Infection proportion
Clavicle	China/ 2020	Plates	285	22	7.7%
Proximal humerus	USA/2011	Plates	514	22	4.3%
Distal radius	Sweden/ 2020	Plates	21,348	1110	5.2%
Pelvis	USA/ 2019	Any kind	112	10	8.9%
Acetabulum	USA/2020	Any kind	628	42	6.7%
Proximal femur	China 2020	Any kind	1941	25	1.3%
Tibial plateau	USA/2022	Any kind	4532	226	4.9%
Tibial shaft	UK/ 2022	Intramedullary nailing	805	94	11.7%
Tibial plafond	USA/ 2022	Any kind	3158	286	9.0%
Calcaneus	China 2022	Any kind	883	19	2.2%

1.5 Why do fractures get infected (Risk factors)

- Patients factor

Cigarette smoking, diabetes, history of stroke, heart failure and numerous prior surgeries are recognized risk factors of OAI [39]. Smoking is associated with higher rates of nonunion and deep surgical site infection after non-pathological fracture treatment. Smoking cessation (\geq four weeks before surgery) is associated with a decreased rate of postoperative wound infection[40].

Immunocompromised patients can present atypically with slow growing atypical organisms and a combination of less fulminant initial clinical features that lead to a delay in diagnosis but later rapidly deteriorate into life-threatening infections [41,42]. Elderly patients, intravenous drug users and socially deprived patients are also shown to be at higher risk. In fragility hip fractures, both mortality and disability are increased with OAI. HIV-infected patients are at risk of osteoporosis, all types of fractures, infection of non-operated fracture hematoma and OAI[42].

A study in Germany revealed some risk factors for fracture related infection to include; arterial hypertension (50.9%), diabetes mellitus type II (20.7%), obesity (10.5%) and chronic kidney failure (12.3%)[43] .

- Fracture type

Open fractures are most commonly associated with OAI. The risk of secondary infection according to the Gustilo and Anderson grading¹⁵ is 2–4% for grades I and II, and between 4% and 52% for class III fractures, depending on the severity of soft tissue damage. Fractures of the lower limbs, especially near the proximal and distal tibia, are at the greatest risk. Severe soft tissue involvement, polytrauma, penetrating, blast, combat injuries and compartment syndrome are significant risk factors for subsequent infection. Irradiation-related fractures, pathological fractures and pelvic fractures requiring arterial embolization are all also at increased risk of OAI. In comparison to acute fractures, fixations of non-unions have double the risk of infection [39].

- Soft tissue injury

A study carried out in Switzerland from 2020- 2018 recorded 145 patients with lower leg FRI, of whom 58 (40%) received Soft Tissue Reconstruction (STR). In total seven patients required secondary STR due to primary flap failure. All failures and flap-related complications occurred within the first three weeks after surgery, secondary STR was successful in all cases. Out of the 43 patients who completed the 9-month follow-up, 11 patients presented with fracture nonunion and 12 patients with a recurrent infection [44].

- **Surgeons and implant factors**

A systemic review carried out in 2017 showed that prolonged surgery duration was associated with a statistically significant increased incidence of SSI [45]. The use of primary external fixators and delayed time to nailing and reaming were equally associated with a high risk of infection [46].

- **Controllable risk factors**

There is robust evidence to show that antibiotic prophylaxis is highly effective in reducing the risk of OAI for both open and closed fractures [39]. A study carried out in Cameroon revealed risk factors of infection to include; delay surgical debridement (83.3%), presence of prosthesis (58%) and surgical wound infections (23%) [36].

1.6 Pathogenesis

FRI generally occurs exogenously due to the trauma itself (e.g. open fracture), during insertion of the fixation device or during disturbed wound healing or late soft tissue coverage in cases of open fractures [18].

For an infection to occur, bacteria needs access to the host (skin break), they also need an environment that offers nutrients and relative safety from host defence. Biofilm formation (it is a surface phenomenon, where bacteria or living organisms live in a very low metabolic state on the surface of dead bone or implants) on the surface of foreign material is crucial in the pathogenesis of FRI [47]. Because it provides a suitable environment for bacterial proliferation with nearby necrotic tissue [48].

The figure below shows changes the bone undergoes during bacterial infection in fracture related infections;

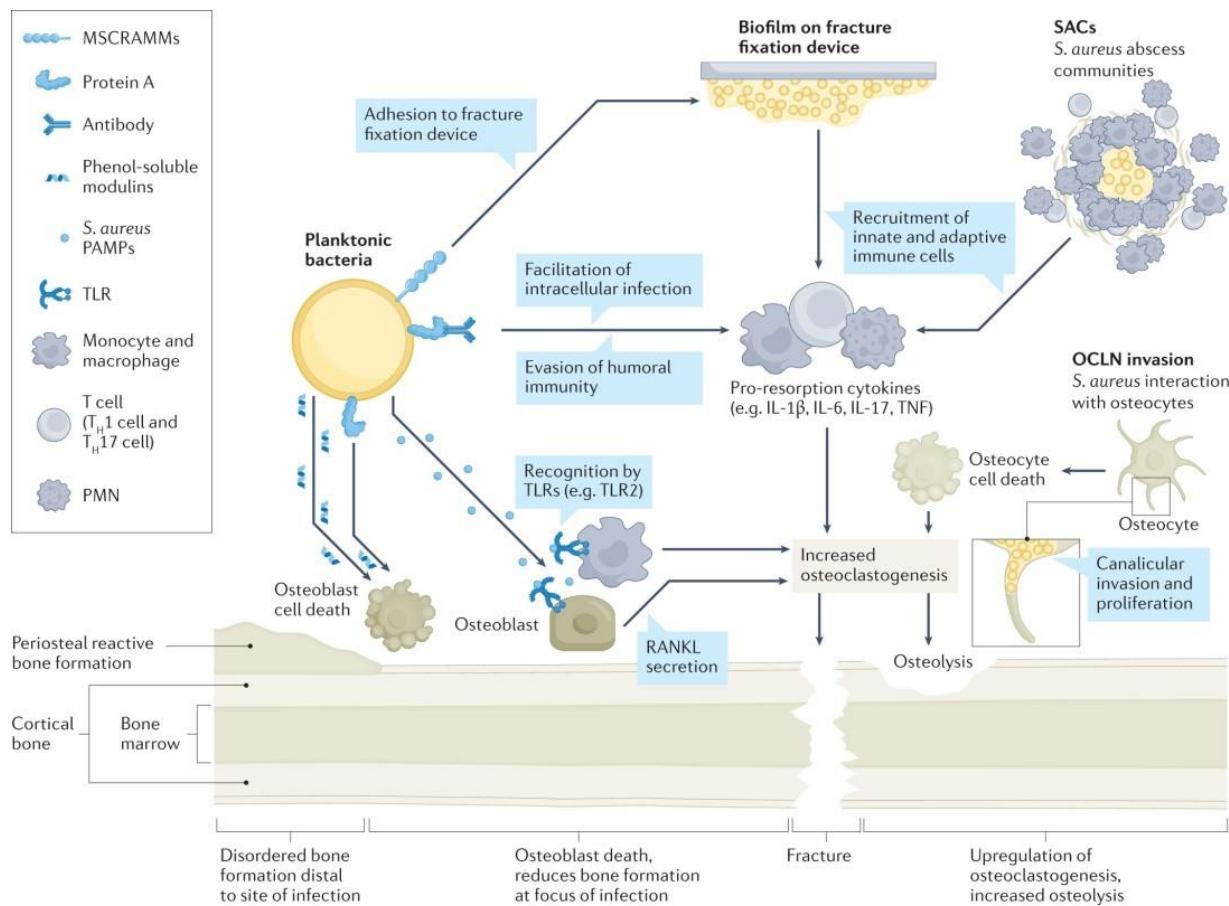


Figure 6 : Mechanisms of bone changes during bacterial infection in fracture-related infection [49]

Microorganisms in a biofilm survive much higher antibiotic concentrations than planktonic ones and, therefore, systematically applied antibiotics mostly do not reach the necessary therapeutic levels [50]. For this reason, successful management of FRI requires a combination of surgical and antimicrobial treatment [48].

FRI generally occurs exogenously due to the trauma itself (e.g. open fracture), during insertion of the fixation device or during disturbed wound healing or late soft tissue coverage in cases of open fractures. Haematogenous infections are rare [51,52]. Polymicrobial infections are frequent (20–35%), and mainly occur in patients with open fractures [8].

The table below gives an overview of the most commonly identified microorganisms causing FRI

Table II : Most common microorganisms in fracture-related infection

Microorganism	Frequency (%)
Staphylococcus aureus	30 - 42%
Coagulase-negative staphylococci	20 - 39%
Enterobacteriaceae	14 - 27%
Anaerobes	16%
Streptococci	11%

Time is an important aspect in the pathogenesis of FRI for the following reasons;

- Maturation of biofilms occurs over the course of weeks and determines the efficacy of antimicrobial therapy [48] .
- Fracture healing leading to bony consolidation is crucial for cure of infection and takes place over the course of weeks to months [53].
- The extent of bone involvement needs consideration when developing a treatment strategy. Preclinical models have shown that within the first 2 weeks after fracture fixation, the bone does not show signs of osteomyelitis or osteolysis, despite the presence of bacteria on the implant [48].

Over the course of the following weeks, histological signs become present. Currently, many classifications are based on these three factors and on time in general [54].

1.7 Classification

Currently no classification is available that is tailored specifically to the FRI patients. Fracture-related infection can be classified according to the time to onset of symptoms after fracture fixation, dynamics of symptoms, route of infection, location, fracture stability and union status, host type, soft-tissue envelope and disease-causing pathogens.

- Willeneger and Roth classification (Infection after fracture fixation - IAFF)
- Cierny – Mader classification
- BACH classification

- **Willeneger et Roth**

Time of onset of symptoms after fracture fixation is the most commonly used and applied modality to classify FRI since it represents the time-dependent pathophysiologic changes of FRIs and may affect treatment decisions. Willeneger and Roth classified FRIs as:

- **Early (< 2 weeks):** Infection presenting early after osteosynthesis is mainly caused by highly virulent pathogens (e.g. *Staphylococcus aureus*). The diagnosis is often made by clinical assessment, since these patients often present with classic local signs of infection as well as wound drainage, which may be accompanied by a local or systemic inflammatory reaction.
- **Delayed (3–10 weeks):** the delay may be due to less virulent organisms or to inadequate early antibiotic use, partially suppressing an early onset of infective symptoms.
- **Late (> 10 weeks):** a mature biofilm as well as bone necrosis and osteolysis may be seen, necessitating thorough debridement and implant removal/exchange [7].

- **Cierny- Mader**

The Cierny-Mader (C-M) classification provides prognostic data and helps in management. It provides anatomical, clinical and radiological features.

For the anatomical classification 4 types exist; Type I (medullary) Type II (superficial) Type III, (localized) Type IV (diffuse). It is most widely used in chronic FRI.

- **Type I (medullary osteomyelitis)** diffusely involves the intramedullary cavity, usually after medullary nailing. The entire medullary canal is involved, and will require surgical clearance (nail removal and reaming).
- **Type II osteomyelitis is superficial,** may be present under a plate, but is rarely, if ever, seen with fracture-site infection.
- **Type III osteomyelitis (localized full-thickness cortical involvement),** will require excision of all necrotic bone. During the excision, the full extent of the necrotic area becomes evident. This may weaken the bone, or produce significant dead space. Soft-tissue cover may be inadequate and therefore require reconstruction. Fracture healing may be a problem requiring additional treatment.
- **Type IV osteomyelitis diffusely** involves the entire circumference of a segment of the bone. The entire bone segment must be removed to eliminate necrotic tissue and persistent bacteria.

The patient is classified as an A, B, or C host.

- **A host** is a patient with normal physiological, metabolic, an immunologic capability.
- **B host** is systemically compromised, locally compromised, or both.
- **C host**, morbidity of treatment is worse than that imposed by the disease itself.

The terms acute and chronic osteomyelitis are not used in this staging system since areas of macronecrosis must be removed regardless of the acuity or chronicity of an uncontrolled infection. The stages are dynamic and interact according to the pathophysiology of the disease. They may be altered by successful therapy, host alteration, or treatment [55].

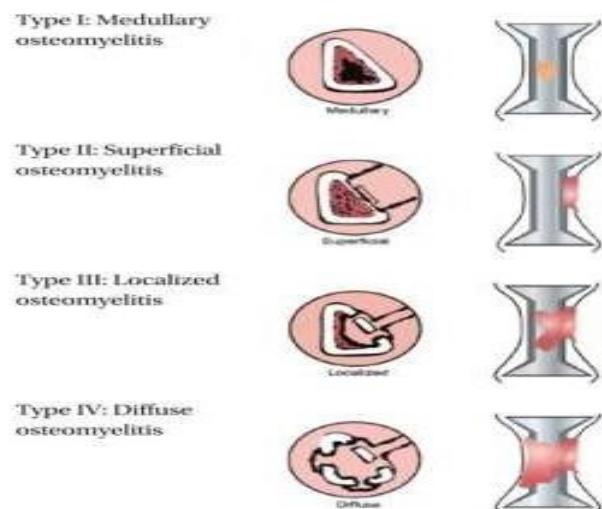


Figure 7 : Cierny - Mader classification [27]

- BACH Classification

In 2017, Hotchen et al. [7] conducted a systematic review to summarize the classification systems for long bone OM, and they totally identified thirteen systems. After analyzing advantages and disadvantages of each system, they recommended that the following four aspects should be emphasized when classifying OM:

- bone involvement (B-variable)
- antimicrobial resistance patterns of the causative pathogens (A-variable)
- coverage of soft tissue (C-variable)
- host status (H-variable)

The bone involvement was divided into three options based on the presence of cavitary involvement (which includes a cortical, medullary, and non-segmental corticomedullary infection) (B1), segmental involvement (B2), or the concomitant involvement of a joint irrespective of the segmental or cavitary infection (B3). The antimicrobial options used the European Society of Microbiology and Infectious Diseases (ESCMID) criteria for stratifying isolates into multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) isolates, and in case of a foreign body, whether an antimicrobial compound with activity against adhering (biofilm) bacteria was available. The coverage of the soft tissues was classified based on whether patients required plastic surgical expertise for skin closure after surgical excision of the infection. The host status stratified patients based on the presence or absence of comorbidities such as diabetes mellitus, vascular or immune compromise, or the presence of recurrent osteomyelitis following previous reconstructive surgery.

Based on the classification of these individual variables, the complexity of osteomyelitis can be determined. Each variable in BACH is stratified into either ‘uncomplicated’ or ‘complex’. In two variables, the antimicrobial options and the host status, osteomyelitis can also be stratified as having ‘few or no options available’. The overall complexity of the osteomyelitis is determined by classification of the most severely classified variable [56].

2. DIAGNOSIS OF FRI

2.1 Patients history and Clinical presentation

Besides information on allergies (e.g. antibiotics), medication (e.g. antibiotics and anticoagulants) and overall medical condition (i.e. host's physiology, risk factors) the medical history concerning the suspected FRI has to be obtained carefully. This includes information on: the initial trauma (mono- or polytrauma), initial fracture pattern with accompanied soft tissue injury (including nerve and vascular injuries), fracture fixation and other surgeries, postoperative wound healing disorders or history of previous FRIs with prior results from microbiology [57].

The clinical presentation of FRI depends on; the preceding trauma and/or surgical procedures, the anatomical localization, the quality of bone and surrounding soft tissue, the time interval between microbial inoculation (trauma, surgery) and manifestation of infection and the type of microorganism [58].

Early postoperative infection (<3 weeks) is generally characterized by erythema, local hyperthermia, protracted wound healing and a secreting wet wound. Thus, wound healing disturbances after internal fixation are highly suspicious of early infection and should be managed as such. The first step is always debridement surgery for diagnostic and therapeutic purposes [58].

Delayed (3–10 weeks) or chronic (≥ 10 weeks) infections are typically due to low-virulence microorganisms such as coagulase-negative staphylococci. However, they may also result from inadequate treatment of early infection. If a patient with wound healing disturbance is treated with a short course of antibiotics without debridement surgery, clinical signs of suppressed early infection typically reappear at a later time. Delayed and chronic infections manifest as persistent pain and/or signs of local inflammation, such as erythema, swelling or intermittent drainage of pus (sinus tract) [58].

2.2 Work-up

Laboratory

- Biological: Blood tests reveal increased CRP levels, leukocytosis and an elevated ESR; it should be remembered, though, that these inflammatory markers are non-specific and may be affected by tissue trauma [4].
- Microbiology: At least 3 deep tissue specimens and if possible, the implant should be

cultured to confirm the presence of a microorganism and determine susceptible antibiotics. Swab cultures have a low sensitivity and a high risk for contamination. Therefore, tissue cultures should be preferred [18].

Imaging

There are 3 indications to request diagnostic imaging for FRI

- To acquire more certainty regarding the presence or absence of FRI,
- To visualize the anatomic details of the disease such as its extension, the presence of sequestrations, sinus tracts, and/or subcortical abscesses, for surgical planning,
- To establish the degree of fracture healing and implant stability. For these purposes, the clinician has a choice of several radiological and nuclear imaging techniques [59].

Such imaging includes: conventional radiography, computed tomography (CT), magnetic imaging resonance (MRI), 3-phase bone scan (BS), fluorodeoxyglucose positron emission tomography (FDG-PET), and white blood cell (WBC) scintigraphy. On a conventional radiography, we could see hyperemia demineralisation lysis (>40percent), lack of peripheral reaction sclerosis [4].

2.3. Positive Diagnosis of FRI

Diagnostic criteria of FRI were proposed by an international consensus in 2018 [1] and updated later, including confirmatory criteria and suggestive criteria. A recent study validates the diagnostic criteria of FRI, and the authors confirmed the excellent diagnostic discriminatory value of the confirmatory criteria. For suggestive criteria, specificities of over 95% were obtained for clinical signs of fever, wound drainage, and local redness. This implies satisfying efficacy of such criteria for FRI diagnosis. [60] .

These criteria can be summarized as shown in the figure below;

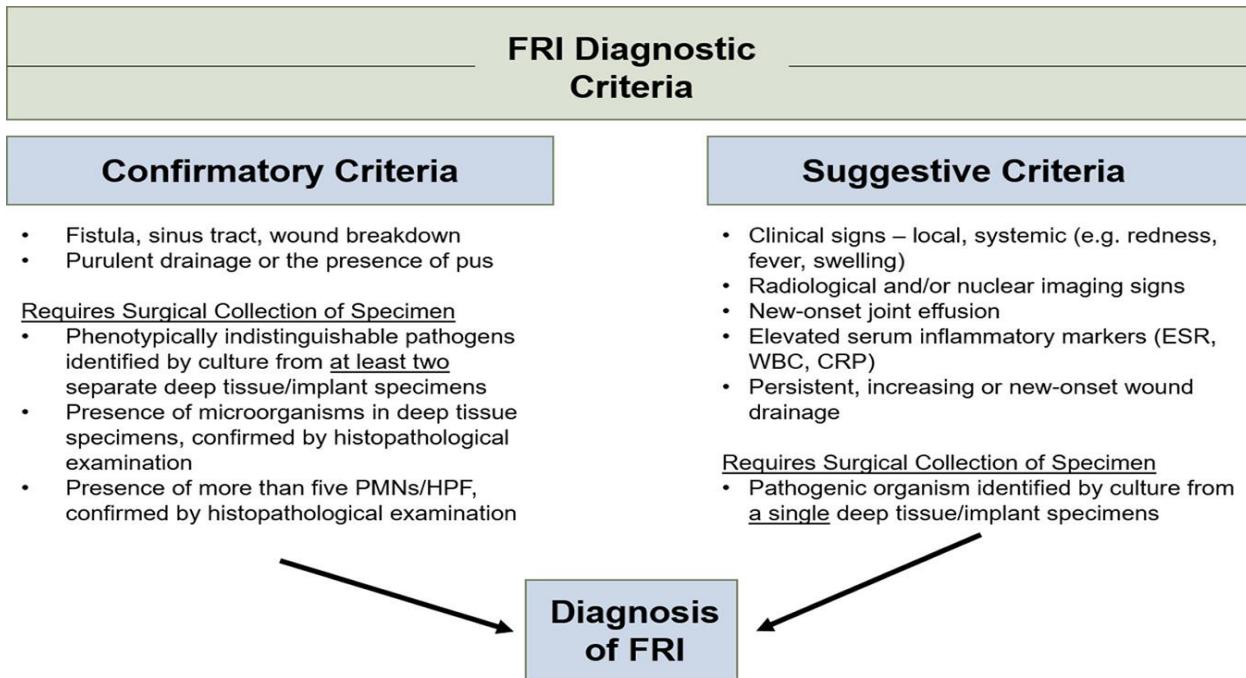


Figure 8 : FRI diagnostic criteria [1]

-For confirmatory criteria, any single criterion is sufficient for a confirmatory diagnosis of FRI.

- For suggestive criteria, identification of any of these criteria should prompt further investigation, which may lead to identifying confirmatory criteria. FRI, fracture-related infection; PMNs (polymorphonuclear neutrophils) HPF (high-power field) ($\times 400$ magnification); ESR, erythrocyte sedimentation rate; WBC, white blood cell; CRP (C-reactive protein) [1].

3. MANAGEMENT OF FRI

Management is multidisciplinary, taking into consideration the patient's condition (their wishes and expectations, comorbidities, drug use, alcohol and smoking) and the injury (type of fracture, if bone loss, soft tissue loss) [61].

3.1 Treatment Goal

- Bone union with fewer complications
- Eradication of infection as the final outcome (in certain cases, initial suppression of infection until fracture consolidation is achieved).
- Healing of the soft-tissue envelope
- Restore limb function
- Avoid complications; soft tissue infection, osteomyelitis, amputation, reduction of limb function, physiological and social dysfunction etc [62].

3.2 Means and Methods

The general treatment principles for FRI include radical debridement, implant handling, systemic and local antibiotics, reconstruction defects of bone and soft tissues, and functional recovery [17]. Management of FRI can therefore be grouped into surgical management and antibiotic therapy.

3.2.1 Surgical principles

Host optimization

- Stop smoking (slows bone consolidation) [41].
- Tissue perfusion and oxygenation are also key components in wound healing. Severe arterial insufficiency should be corrected prior to definitive treatment [63].
- Surgery induces a stress on the body resulting in the release of catecholamine, cortisol and glucagon, thereby causing surgery induced hyperglycaemia. Blood sugar level should be maintained between 140 mg/dL and 180 mg/dL [64].
- If the patient appears nutritionally at risk, oral nutritional supplementation can be considered prior to surgery, in consultation with professionals. If the malnourishment is severe, the combination of oral nutritional supplementation with parenteral nutritional support should be

considered prior to surgery. In such cases, if the patient's clinical status allows it, it is advisable to delay surgery until the nutritional status is under control

- Vitamin D supplementation to improve bone healing for those patients who are considered at risk, like postmenopausal women.
- Stop antibiotics 2 weeks prior to debridement.
- Manage immuno-compromised states

NB : Intra- operating sampling :Deep sterile samples (tissue, not swap) should be taken using separate clean instruments each time care ,taking care not to touch skin and the sample placed straight into container, 5/6 microbiology + 1 biological.

Radical debridement and optimization

- Debridement remains an important surgical tool in the treatment of FRI.
- In general, debridement should include the excision of necrotic (i.e. non-bleeding) bone or tissue, excision of poorly perfused tissue (it will not contribute to wound healing and antibiotic delivery) and removal of all non-essential foreign bodies (e.g. broken screws, sutures) [48] .
- The debridement styles may differ among different C-M anatomical classifications and infection sites. For example, the RIA system is often applied for type I intramedullary infection, while for type III localized calcaneus infection, an “eggshell-like” debridement has been proved to be effective [4].
- Irrigation aims at decreasing the bacterial load and removal of loose debris. It should be performed using normal saline at low pressure to avoid bacterial seeding in soft tissue and bone
 - A sufficient amount (i.e. depending on the anatomic location) of irrigation fluid should be used in order to thoroughly clean the surgical field and to lower the bacterial load after debridement [48].

Improving response to antibiotics [65]

- Eradication of biofilm.
- Use local antibiotic delivery systems. e.g: carentment G.
- Improve local delivery of systemic A by transfer of vascularised tissues

Dead space management [66]

- Dead space is the cavity or the space left behind by the act you have done (debridement) and to be filled for adequate healing
- Walls of infected cavity are rigid (because comprise of bone or fascia)
- The cavity does not collapse on itself after debridement
- Dead space elimination is essential in the prevention of reoccurrence
- Ideal dead space filler still eludes

Bone defect treatment and instability [67]

- Segmental bone defects of long bones are challenging, especially when associated with infection.
- In infected cases we prefer external fixation although internal fixation may be used in certain anatomical regions (hip bone)
- External fixation provides stable fixation, minimal surface area for biofilm formation, corrects bone deformity, recreate lost bone

Soft tissue reconstruction [68]

- Meticulous debridement of all non-viable tissue may result not only in bone defects, but also in major overlying soft tissue loss
- Reconstruction should be done with vascularised tissues
- Provides coverage
- Provides vascularity
- Increases antibiotic delivery to area

3.2.2 Surgical treatment strategies

Surgery remains one of the cornerstones of the treatment of FRI. All surgical approaches have one important element in common; a judicious well-planned debridement with removal of all dead tissues and acquisition of deep tissue biopsies for microbiology and histopathology .Following the debridement and sampling, the fracture fixation needs to be addressed. This can either be removed, retained or revised. Repair or reconstruction of the soft tissue envelope is essential, irrespective of what approach is used in terms of the fracture fixation and skeletal reconstruction i.e. whether the initial implant is retained, exchanged or removed. A thorough debridement entails excising all

necrotic or ischemic tissue, including scarred soft tissue. The soft tissue envelope then needs to be reconstructed with well-vascularized tissue. This can be done at the same time as the debridement (one stage procedure) or as a subsequent surgical procedure (two stage soft tissue reconstruction) [69].

Selecting the appropriate surgical strategy depends on numerous factors related to the ability to perform a proper debridement (e.g. considering implant type). This is illustrated by the fact that the rate of treatment failure in case of implant retention is higher in the presence of an intramedullary nail than plate osteosynthesis. This can be explained by the fact that the intramedullary canal cannot be debrided in the presence of an implant. Other factors that may affect the choice of surgical strategy include; patients factors, pathogen, bone and soft tissue. In selected cases, where fractures are judged to be in the optimal mechanical and biological environment to unite, the infection may be suppressed and implants retained until fracture union. In these scenarios, the subsequent surgery is much less complex when the fracture is united. If there is an established non-union present or if fracture union is deemed unlikely to occur, exchange/revision of the fixation is indicated. Exchange of the fixation is typically performed as either a single or a two-stage procedure. This approach can be likened to the one- or two-stage revision in periprosthetic joint infection (PJI) [69].

The flow chart below shows a treatment algorithm describing the basic treatment principles for FRI

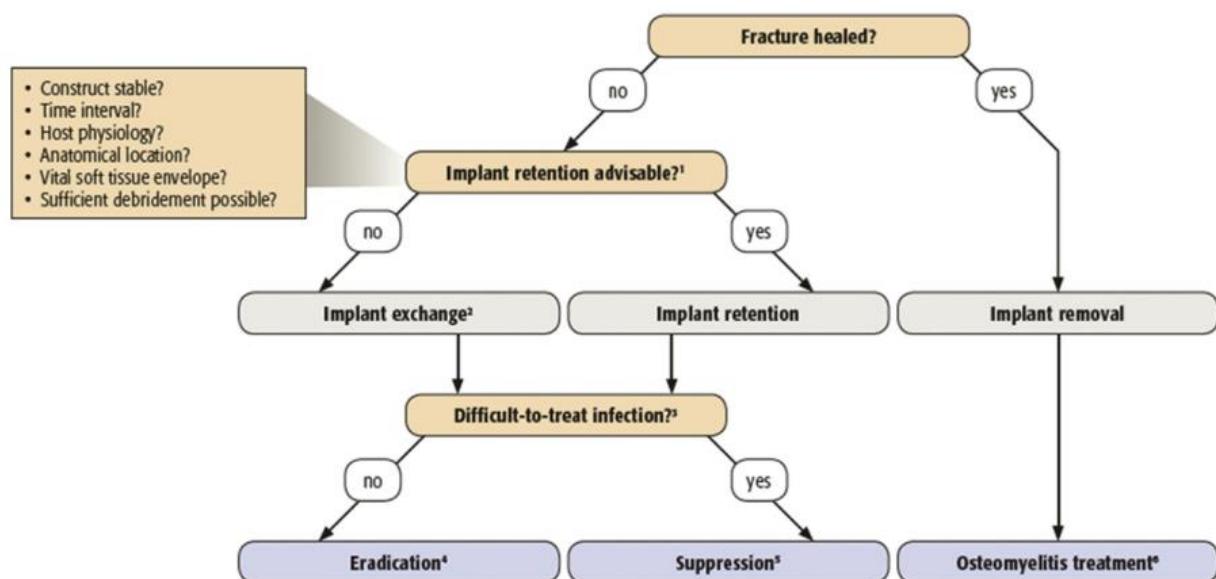


Figure 9 : Algorithm describing the basic treatment principles for fracture-related infection [18]

3.2.2.1 Implant Removal

If the fracture is united, treatment is typically less complex because of the absence of instability; thus there is no need to perform internal or external fixation. This is one of the main reasons why achieving fracture union remains the main priority when dealing with FRI in the setting of an ununited fracture. In the case of a healed fracture, either a curative approach or palliative approach can be followed. In the vast majority of cases a curative strategy is employed, which involves debridement and implant removal. Very rarely, when the patient is deemed unfit for surgery, a palliative treatment strategy may be indicated. In this scenario, suppressive antibiotics are typically administered for a limited period of time while the patient is optimised for surgery. Rarely, long-term suppression or even amputation may be indicated when patient cannot be optimised for surgery. In the absence of union, the choice is between retention or revision of the fixation [18].

3.2.2.2 Debridement Antibiotics Implant Retention (DAIR)

Retention of the original implants is often tempting, as it would negate having to redo the fixation, which could involve unintentional loss of reduction, additional soft tissue stripping or even further bone loss. However, the reported success rates of debridement, antimicrobial therapy, and implant retention (DAIR) are highly variable and dependent on a number of factors. An adequate debridement resulting in reduced bacterial burden and a vital well-perfused soft tissue envelope, are prerequisites. The first priority in the management of FRI is fracture union, therefore the original implants should only be retained if the fracture is stable and there is a high likelihood of fracture union under the prevailing mechanical and biological environment. Once this decision is made, the other factors associated with increased risk of treatment failure with implant retention need to be considered [70].

With an increase in the duration of the infection and the time from the index surgery, there is a corresponding rise in the failure rate due to recurrence of infection. Other factors associated with an increased risk of failure include: local or systemic compromising host factors (such as smoking, diabetes, or peripheral vascular disease), the location and nature of the injury (with lower extremity and open fractures being at higher risk), the type of implant present (intramedullary nails being associated with a higher risk), multiple debridement, failure to obtain primary soft tissue closure, the use negative pressure wound therapy following the debridement and difficult-to-treat pathogens (such as rifampin-resistant staphylococci or bacteria resistant to biofilm active antibiotics) [71].

3.2.2.3 Implant exchange

If implant retention strategy is not deemed advisable, further decisions need to be made with regards to: 1) The need to reconstruct a bone defect, 2) The type of fixation that will be used following removal of the original implants, and 3) The timing of the exchange of fixation, i.e. whether it will be done in a single sitting or in stages [69].

The first question to ask when implant exchange is being considered is: Is there a critical bone defect? A critical bone defect can be defined as any defect that will not heal without further surgical intervention. The treatment of post-infective bone defects is complex; there are numerous treatment options and many factors that influence the decision making. There is currently limited robust evidence to guide treatment strategy selection in the management of bone defects and in many cases is based on the surgeons experience and preference. The choice of reconstruction option is dependent on the site, size and shape of the defect, the quality of the soft tissues and bone, and the presence of deformity, joint contractures or leg length discrepancy [72].

The next question to answer is: What type of fixation that would most reliably achieve union at the fracture site? The choice of fixation is also influenced by a variety of other factors, including the anatomic location of the fracture, the fracture configuration, the bone quality, the presence of a bone defect and the soft tissue envelope. If there is a critical bone defect the fixation would typically depend on the techniques selected to treat the bone defect [73].

Fracture union remains the priority in the treatment of FRI. Therefore the fixation method that would most reliably yield fracture union should be selected. For this reason internal fixation may be an option when performing implant exchange in certain cases of FRI involving the upper limb. There is however a lack of comparative data with regards to the optimal method of fixation. McNally et al. have looked at the factors associated with failure of treatment in FRI and noted comparable failure rates with exchange to new internal fixation and conversion from internal to external fixation (12.5 % vs 10.3 %) [74].

The authors have previously proposed that internal fixation can be considered in selected patients, who are Cierny & Mader type A hosts, with less than 2 cm bone defects, good bone stock and soft tissue quality, and no multi-resistant organisms. They noted that, in their experience, internal fixation was used in less than 5 % of infected non-unions.⁷⁰ With the increased use of local antibiotics there has, however, been an increase in the use of internal fixation in infection, for example with the use of antibiotic coated intra-medullary nails [74].

The final question when embarking on an implant exchange treatment strategy is whether a single stage procedure is advisable. In a case with acute severe systemic or local sepsis (such as significant pus accumulation or significant cellulitis) a staged approach may be more appropriate and less risky. In its absence, the decision is not as simple. There are several other factors that may also influence the decision to embark on a staged approach, like concerns about the viability of the remaining bone, poor quality soft tissues, significant host impairment due to comorbidities and a multi-resistant difficult-to-treat pathogen [69].

More recently, cases series utilizing either one- or two-stage procedures have shown good results. McNally reported eradication of infection in 96 % of tibial nonunions treated with a single stage procedure and circular external fixation at a mean follow-up of 40 months.⁷³ Union was ultimately achieved in 91 % of patients. On the other hand, Zhang et al. reported a union rate of 90 % at 2-year follow-up with a staged approach in infected nonunion of long bones. Union occurred in 91 % of cases with negative cultures at time of definitive fixation, compared to 63 % of cases who were culture positive [75].

Treating large (>5 cm) segmental bone defects in the lower limbs is particularly challenging. While there was initially significant enthusiasm about the induced membrane technique, as popularized by Masquelet, this has waned with studies showing complication rates of up to 50 %. Concern has been raised about the use of this technique in segmental tibial bone loss, in particular, having been shown to have a low success rate. Recently, Feltri et al. showed in their meta-analysis on diaphyseal bone defects (not exclusively resulting from infection) that bone transport yielded the highest rate of primary union (91 %), as well as the lowest reintervention rate, when comparing it with bone graft procedures. However, the limitation of this study was that a heterogeneous group of cases were pooled together involving a variety of diagnoses and defect sizes. Another meta-analysis has shown that the use of distraction osteogenesis is associated with a high rate of resolution of infection for the treatment of long bone defects in the lower limbs. However, bone transport is a complex, lengthy procedure with a high demand being placed on both the surgeon and the patient. Vascularized free fibula autograft is another option to consider for large segmental defects, particularly in the upper limb. Potential advantages include a shorter time to union and lower number of surgeries, however fracture and fracture remains a concern [76].

3.2.2.4 Masquelet technique

Masquelet technique for osseous defects serves as an alternative method to bone transport when addressing large osseous defects. Masquelet et al originally described the induced membrane technique as a novel method to fill a large bony defect with a cement spacer while awaiting definitive reconstruction and coverage. This method focuses on avoiding iatrogenic injury and surgical devitalization of the local area, while the cement spacer fills the bony void. It is a 2- stage technique that avoids microsurgery and can be used in the acute trauma setting. It does not require immediate grafting and can be performed in the case of contaminated wounds where bone grafting would be contraindicated [77].

To perform, the first stage involves a cement spacer to be implanted within the intramedullary canal and over the cortical edges to optimally maintain the space for bony reconstruction. In the cases of infection or gross contamination, an antibiotic cement spacer could be used but may conceal a low-grade recurrence of infection. Masquelet describes returning to the surgical site 6–8 weeks later to find an induced membrane around the cement spacer, which is abundant with vascular endothelial growth factor [77].

The second stage requires explanation of the cement spacer while minimizing disturbance to the overlying membrane and filling the residual void with bone graft. This is performed through careful exposure of the cement spacer, which is explanted using osteotomes to break the spacer into smaller pieces and removed in its entirety being mindful to keep the surrounding membrane intact. Once thoroughly irrigated to remove any residual cement, the adjacent medullary canals are curetted to obtain further autograft and also allowed for further bleeding into the graft site. Autograft serves as the gold standard for this stage and may be augmented with bone substitutes, bone marrow aspirate, or allograft [77].

Although the induced membrane technique requires 2 surgical stages and a significant amount of autograft with potential donor site morbidity, it serves as an alternative method to vascularized fibular autograft or distraction osteogenesis, both of which have their own technical challenges and associated morbidities [77].

Dead space management

Debridement in FRI often creates a dead space, which is a poorly perfused defect allowing bacterial proliferation. This environment of low oxygen and pH is ideal for the development of biofilm and bacterial persistence. Therefore, local antimicrobial delivery systems are often used as temporary or definitive strategies for dead space management. The chosen antibiotic must provide coverage against a wide range of pathogens (i.e. broad-spectrum antibiotic) or against a specific pathogen identified by culture, it must be compatible with and achieve an adequate release from the chosen carrier, and it must have a good toxicity and hypersensitivity profile, and a low rate of resistance. In clinical orthopedics practice, gentamicin, tobramycin, vancomycin, and clindamycin are the most common commercially available formulations for local antibiotic delivery. They are industrially incorporated into bone cement, collagen, and other bone void fillers that are available for clinical use [78].

Antibiotic impregnated bone grafting has recently been considered as a treatment option for bone voids. Before its introduction, bone graft was avoided in the setting of an active infection because of the risk of devascularised graft becoming a source of sequestrum. Bone graft serves as a superior scaffold for restoring osseous anatomy that theoretically would not compromise substrate strength and decrease the risk for mechanical failure [78].

3.2.3 Antimicrobial therapy

After surgical debridement and sampling, empirical antibiotic therapy should be started in case of high suspicion of infection. The choice of empiric therapy depends on the local epidemiology of microorganisms and individual risk factors of the patient (i.e. previous antibiotics, comorbidities, allergies, previous hospitalizations, previous debridement at the same site, previously recovered pathogens). As a rule, initial empiric therapy should include a lipo/glycopeptide and an agent against GNB, thereafter it should be adapted according to culturing results as soon as possible. In most cases, antimicrobial therapy can be delayed until after deep tissue sampling. Immediate antibiotic therapy is only given to patients with sepsis and after obtaining blood for culture.

Empiric IV antimicrobial therapy should be started as soon as tissue samples are taken and maintained until culture results are available. The choice of empiric therapy depends on the local epidemiology of antibiotic resistance rates, antibiotic formularies and the risk factors of each individual. In suspicion of biofilm-related infection, biofilm-active antibiotic agent is suggested,

which had been certified of rifampicin combinations against staphylococci and fluoroquinolones against Gram-negative bacteria. Recent studies showed that **daptomycin**, **dalbavancin** are also efficient in management of osteomyelitis [79].

Frequently locally used antibiotics are gentamicin, tobramycin, vancomycin, and clindamycin. Other antibiotics that had been reported for local use include cefazolin, daptomycin, erythromycin, polymyxin, linezolid, amphotericin, voriconazole, and amikacin [79].

Duration of antimicrobial therapy is controversial and not well investigated. Overall, regimes of 6–12 weeks are common and should be decided with advice from the MDT. A recent randomized controlled trial showed that patients treated with up to 7 days of IV (intra-venous) antibiotics followed by oral therapy had the same outcome as those with prolonged IV therapy (usually 6–12 weeks) [79].

Patients should have a baseline blood analysis available, especially patients who will receive IV antimicrobial therapy, including baseline inflammatory markers [e.g. C-reactive protein (CRP)], full blood count, electrolytes and liver- and renal function tests. Depending on the type of antibiotic and local preferences, some specific blood parameters (e.g. liver function tests for rifampicin, electrolyte levels and full blood count for fluoroquinolones, etc.) should be monitored at least twice weekly, as common side effects of high-dose IV antibiotics include bone marrow suppression, hepatitis and nephrotoxicity [79].

Following a study in Cameroon, out of 31 samples, 29 yielded positive culture giving rise to 48 bacteria isolates. Fourteen samples (48%) were polymicrobial. The most predominant species was Escherichia coli (29%), followed by Staphylococcus aureus, Pseudomonas aeruginosa and Klebsiella pneumoniae (all 22.6%). The gram-positive organisms showed good sensitivity to Imipenem, Rifampicin, Fucidine, Lincomycin, and to Vancomycin whereas the gram-negative bacilli were mostly sensitive to Imipenem (96.7%), Amikacin (82.1%) and to a lesser extent Quinolones (54%) and Piperacillin/Tazobactam and Ceftazidime (48%). Conclusion: Nosocomial bacteria dominate the bacterial flora of posttraumatic osteomyelitis in our setting and many multidrug resistant strains are emerging thus emphasizing on the importance of hygiene and targeted antibiotic therapy [36].

Based on these concepts, treatment duration and mode of administration will be discussed below

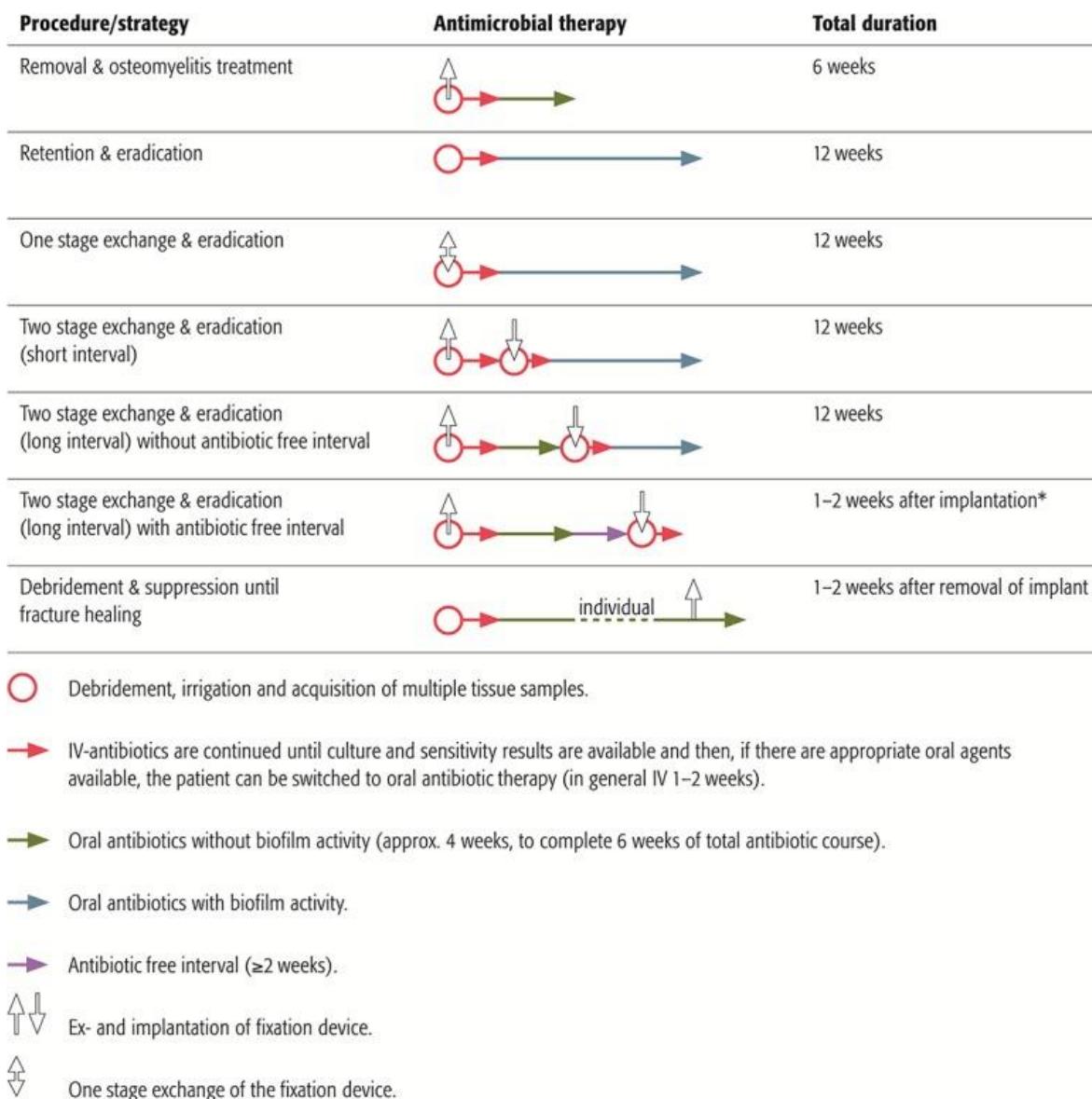


Figure 10 : Duration of antimicrobial therapy according to treatment strategy.

- Suppression therapy

In the case of a late onset FRI with biofilm maturation where the fracture is not yet consolidated, the goal of treatment can be to suppress the infection till fracture consolidation, then implant removal is done. If the planned goal is suppression therapy until the fracture is consolidated, oral monotherapy can be given depending on the pathogen and should be continued until 2 weeks after implant removal [62].

Treatment guidelines of FRI

Standardized guidelines for treatment of fracture-related infection (FRI) are lacking. Worldwide, many treatment protocols are used with variable success rates [80]. Consolidation of the fracture while avoiding osteomyelitis is considered the primary goal in the treatment of FRI. Careful planning of the treatment strategy is therefore essential. Contrary to the therapy in PJI, infection eradication is not always mandatory. It must be determined whether implant removal is possible, infection eradication should be attempted with the implant in place, or whether infection suppression with suppression therapy until bone consolidation with subsequent implant removal and healing of the infection is an option. Suppression therapy shows good results when the bone is vital and low-virulence pathogens are detected [81].

- **Consolidated fracture**

If FRI occurs after consolidation of the fracture, thorough debridement with complete removal of the implant material is recommended. The duration of antimicrobial therapy is based on the treatment of acute osteomyelitis and includes a total of at least 6 weeks [81].

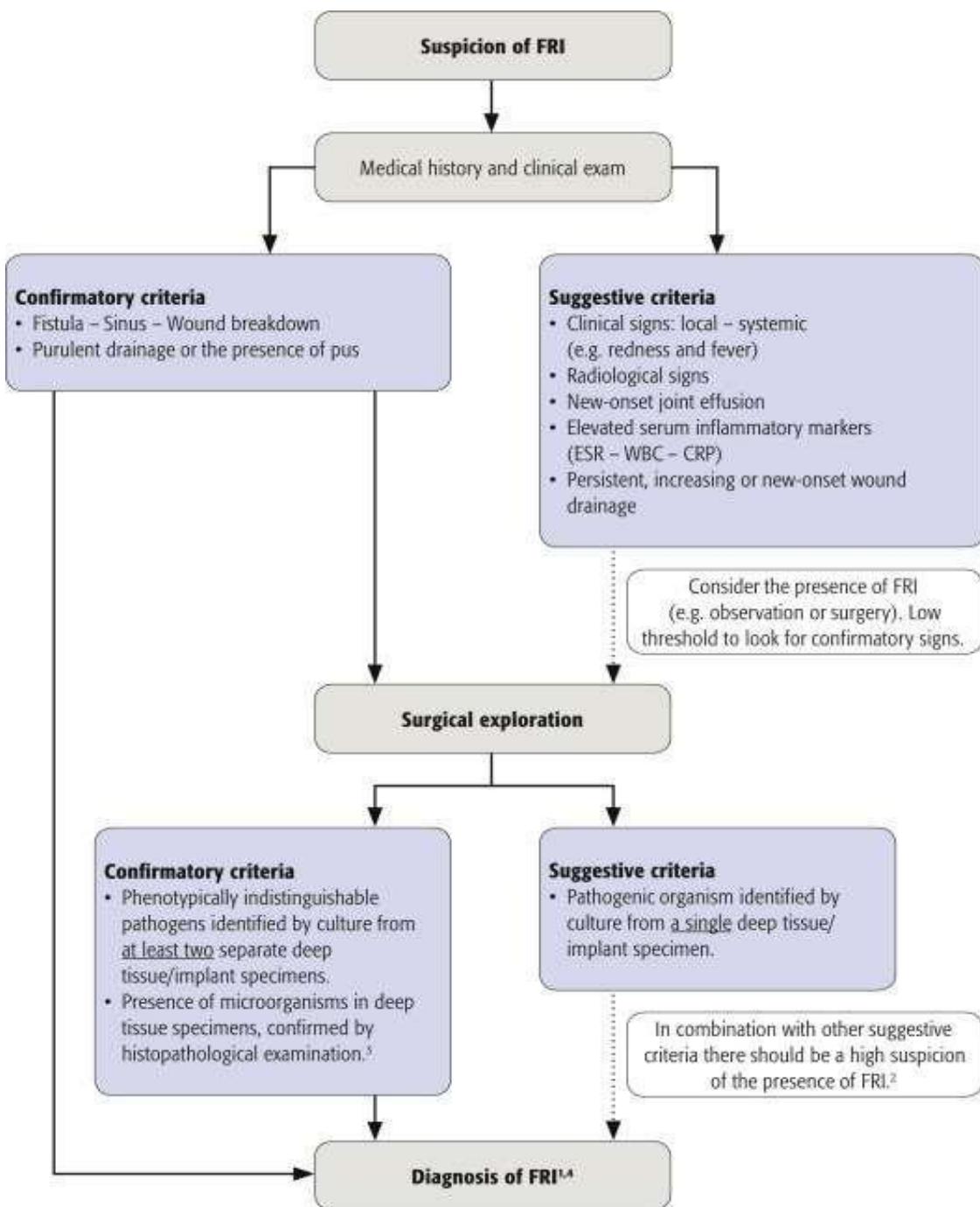
- **Early infections**

In the case of acute FRI with incomplete fracture healing, implant retention should be aimed for depending on the pathogen detected. A prerequisite for success is careful surgical debridement in combination with biofilm-effective antimicrobial therapy. Studies show success rates of up to 90% with a symptom interval of 3 weeks, 70% after 6 weeks, and 50% with existing FRI for 10 weeks [69].

- **Late infections**

Implant replacement is mandatory for infection eradication in chronic FRI. For uncomplicated infections with adequate soft tissue status and for pathogens that can be treated with biofilm effect, a single-stage procedure is possible. For extensive soft tissue compromise and evidence of difficult to treat pathogens, a two-stage procedure should be performed [2]. The treatment algorithm as a possible approach is shown in the Figure below.

Regardless of the surgical therapy chosen, the importance of surgical debridement must be emphasized. Surgical expertise ensures that radical but not reckless debridement, in combination with antimicrobial therapy appropriate to the identified pathogen, leads to successful infection eradication [82].



¹ In cases of purulent drainage or fistula/sinus/wound breakdown, the presence of pathogens identified by culture is not an absolute requirement (e.g. in the case of chronic antibiotic suppression).

² If the positive culture is from sonication fluid, it is highly likely that FRI is present. This is especially true when virulent bacteria (i.e. *Staphylococcus aureus*) are present.

³ The presence of microorganisms is confirmed by using specific staining techniques for bacteria and fungi.

⁴ Future research is required on the following criteria: acute inflammatory cell infiltrate on histopathological examination (e.g. PMN count), molecular diagnostics (e.g. PCR) and nuclear imaging (e.g. WBC scintigraphy).

Figure 11 : Descriptive flow chart of FRI [16]

4. FOLLOW-UP

- Early individualized functional rehabilitation is a critical aspect for every orthopaedic trauma patient and particularly when infection arises. It needs the collaboration of physical therapists, physiotherapies, nurses, rehabilitation physicians etc
- Patient optimization principles, as discussed in “Host optimization”, should also be implemented in the postoperative and follow-up period
- A follow-up of minimum 12 months after cessation of (surgical and antibiotic) therapy is required
- Follow-up outpatient visits generally consist of a wound inspection, radiological evaluation of the fracture and monitoring for complications or recurrence of infection.
- In case of deterioration of the patient’s health status (e.g. sepsis), CRP levels can help the decision-making process, although physicians should be aware that the evidence for the use of serum markers as diagnostic and follow-up parameters is scarce.
- Regarding the standard removal of implants after consolidation/healing of a sustained FRI, currently insufficient evidence exists to recommend this at a routine basis [61].

5. OUTCOME AND PROGNOSIS

Primary outcome measures include re-operation rates, non-union, infection recurrence, amputation and death. Standardized outcome measures for FRI patients are currently lacking. Such outcomes include clinical outcomes, functional outcomes, general health-related outcomes, and satisfaction with the process of care. Clinical outcomes (such as range of motion, radiographic union, implant loosening, and ongoing or recurrent infection) have been the focus of clinical research in orthopedic surgery [74].

These outcome can be evaluated using either bone union following the Modified Radiologic Union Score for Tibia fractures (mRUST) criteria [11] or through the recurrence of infection.

- mRUST Criteria

More recently, researchers developed the standard Radiographic Union Scale for Tibial fractures (RUST) and modified RUST (mRUST) scoring tools to assess healing status of tibial fractures using radiographic analysis. These tools use the presence of bridging callus and obliteration of fracture lines on anteroposterior (AP) and lateral radiographs in order to assign a numerical value for a healing tibial shaft fracture. In the standard RUST instrument, raters are asked to score each of 2 cortices visible on both AP and lateral radiographs of a tibial fracture. Each of the 4 (total) cortices is scored based on the following guidelines: 1 = no callus, 2 = bridging callus, 3 = remodeled. For mRUST, a fourth option (“callus present”) was added to the rating scale to differentiate between nonbridging and bridging calluses. This corresponds to a rating system of 1 = no callus, 2 = callus present, 3 = bridging callus, 4 = remodeled. Scores range from 4 to 12 (for standard RUST) and 4 to 16 (for mRUST), with lower scores indicating a less healed fracture and higher scores suggesting a more advanced stage of healing. The reliability (agreement in scoring among surgeons) and validity (correlation between scores and patient-relevant outcomes) of RUST and mRUST have been demonstrated in several studies [83].

- Recurrence of infection

In the UK, the eradication of infection was successful in 86.4%, and 86% of unhealed infected fractures were healed. Outcome of FRI was not dependent on age, BMI or time from injury, the presence of an internal fixation at presentation did not adversely affect the outcome, compared to FRIs without implants. Tobacco smoking at the time of surgery increased the chance of failure by three times [84] .

In addition, Secondary evaluation is possible using LEFR (lower extremity functional scale), UEFS (Upper Extremity Functional Scale) and the ability to go back to work.

- **Lower Extremity Functional Scale (LEFS)**

The Lower Extremity Functional Scale (LEFS) is a self-reported outcome measure used to assess the functional status of a patient's lower limb. It is a widely used tool to evaluate the extent to which lower limb pain or disability is affecting a patient's activities of daily living. The LEFS questionnaire consists of 20 items that evaluate a patient's ability to perform basic functional activities, such as walking, climbing stairs, and getting in and out of a chair. Each item is scored on a scale of 0 to 4, with a higher score indicating better function. The total score ranges from 0 to 80, with higher scores indicating better lower limb function.

The LEFS can be used in a variety of settings, including physical therapy, sports medicine, and orthopedic surgery. It is commonly used to assess the effectiveness of interventions, such as physical therapy, rehabilitation, or surgery, in improving lower limb function. The LEFS is appropriate for use in patients with lower limb injuries or disabilities, such as those with hip or knee osteoarthritis, ankle sprains, fractures, or ligament injuries. It is also used in patients who have undergone lower limb surgeries, such as total hip or knee replacement or ligament reconstruction.

The Lower Extremity Functional Scale (LEFS) is scored on a scale of 0 to 80, with higher scores indicating better lower limb function. The interpretation of the scores can be based on the following categories:

6. 0-20: Severe functional limitation
7. 21-40: Moderate functional limitation
8. 41-60: Mild to moderate functional limitation
9. 61-80: Minimal functional limitation or normal function

Normal scores for the LEFS may vary depending on the patient population and the specific lower limb condition being assessed. However, scores in the range of 61-80 are generally considered normal or indicative of minimal functional limitation. Scores in the range of 41-60 may indicate mild to moderate functional limitation, while scores in the range of 20-40 may indicate moderate to severe functional limitation. Scores of 0-20 indicate severe functional limitation [85].

- **Upper Extremity Functional Scale or Index (UEFS or UEFI)**

The UEFS is commonly used by healthcare professionals such as physical therapists, and orthopedic surgeons to assess the functional limitations of patients with upper limb impairments, such as those resulting from musculoskeletal injuries, nerve damage, or arthritis. It can be used to monitor changes in functional status over time, as well as to evaluate the effectiveness of treatment interventions.

The columns on the scale are summed to get a total score. The maximum score is 80. A higher score indicates better upper limb function. There are no established "normal" results for the UEFI, as the scores can vary depending on the individual's age, sex, occupation, and the severity of their upper limb impairment. Instead, the UEFI is used to compare the patient's current functional status to their previous status or to the status of other patients with similar conditions [13].

- **Short Form (SF) – 12 score**

The SF-12v2 is a health-related quality-of-life questionnaire consisting of twelve questions that measure eight health domains to assess physical and mental health. Physical health-related domains include General Health (GH), Physical Functioning (PF), Role Physical (RP), and Body Pain (BP). Mental health-related scales include Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH) [14].

6. PREVENTION

FRI is a catastrophic complication of fractures for both patients and clinical physicians, and prevention is better than cure. In order to effectively lower FRI incidence, comprehensive understanding of the pathogenesis of this disorder is necessary. Improvements in both prevention and treatment will be required to achieve better patient care in the coming decades. Such improvements may range from better-defined and controlled peri-operative antibiotic prophylaxis, to more rapid and specific diagnostics of even sub-acute infection, to increased availability of antimicrobial functionalized medical devices or bone void fillers and graft material[86]. The central tenets of preventing FRI include systemic and local antibiotics, skin antisepsis at the time of surgery, and the surgical approach itself, which includes fracture stabilization debridement in case of open fractures, and soft tissue management [87].

- Perioperative antibiotic prophylaxis

Perioperative antibiotic prophylaxis (PAP) has been demonstrated to be highly efficacious in preventing infection following fracture surgery. Antibiotic administration following a closed fracture is typically only necessary when a surgical procedure is needed, and as for other clean or clean-contaminated procedures, the optimum time of administration is a single dose 1 hour prior to surgical incision. An antibiotic with good Gram-positive coverage and pharmacokinetic profile to penetrate the surgical site is recommended, primarily first-generation cephalosporins [87,88].

In open fractures the considerations regarding PAP are different and guided by the injury severity. Due to historical use of the Gustilo and Anderson classification however, PAP guidelines are still reported according to this description. Overall, type and duration of PAP still remain controversial and uniformly accepted guidelines are lacking. As in closed fractures, first-generation cephalosporins are recommended, with limited evidence for the additional administration of an antibiotic with broad-spectrum gram-negative coverage in case of severe soft tissue damage (i.e. Gustilo-Anderson type III injuries). Furthermore, current guidelines state that in patients with Gustilo-Anderson type I-II injuries, duration should not exceed 24 hours. In patients with Gustilo-Anderson type III injuries the duration is less clear, due to a lack of comparative studies [88].

In case of complex open fractures, systemic antibiotics alone are often not sufficient because the surrounding tissues and blood vessels by which systemic antibiotics would normally reach the tissue-implant interface may be damaged as well. Studies show that local administration of antibiotics could have a positive influence on infection prevention. Local prophylaxis can be

administered by cement spacers, which are made of polymethyl methacrylate (PMMA), collagens, coatings (e.g. antibiotic-coated tibial nails) and hydrogels [87].

- **Debridement and soft tissue management**

A thorough surgical debridement to remove all contamination and non-viable tissue is considered crucial to prevent FRI. Historically, it has been considered that this should occur urgently (within 6 hours), however a number of retrospective reviews have not supported this notion with longer timeframes (e.g. 12 hours) having similar rates of subsequent FRI [87]. Time to debridement is currently regarded as independent of infection risk if performed within 24 h provided there is no gross contamination. The use of low flow normal saline has been shown as a low-cost alternative and is optimal for the irrigation of open fractures [89].

Following initial debridement, an open fracture should be stabilized and the wound closed primarily or delayed if primary closure is not possible due to the injury severity (Gustilo- Anderson type III injuries). As soft tissue coverage is needed to support fracture healing, prevent nosocomial contamination and aid systemic antibiotic delivery, early reconstructive protocols are preferred [88].

- **Operating room and personal sterility**

Trauma procedures with implants should be ideally be performed in orthopedic dedicated theatres with clean areas for implant storage, and minimal personnel movement. There is debate with regard to the effects on SSI and FRI rates when using laminar flow ventilation systems in the context of trauma. Use of meticulous hand hygiene techniques by all members of the surgical team is important [88]. Hand hygiene is a very important factor for infection control and is included in the WHO guidelines. A major transmission route of micro-organism causing nosocomial infections are contaminated hands of healthcare workers. Furthermore, healthcare workers should disinfect their hands with an alcohol-based antiseptic before and after each patient contact, after contact with the patient's surroundings, after exposure to bodily fluids and mucous membranes and before a clean or aseptic procedure [88]. Current recommendations support the use of alcohol-based solutions complying with a recommended hand-washing technique of no less than 90 s duration. Appropriate surgical attire should always be worn and changed when visibly soiled. Use of face masks is strongly recommended. Despite the lack of robust evidence, the use of double gloving technique is also recommended due to the documented high rates of perforation and contamination in orthopaedic surgery [90].

- **Wound drainage**

Wound drains have been used to prevent fluid accumulation, and some debate remains on the difference between using and not using drains. Several studies in the orthopedic domain indicate that there is no advantage in using a wound drain for implant-related surgery. In a randomised controlled trial, Li et al. studied the use of wound drains in total knee arthroplasty surgery and reported no significant advantage associated with their placement [91]. For musculoskeletal trauma surgery, these types of studies are again lacking.



Figure 12 : Summary of FRI [89]

7. STATE OF THE ART

Due to the importance of the outcome of Fracture related infections and the factors affecting its prognosis, some studies have focused on this subject.

In developed countries, an international multicentre study involving the United Kingdom and Netherlands in 2022, investigated on what factors affected outcome in the treatment of FRI. A total of 453 patients were studied. Concerning the management of FRI, when the fracture was unhealed 48.1% went through DAIR and 31.6% through DAIEX. In 20.3% the fixation was removed from if the fracture was healed. Overall, the eradication of infection was successful in 86.4%, and 86.0% of unhealed infected fractures were healed at the final review. In total, 3.3% required amputation, equally divided between those with infection recurrence. A recurrence of infection occurred in 10% of patients who received local antibiotic therapy and in 18.7% of those who did not. Generally, patients who were treated with local antibiotics had a longer interval from injury to FRI surgery, but time from injury was not an independent determinant of recurrence in the multi-variate analysis. The successful treatment of FRI was multi-factorial. These data suggested that treatment decisions should not be based on time from injury alone, as other factors also affected the outcome [84].

In the United Kingdom, another retrospective observational study was performed from January 2015 to January 2021 to determine the prognostic factors associated with the outcome of FRI. 102 patients were enrolled, treatment failure occurred in 23.5%, 20.6% had recurrent infection and 2.9% required an amputation. Prognostic factors associated with FRI management failure were obesity, diabetes and implant retention [74].

In Belgium, all patients with a clavicle fracture who underwent open reduction and internal fixation (ORIF) between 1 January 2015 and 1 March 2022 were retrospectively evaluated to determine what the outcome of FRI was. 626 patients were evaluated with 630 clavicle fractures who underwent ORIF. 28 patients were diagnosed with an FRI. Of these, 29% underwent definitive implant removal, 18% underwent debridement, antimicrobial treatment and implant retention, and 50% had their implant exchanged. One patient (3.6%) underwent resection of the clavicle. The functional outcome was satisfactory, with 26 out of 28 patients (93%) having full range of motion. [92].

In Norway, a study was conducted to identify risk factors for FRI in patients operated for ankle fractures. A cohort of 1004 patients surgically treated for ankle from 2015 to 2019 was studied retrospectively. FRI was confirmed in 87 (9%) of 1004 patients. Congestive heart failure (CHF),

peripheral artery disease (PAD) and current smoking were identified as risk factors for FRI. PAD and CHF were the risk factors displaying the strongest [93].

In Africa, precisely in Togo, a retrospective cohort study was conducted between January 2015 and December 2020 in Lome. The aim was to focused on the clinical, paraclinical and therapeutic features of Infection related to implant and its outcome. A total of 1621 patients were included in the study, a total of 161 patients presented with an infection, hence the incidence was 9.9%. The time to onset of was: early in 15 (25%); delayed in 18 (30%) cases and late in 27 (45%) cases. *Staphylococcus aureus* was the most common germ (56%) followed by *Pseudomonas Aeruginosa* (14%). Surgery was performed in 28.3%, DAIR in 18.3%, DAIEX in 8.3% and Distraction osteogenesis in 1.6%. The remaining 71.7% were managed using local wound dressing and antibiotics, the initial antibiotic treatment was probabilistic then adapted based on the antibiogram. The evolution was marked by consolidation in 71.6% patients, and to vicious callus in 28.3% patients. Recurrence of infection was noted in 5% [94].

In Cameroon, No study was found on the outcome of FRI in Yaoundé. A descriptive cross-sectional study was carried out between November 2016 and May 2017 at the Yaoundé Central Hospital (YCH) to determine the epidemiological and susceptibility profile of bacterial isolates in posttraumatic osteomyelitis. A total of 31 patients were included in the study, eighteen (58%) patients had infections on prosthetic devices. Sixteen patients (52%) had acute osteomyelitis (symptoms had been evolving for less than 6 weeks) while the remaining 48% had a chronic bone disease. Out of the 31 samples analysed, 29 (93.5%) positive culture results were found; Enterobacteria represented 62.5% of the isolates followed by non-fermenting Gram negative bacilli (18.8%) and Gram positive cocci (18.8%). The most predominant species was *Escherichia coli* with a prevalence of 29%, followed by *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (all 22.6%) [95].

METHODOLOGY

1. STUDY DESIGN

This study was a prospective cohort study.

2. SITE OF STUDY

The study was carried out in 4 hospitals in Yaoundé-Cameroon; Yaoundé General Hospital, Yaoundé Central Hospital, the Yaoundé Emergency Center and the Yaoundé Military Hospital.

3. DURATION OF STUDY

This study was carried out over a period of 17 months, from December 2022 to May 2024.

4. STUDY POPULATION

a. Source population

All patients that sustained a fracture and followed-up in YCH, YGH, Military hospital of Yaoundé and Yaoundé Emergency center.

b. Target population

Patients presenting a FRI treated and followed-up in one of the study setting

c. Inclusion criteria

We will include in our study;

- Patients presenting a FRI according to the consensus diagnostic criteria [1] treated and followed for a period of at least 3 months in one of the study setting.
- Patients have given their free and informed consent to participate in the study.

d. Exclusion criteria

Will be excluded;

- FRI of the skull/facial bones, spine.
- Those lost to follow-up within 3 months of initial FRI treatment.

5. SAMPLE SIZE ESTIMATION

The minimum sample size for the study was estimated using the COCHRANE formula, considering a 95% confidence interval and 3.4% [5] as the prevalence of FRI [96] formula.

$$n = \frac{Z^2 pq}{e^2}$$

$$n = \frac{(1.96)^2 \times (0.034)(0.966)}{(0.05)^2}$$

Where:

n = sample size,

Z = **1.96** (at 95% confidence level)

e = the desired level of precision (i.e. the margin of error) = **5%**

p = the estimated prevalence of FRI; considered as **3.4%**

q = $1 - p = 0.966$

This gives us an approximated sample size of **50**

6. MATERIAL

➤ Materials for data collection

- Human resources: Medical personnel for data collect
- Census and Survey Processing system (CSPro) 7.5

➤ Data collection entry form

- Pen
- Examination gloves
- Gauze

➤ Material for data analysis

- Microsoft® Office Excel 2016
- IBM SPSS (Statistical Package for Social Sciences) version 26.

7. PROCEDURE

Once the research protocol was validated by the supervisor of thesis and authorized by the administrative authorities, an ethical clearance was gotten from the Ethics Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. An application was then deposited at the research sites, requesting for authorization for data collection. Once this is done, recruitment of participants was carried out at the different hospitals by looking through medical files, attending rounds and out-patient consultations in search of patients who have been diagnosed with FRI or present signs and symptoms in line with the diagnostic criteria of FRI (presence of sinus, fistula, wound break down or purulent effusion at the surgical site). We then went on to the collection of data with the help of the questionnaires.

Data collection: After approval and signing of consent forms by the participants, we interrogated them and filled our established questionnaires. These questionnaires provided information on the socio-demographic status of our participants, their comorbidities, information about their initial trauma, the method of initial management, clinical signs and symptoms of the presenting condition, the method of management and their follow-up. Interrogation was followed by clinical examination to evaluate clinical features. The results of biological tests and culture results from recognized laboratories were recorded and analyzed, with the x-rays done during the hospital stay, which were analyzed by a radiologist and 2 orthopedic/trauma surgeons. The patients were then followed up for a minimum of 3 months after definite management to determine the outcome. A good outcome was defined by the absence of clinical signs of infection initially present at the time of diagnosis, the absence of radiological signs of infection and bone union determined by 2 orthopedic/trauma surgeons. The primary outcome measures were; bone union following the mRUST criteria and recurrence of infection. Secondary outcome measures were; functional evaluation using the LEFS or UEFS. Quality of life was evaluated using the SF -12 score. Photographs of the infected sites were taken at intervals. The data obtained was then processed to obtain results.

Primary outcome measures

- Bone union following the Modified Radiologic Union Score for Tibial fractures (mRUST) criteria [11]
- Recurrence of infection

Secondary outcome measures

- Functional evaluation using the LEFS (lower extremity functional scale) [12] or using the UEFS (Upper extremity functional sale) [13]
- Quality of life evaluation using the Short Form (SF)- 12 score [14]

Data analysis: data collected was entered and coded using CS Pro (Census Survey Processing) software and extracted to SPSS (Statistical Package for Social Sciences) version 26.0 software for statistical processing and analysis. Tables and graphs were made using Microsoft® Office Excel 2016 and S.P.S.S version 26.0. In the case of quantitative variables, mean and standard deviations were calculated to extract the information they contained. The Student test was used to measure the relationship between quantitative and qualitative variables, and the Chi-square test of independence to measure the relationship between qualitative variables. Finally, prognostic factors were determined using the Multivariable logistic regression. The significance level was set at 5%. A p-value of less than 0.05 was therefore considered statistically significant.

8. ETHICAL AND ADMINISTRATIVE CONSIDERATIONS

The study was carried out in full consideration of the ethical principles of the Helsinki declaration and in strict compliance with the fundamental principles for human health research in Cameroon. An ethical clearance was obtained from the “Institutional Ethics Committee for Research” of the Faculty of Medicine and Biomedical Sciences (FMBS) of the University of Yaoundé I. Authorizations for research were acquired from the different hospitals where research was carried out. The participants were free to be part and to withdraw from the study at any time they pleased. Participants were given consent forms to sign after they had been explained the details (nature and benefits) of the study. Data was collected in strict compliance to medical confidentiality and the survey forms were made anonymous and coded in order to ensure data confidentiality throughout the collection process. The rights of the participants, their dignity, privacy and confidentiality were protected during the study. Participants were not given any benefits by providing consent for the study but that the information obtained at the end of the study will improve scientific knowledge and help in their management.

RESULTS

Distribution of patients by study site

The study included a total of 146 confirmed fracture-related infections according to the consensus definition[16]. In the course of the study, 42 participants were lost to follow-up. Hence, 104 participants were present at final evaluation. The distribution by study site was as follows;

Table III : Distribution of patients by study site

Site	Frequency (N=104)	Percentage(%)
Yaoundé Central Hospital	47	45%
Yaoundé General Hospital	32	31%
Yaoundé Emergency Center	13	13%
Yaoundé Military Hospital	12	12%

During the study period from December 2022 to May 2024, there were 329 open fractures and 118 closed fractures registered at the study sites giving a total of 528 fractures. Thus, the incidence of FRI in Yaoundé within the study period was 27.65%.

SECTION I: PATIENTS DEMOGRAPHICS

1.1 Age

The mean age of the patients was 40.46 (± 14.98) years, ranging from 5 to 80 years (Figure 13).

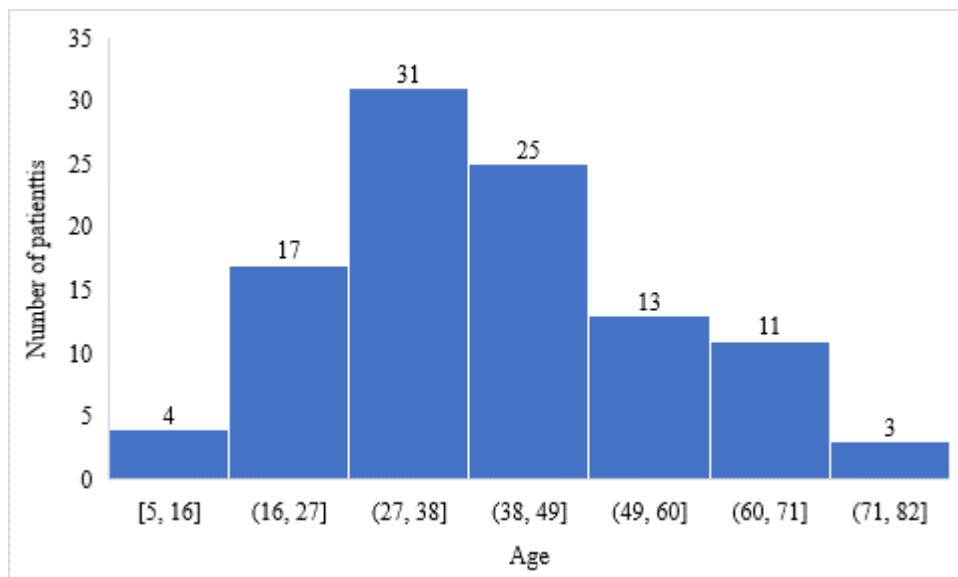


Figure 13: age distribution

1.2 Gender

We found out that the population was made up of 76 (73.08%) males and 28 (26.92%) female, with a gender ratio (**M: F**) of 2: 9 (Figure 14).

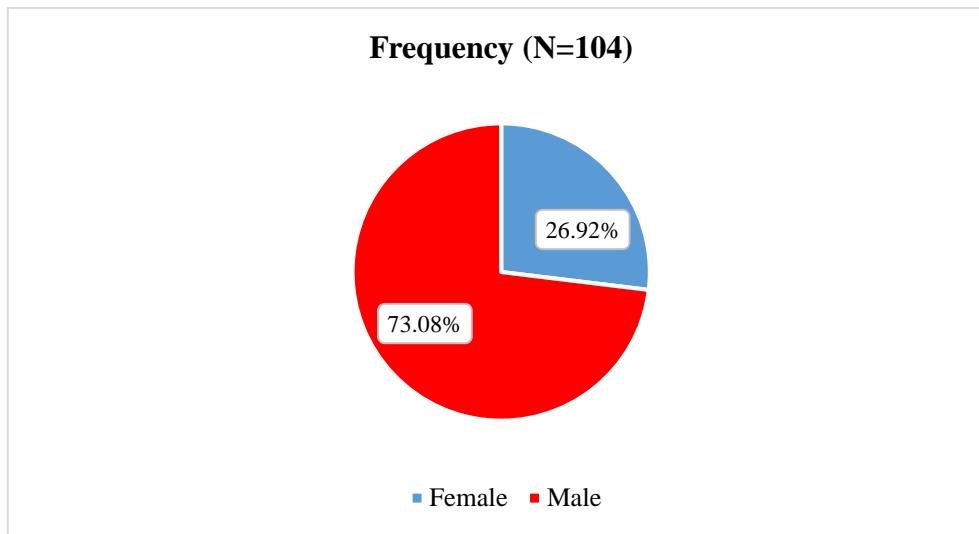


Figure 14: gender distribution of patients with FRI

1.3 Socioeconomic status, education and profession

Forty-four (42.31%) participants had gone through at least secondary school, 46 (44.23%) patients had a fair socio-economic status (monthly income between minimum wage and 150,000FCFA) and 21 (20.19%) participants were traders (Table IV).

Table IV : Demographic of patients with a FRI

Variable		Frequency (N=104)	Percentage (%)
Social class	Class 1	8	7.69%
	Class 2	46	44.23%
	Class 3	35	33.65%
	Class 4	12	11.54%
	Class 5	3	2.88%
Level of education	Primary	18	17.31%
	Secondary	44	42.31%
	University	42	40.38%
Profession	Trader	21	20.19%
	Student	15	14.42%
	Civil servant	10	9.62%
	Housewife	10	9.62%
	Farmer	9	8.65%
	Retired	7	6.73%
	Carpenter	7	6.73%
	Driver	5	4.81%
	Military	5	4.81%
	Jobless	4	3.85%
	Teacher	3	2.88%
	Bike rider	2	1.92%

SECTION II: Comorbidities

In the study population, the average BMI was 26.02 kg/m² ranging from 10.88 to 39.25. Also, 14 (39%) participants were smokers and had an average tobacco index of 5.77 (± 10.13) pack-years

ranging from 0 - 40 pack years. Six (17%) had Diabetes and eleven (33%) were carrying the HIV (Figure 15).

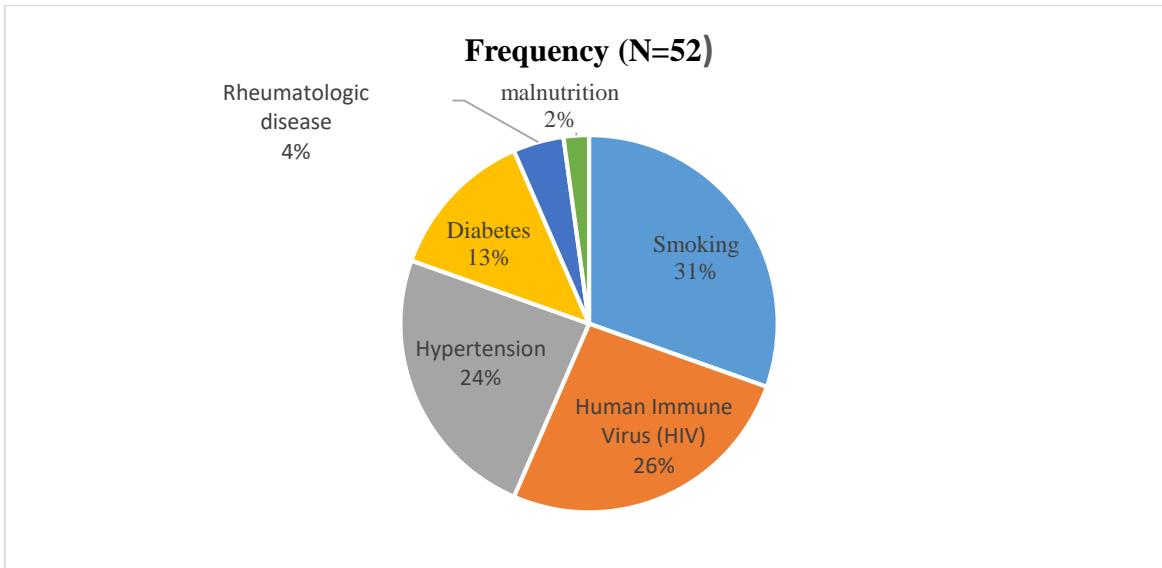


Figure 15: Comorbidities of patients with FRI

SECTION III: PAST HISTORY

3.1 Circumstance of injury

Road traffic accidents were responsible for 78 (75%) fractures that developed FRI in this study (Figure 16).

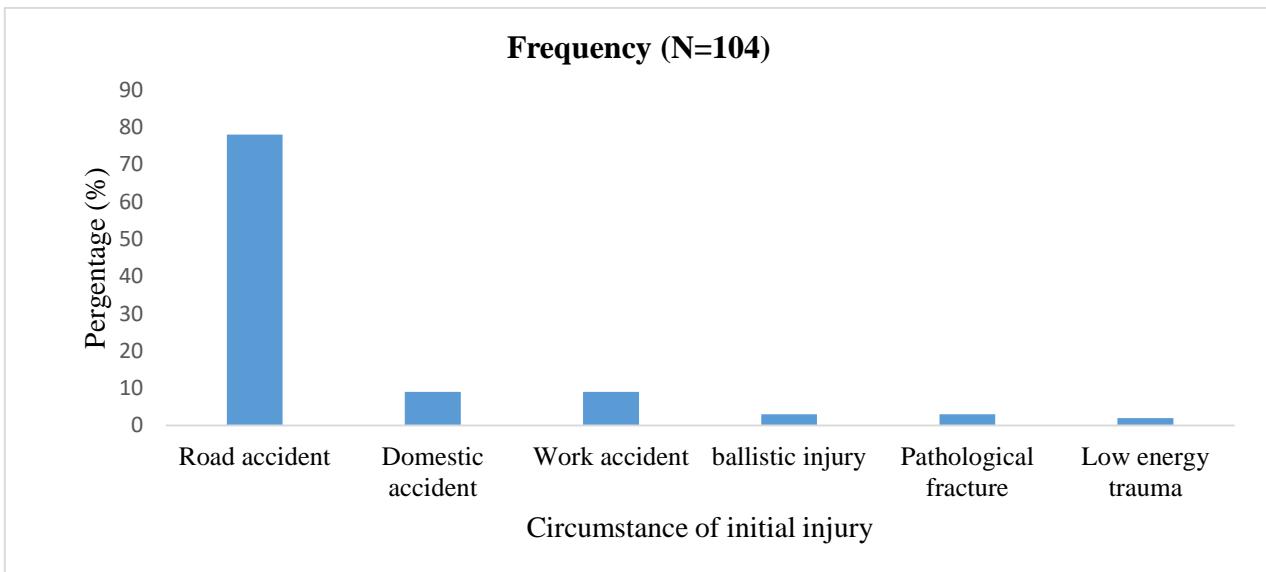


Figure 16 : Repartition of patients with respect to circumstance of injury

3.2 Fracture type

There were 69 (66.35 %) open fractures and 35 (33.65%) closed fractures in the study (Figure 17).

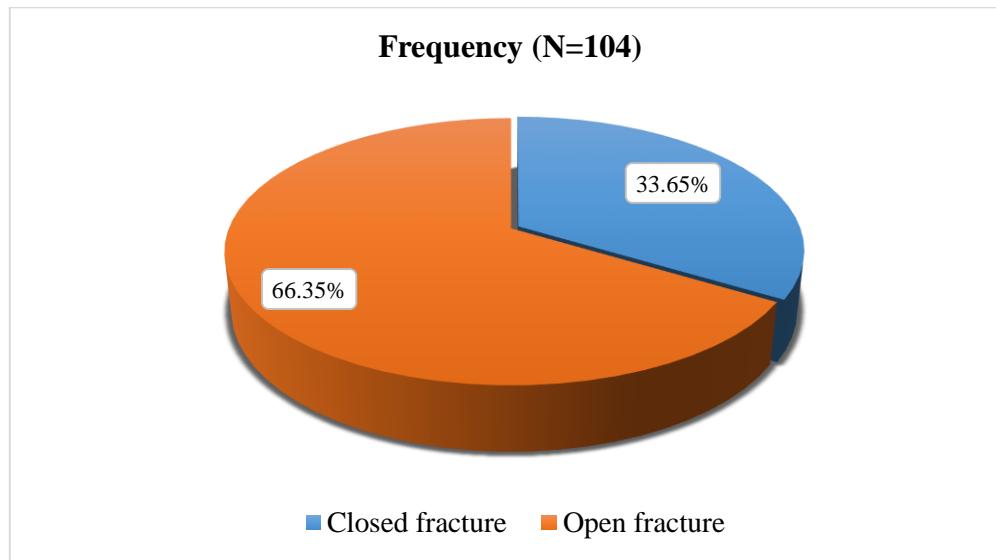


Figure 17 : Fracture type of FRI

3.3 Open fracture classification

Gustillo and Anderson type III fractures were the most represented class of open fractures with 40 (59.7%) cases (Figure 18).

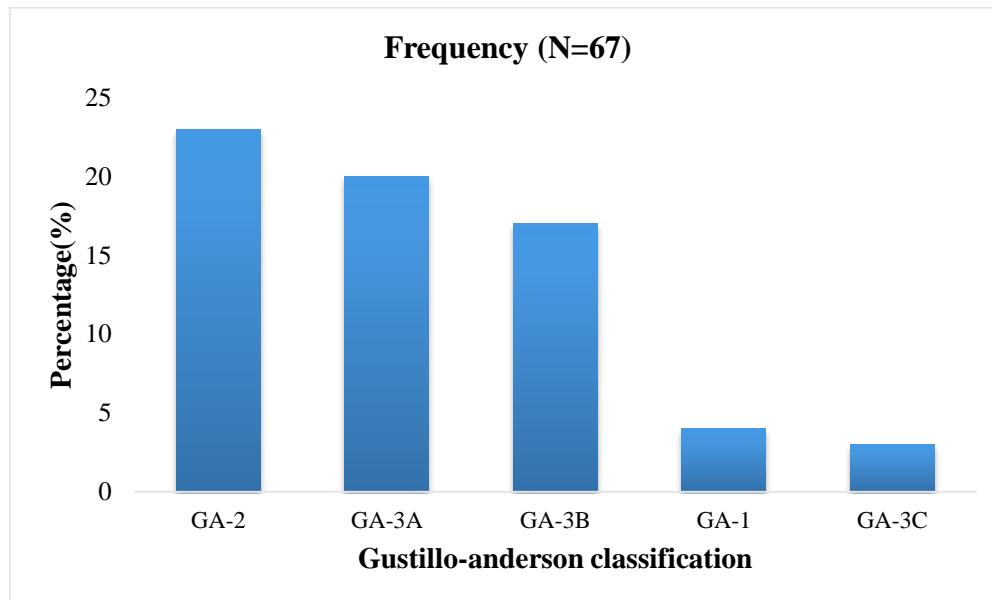


Figure 18 : Open fracture classification by Gustilo-anderson for FRI patients

3.4 Delay of admission

The mean duration between the accident and admission was $8.88 (\pm 22.56)$ hours. Meanwhile the mean time delay between the accident and first washing/debridement for open fractures was $10.26 (\pm 23.23)$ hours and the delay between initial trauma and the onset of antibiotic administration in open fractures was $11.87 (\pm 26.98)$ hours (Table V).

Table V : Delay of admission, fist wash and delay of antibiotic for FRI patients

Indicator	Delay of admission (in hours)	Delay of first wash (in hours)	Delay of Antibiotics (in hours)
mean	8.88	10.26	11.87
min	1	2	1
max	168	170	170
SD	22.56	23.23	26.98

3.5 Delay of surgery

The mean delay between initial trauma and surgery for bone fixation was 30.3 ± 64.8 days, ranging from 1 to 376 days. The mean delay to surgery for closed fractures was 43.4 ± 67.88 days and for open fractures was 23.32 ± 62.89 days.

3.6 History of prior FRI

From the participants, there were 43 (42%) cases of recurrent FRI with a median delay for onset of initial infection of 28 days, ranging from 3 to 10220 days after initial surgery

3.7 Initial fracture management

Initial fracture management was by open surgery in 52 (97 %) of the 53 patients who were operated for fracture fixation prior to the onset of FRI. The remaining 51 patients presented with open fractures which were not operated prior to the onset of FRI.

External fixators were used in 44 (43.14 %) cases during initial surgery. From the cases registered, 22 (21.15 %) underwent traditional therapy with bone setters in the period between the initial fracture and the onset of FRI. (Figure 19).

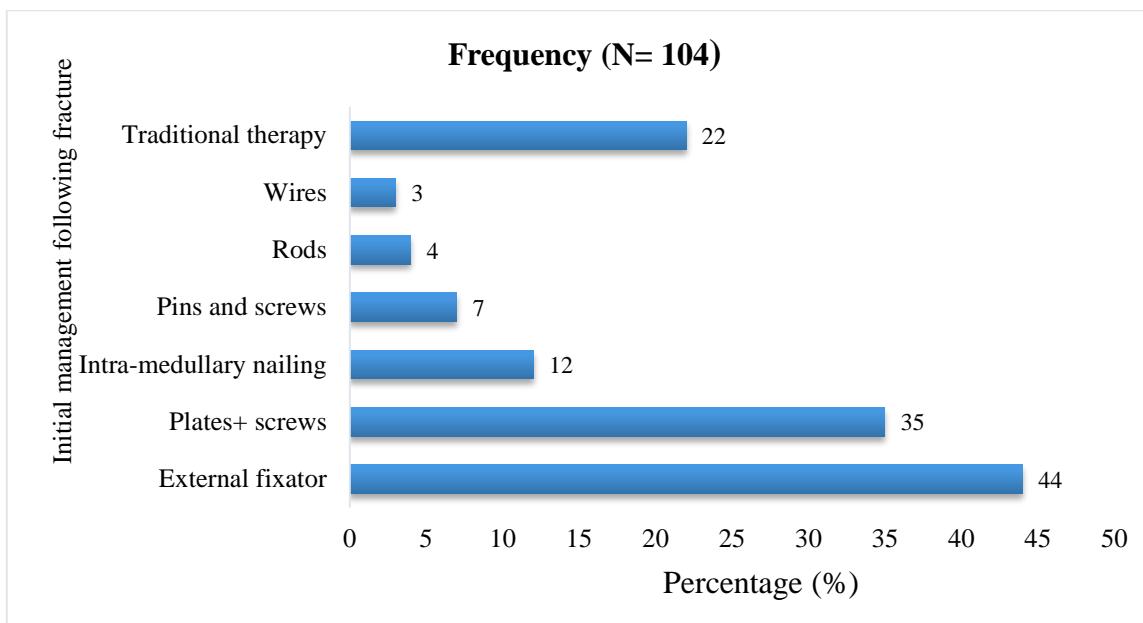


Figure 19 : Initial management following fracture

SECTION 4: CLINICAL FEATURES AND WORK-UP OF CURRENT FRI

4.1 Onset of Infection

Infections were post-operative (presented with clinical signs of infection after surgical management of the fracture) in 68 (65.38%) cases (Figure 18).

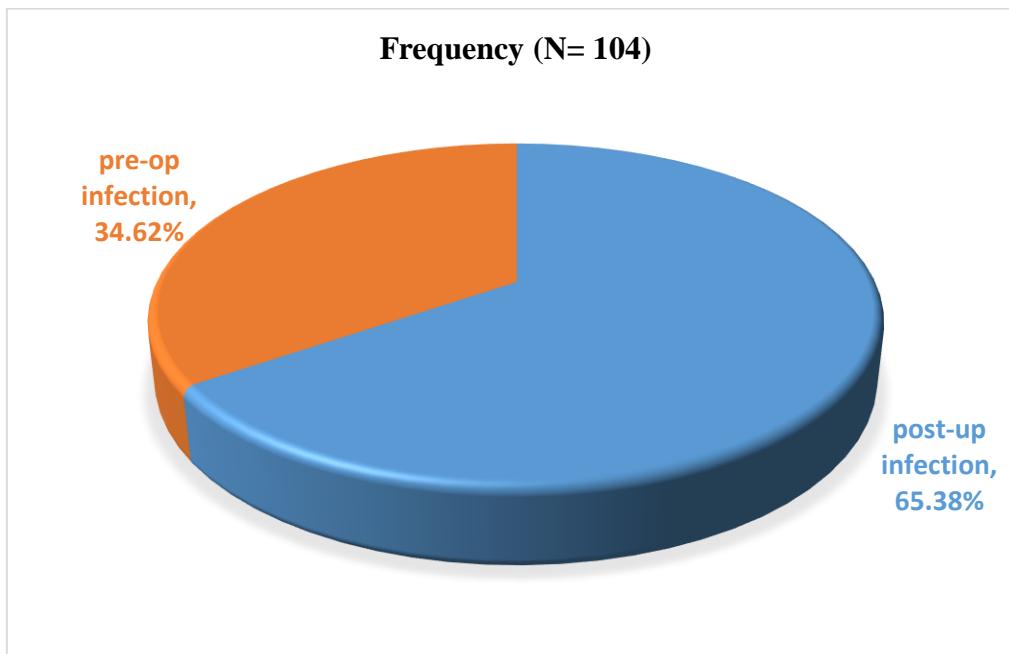


Figure 20 : Onset of FRI

4.2 Delay of onset of infection

The mean duration from initial injury to onset of infection in the case of pre-operative infections was 12.97 (SD 21.15) days. On the other hand the mean duration from initial surgery to onset of infection in the case of post operatory infection was 68 (SD 14.68) days.

4.3 Location of infected fracture

Infected fractures were located at the tibia in 28 (26.92%) participants. Twenty- eight (25%) cases had infected fractures located at the tibia + fibula (Table VI).

Table VI : Location of infection

Affected bone	Frequency (N=104)	Percentage (%)
Tibia	28	26.92%
Tibia + Fibula	26	25.00%
Femur	25	24.04%
Humerus	8	7.69%
Pelvis	6	5.77%
Foot	4	3.85%
Patella	3	2.88%
Radius	2	1.92%
Fibula	1	0.96%
Radius + Ulna	1	0.96%
Total	104	100%

4.4 Clinical signs of infection

The most prevalent clinical sign of infection was purulent wound drainage which presented in all 104 patients (Figure 21).

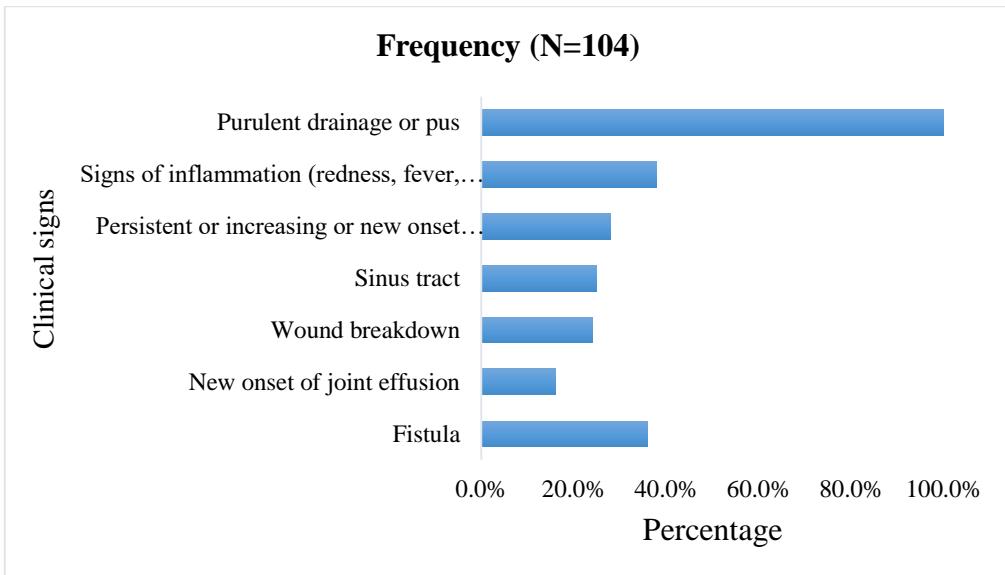


Figure 21 : Clinical signs of FRI

4.5 Radiological signs of infection

Radiological signs were observed in 25 (24%) cases. The main radiological sign was bone lysis which was present in 20 (83%) cases (Figure 22).

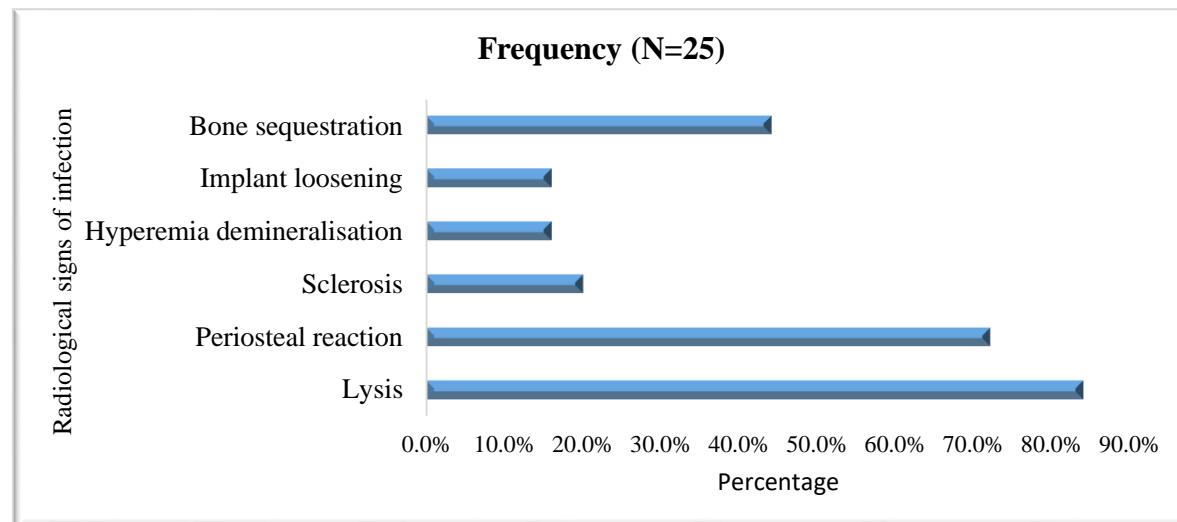


Figure 22 : Radiological signs of infection

4.4 Biological features and histopathology

White Blood Cells were elevated in 39 (75%) cases, C - reactive protein was elevated in 27 (51.9%) and ERS was elevated in 12 (23.1%) of patients that undergone laboratory testing.

NB: Histopathologic examination was not done for any case of FRI during our study

SECTION 5: BACTERIOLOGICAL PROFILE

5.1 Specimen culture and sampling

Specimen for culture from the infected fracture site was collected from 83 (81%) participants. Of the specimens taken for culture, 42 (51.24%) were taken by deep tissue biopsy during surgery and a two specimen sample was collected in 45 (54.05%) cases (Table VII).

Table VII : Specimen collection

Methods of specimen collection	Frequency (N=83)	Percentage (%)
Wound swab	14	17.07
Pus aspiration	27	31.71
Deep tissue biopsy	42	51.24
Number of specimens collected for culture		
2	45	54.05
1	33	40.54
3	5	5.41

5.2 Culture results

From the specimens collected from the infected fracture site, there were 46 (79.22%) positive cultures from which 45 (73.77%) were polymicrobial (having more than 1 bacterial type isolated) (Table VIII).

Table VIII : Culture results

Variable	Frequency (N=83)	Percentage (%)
Positive culture results	64	77.88
Negative culture results	19	22.12
Total	83	100
Number of bacteria per culture		
1	22	26.92
2	47	56.73
3	14	16.35
Total	83	100

The most isolated bacteria species were *Staphylococcus aureus* in 23 (37.7%) cases, *Klebsiella pneumonia* in 14(23%), *Escherichia coli* in 13(23%) and *Enterobacter cloacae* in 12 (19.7%) (Table IX).

Table IX : Bacteriological profile

Bacteria	Frequency (N=121)	Percentage (%)
<i>Staph aureus</i>	23	37.7%
<i>Klebsiella pneumonia</i>	14	23.0%
<i>E. coli</i>	13	21.3%
<i>Enterobacter cloacae</i>	12	19.7%
<i>Pseudomonas aeruginosa</i>	8	13.1%
<i>Proteus mirabilis</i>	8	13.1%
<i>Enterococcus faecalis</i>	6	9.8%
<i>Morganella morganii</i>	5	8.2%
<i>Citrobacter koserii</i>	4	6.6%
<i>Streptococcus group b</i>	3	4.9%
<i>Peptoniphilus asaccharolyticus</i>	3	4.9%
<i>Enterococcus hirae</i>	3	4.9%
<i>Klebsiella spp</i>	2	3.3%
<i>Citrobacter sedlakii</i>	2	3.3%
<i>Citrobacter freudi</i>	2	3.3%
<i>Providencia stuartii</i>	2	3.3%
<i>Staph saprophyticus</i>	2	3.3%
<i>Acinobacter baumannii</i>	2	3.3%
<i>Enterobacter hormaechei</i>	1	1.6%
<i>Staph coagulase negative</i>	1	1.6%
<i>Enterococcus spp</i>	1	1.6%
<i>Enterococcus avium</i>	1	1.6%
<i>Salmonella</i>	1	1.6%
<i>Staph hemolyticus</i>	1	1.6%
<i>Cornyebacterium striatum</i>	1	1.6%

SECTION 6: CLASSIFICATION

Following the Willeneger and Roth classification [17], 69 (66.3%)cases of FRI were early infections while 21 (20.2%) cases were classified as late infections . Also, 83 (79.8%) participants were classified as uncomplicated according to the BACH classification [89]. According to the Cierny-Mader classification [38], 91 (87.5%) cases were classified stage I and 73 (70.2%) cases no radiological signs of chronic infection (Table X).

Table X : Classification of FRI

	Classification	Frequency	Percentage (%)
Willenegger and Roth	Early	69	66.3%
	Delayed	14	13.5%
	Late	21	20.2%
BACH	Uncomplicated	83	79.8%
	Complex	20	19.3%
	Limited option	1	1.0%
Cierny Mader (Physiologic Host)	A Host (Normal)	91	87.5%
	B Host ; Bs (Systemic compromise)	11	10.6%
	C Host (Treatment worse than disease)	2	1.9%
Cierny-Mader (Anatomic Type)	Normal	73	70.2%
	Type 1 (Medullary osteomyelitis)	11	10.6%
	Type 2 (Superficial osteomyelitis)	1	1.0%
	Type 3 (Localised osteomyelitis)	16	15.4%
	Type 4 (Diffused osteomyelitis)	3	2.9%

SECTION 7: DIAGNOSIS

Following the consensus criteria for the FRI, all participants recruited for our study presented with at least 1 confirmatory sign for FRI, which was the presence of purulent wound effusion at the fracture site. Also, 9 (8.65%) cases had 2 bacteriology exams which presented with identical bacteria, thus confirming an FRI following the 2018 consensus guidelines.

SECTION 8: MANAGEMENT

8.1 Pattern of management

Concerning the management of patients with FRI, 35 (34%) cases were managed by suppression therapy (wound dressing + antibiotics), and 19 (18%) cases were managed by Debridement Antibiotics Implant retention (Figure 23).

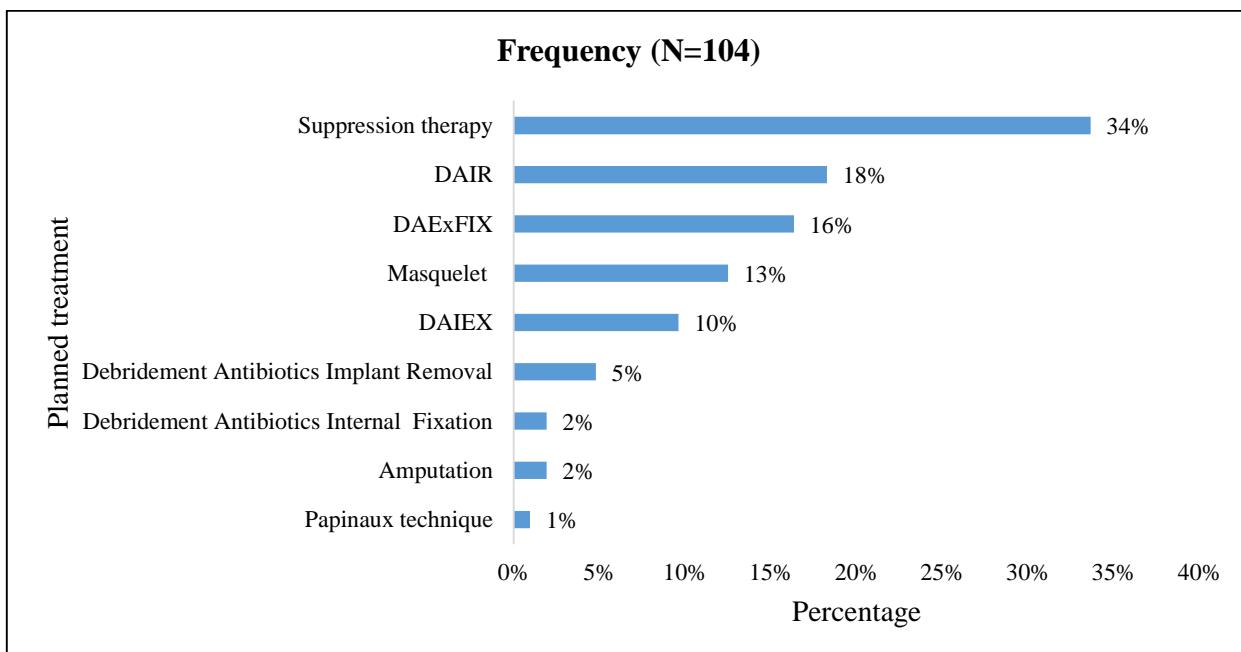


Figure 23 : Treatment of FRI

Twenty-five (24.04%) of those presenting with post-op infection were managed using antibiotics and wound dressing and 14 (13.35%) cases presenting with pre-op infection were treated by DAExFIX (Table XI).

Table XI : Treatment plan according to onset of infection

Planned treatment	About the Infection	
	Post-op infection	Pre-op
Amputation	2 (1.92%)	1 (0.96%)
DAExFIX	3 (2.88%)	14 (13.35%)
DAIEX	8 (7.69%)	2 (1.92%)
DAIR	12 (11.54%)	7 (6.73%)
Debridement Antibiotics Implant Removal	4 (3.85%)	1 (0.96%)
Debridement Antibiotics Internal Fixation	1 (0.96%)	1 (0.96%)
Masquelet technique	13 (12.5%)	0 (0.00%)
Papineau technique	1 (0.96%)	0 (0.00%)
Suppression therapy	27 (24.04%)	9 (9.62%)

From the patients who had early infections according to the Willenegger and Roth classifications, 34 (32.69%) cases were managed by suppression therapy which consisted of administration of antibiotics and doing regular wound dressing. Two patients were amputated following the onset of an early FRI as shown in the table below.

Table XII : Willenegger and roth classification of FRI according to management

Planned treatment	Early	Delayed	Late
Masquelet technique	4 (3.85%)	4 (3.85%)	5 (4.81%)
DAExFIX	12 (11.54%)	3 (2.88%)	2 (1.92%)
DAIR	10 (9.62%)	6 (5.76%)	3 (2.88%)
Debridement Antibiotics Implant Removal	1 (0.96%)	1 (0.96%)	3 (2.88%)
DAIEX	5 (4.81%)	0 (0.00%)	5 (4.81%)
Suppression therapy	34 (32.69%)	0 (0.00%)	1 (0.96%)
Amputation	2 (1.92%)	0 (0.00%)	0 (0.00%)
Debridement Antibiotics Internal Fixation	1 (0.96%)	0 (0.00%)	1 (0.96%)

8.2 Respect of international guidelines

In the course of our study, up to 73 participants (70.19%) were not treated according to the recommended international guidelines [62] as shown in the table below.

Table XIII : Respect of international guidelines

Respect of international guidelines	Frequency	Percentage (%)
No	73	70.19%
Yes	31	29.81%
Total	104	100%

SECTION 10: OUTCOME OF FRI

One hundred and four participants were present at final evaluation and were followed-up for a minimum of 3months. Out of which 50 (48.08%) participants had a good outcome defined by the clinical absence of infection and bone union. Forty-five (40.38%) participants still presented with an infection while 62 (59.62%) participants had their infection controlled. Fifty-eight (55.76%) cases had consolidated compared to 46 (48.24%) that did not consolidate at final evaluation. These information are represented in the table below.

Table XIV : Primary outcome of FRI

Bone union	Infection		Total
	No	Yes	
No	12 (11.54%)	34 (32.69%)	46 (55.76%)
Yes	50 (48.08%)	8 (7.69%)	58 (55.76%)
Total	62 (59.62%)	42 (40.38%)	104 (100%)

From the we concluded that the treatment of FRI in the course of ours study was successful (good outcome) in 50 (48.08%) cases compared to 54 (51.92%) cases that were the management failed as shown in Figure 24 below.

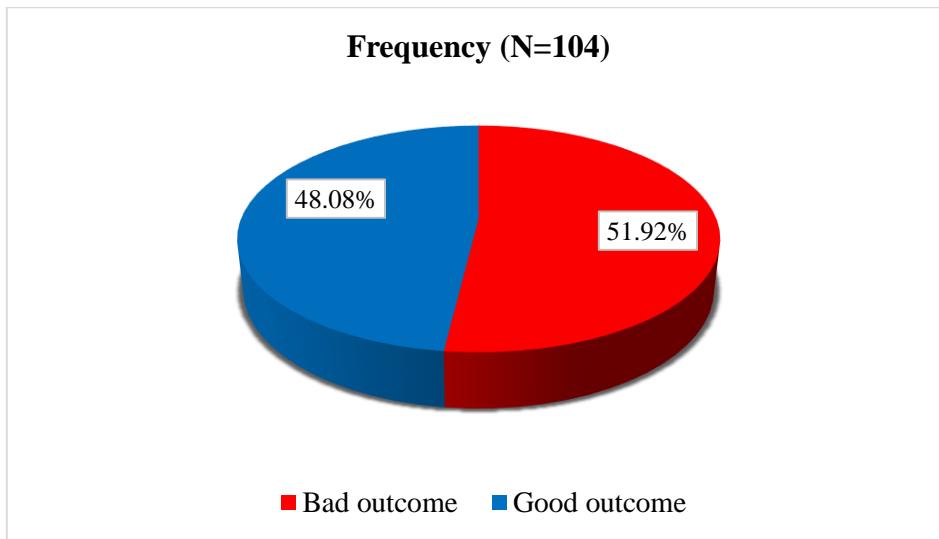


Figure 24: Outcome of Fracture – Related Infection

SECTION 11: FUNCTIONAL EVALUATION AND QUALITY OF LIFE

11.1 Functional evaluation

The mean Lower Extremity functional scale (LEFS) in our study 12 months after initial management of FRI was 56.6 ± 9.9 while the mean Upper Extremity Index (UEFI) 12 months after initial management was 69.7 ± 8.5 .

11.2 Quality of life

Following the Short Form-12 score, the mean 12 months after initial management of FRI was 38.75 ± 8.32 for Physical score and 49.42 ± 9.42 for mental score.

SECTION 12: PROGNOSTIC FACTORS OF FRI

12.1 Bivariate analysis

- Relationship between age, BMI, delay of onset of infection and outcome**

The data showed that various management delays were significantly higher in patients who had a bad outcome including; delay of surgery ($p = 0.04$), antibiotic duration ($p = 0.00$) and the delay of first wash ($p = 0.03$). There was no association between age, BMI and outcome (Table XV).

Table XV : Relationship between age, BMI, delay onset of infection and outcome

Variable	Bad outcome	Good outcome	P-value
Age	40.91 (14.90)	39.98 (12.65)	0.75
BMI	27.37 (3.66)	24.64 (4.04)	0.67
Delay of surgery (in days)	38.02 (23.57)	16 (17.98)	0.04
Antibiotic duration (in days)	107.70 (90.92)	62.36 (65.16)	0.00
Delay of first wash (in hours)	26.35 (32.60)	26 (31.63)	0.03

➤ **Patients demography and past history**

There was an association between gender and outcome; men had a higher rate of bad outcome (53.9%) compared to women (46.4%) ($p < 0.001$). Also, Tobacco smoking (71.4%) was significantly higher in patients with a bad outcome ($p < 0.001$). There was no relationship between HIV, Diabetes and outcome (Table XVI).

Table XVI : Relationship between gender, comorbidity and outcome

Variable	Bad outcome	Good outcome	p-value
Gender	Female	13 (46.4%)	15 (53.6%)
	Male	41 (53.9%)	35 (46.1%)
Comorbidities	Diabetes	3 (50.0%)	3 (50.0%)
Comorbidities	Smoking	10 (71.4%)	4 (28.6%)
	HIV	5 (41.7%)	7 (58.3%)

- Clinical features and relationship with outcome**

We found out that there was a relationship between the infected bone part and outcome; infections located at the tibia had a higher rate of bad outcome (67.86%) compared to infections located at the humerus (25%) ($p < 0.001$). A relationship between clinical signs and outcome also existed; Participants with a Fistula/sinus tract had a lesser rates of good outcome (38.9%) compared to participants with signs of inflammation (55.3%) ($p < 0.001$) as shown below.

Table XVII : Relationship between clinical features and outcome

Variable		Bad outcome	Good outcome	P-value
		(N=54)	(N=50)	
Infection location	Femur	16 (64%)	9 (36%)	0.03
	Foot	0 (0.00%)	4 (100%)	
	Humerus	2 (25%)	6 (75%)	
	Patella	1 (33.33%)	2 (67.33%)	
	Pelvis	3 (50%)	3 (50%)	
	Radius	0 (0.00%)	2 (100%)	
	Radius + Ulna	0 (0.00%)	1 (100%)	
	Tibia	19 (67.86%)	9 (32.14%)	
Clinical signs	Tibia + Fibula	15 (57.69%)	11 (42.31%)	0.00
	Fistula	22 (61.1%)	14 (38.9%)	
	Sinus tract	16 (64.0%)	9 (36.0%)	
	Wound breakdown	14 (58.30%)	10 (41.70%)	
	New onset of joint effusion	11 (68.8%)	5 (31.20%)	
	Signs of inflammation	17 (44.74%)	21 (55.30%)	
	Purulent drainage / pus	56 (53.85%)	48 (46.15%)	
	Persistent or increasing or new onset wound drainage	17 (60.70%)	11 (39.30%)	

Relationship between Radiologic signs, culture results and outcome

There was no association between culture results (**p = 0.35**), radiologic findings (**p = 0.05**) and outcome as shown in the table below.

Table XVIII : Relationship between work-ups and outcome

Variable		Bad outcome	Good outcome	p- value
Radiological findings	Lysis	14 (67.7%)	7 (33.3%)	0.35
	Periosteal reaction	11 (61.1%)	7 (38.9%)	
	Bone sequestration	8 (72.7%)	3 (27.3%)	
	Sclerosis	4 (80.0%)	1 (20.0%)	
	Hyperemia demineralisation	4 (100.0%)	0 (0.0%)	
Culture result	Implant loosening	2 (50.0%)	2 (50.0%)	0.05
	Negative	9 (56.3%)	7 (43.8%)	
	Positive	29 (47.5%)	32 (52.5%)	

- Relationship between management of FRI and outcome**

There was a relationship between onset of infection and outcome. Patients with post-operative infections had a higher rate of good outcome (48.53%), than those with pre-operative infections (45.22%) ($p = 0.98\%$). We also found a relationship between the treatment of FRI and outcome. Patients treated by the DAIR (68.42%) had a higher rate of bad outcome compared to those treated by the Masquelet technique (23.08%) ($p = 0.03$). Participants managed by suppression therapy had a higher rate of bad outcome than those managed by DAExFIX (60%) ($p = 0.03$) These infomations are represented in the table below.

Table XIX : Relationship between management and results of FRI

Variable	Label	Bad outcome (N=54)	Good outcome (N=50)	p-value	
About the Infection	Post-operative	35 (51.47%)	33 (48.53%)	0.01	
	Pre-operative	19 (54.78%)	17 (45.22%)		
Planned treatment	Amputation	3 (100%)	0 (0.00%)	0.03	
	DAExFIX	9 (52.94%)	8 (47.06%)		
	DAIEX	6 (60%)	4 (40%)		
	DAIR	13(68.42%)	6 (31.58%)		
Planned treatment	Debridement Antibiotics	1 (20%)	4 (80%)	0.03	
	Implant Removal				
	Debridement Antibiotics	1 (50%)	1 (50%)		
	Internal Fixation				
	Masquelet technique	2 (23.08%)	10 (76.92%)		
	Papinaux technique	1 (100%)	0 (0.00%)		
	Suppression therapy	23 (65.71%)	12 (34.29%)		

Relationship between Classifications and outcome

The Willenegger and Roth classification of FRI was associated with outcome of FRI; Participants with late infections had greater rates of bad outcome (57.14%) compared to patients with early infections (50.72%) ($p=0.04$) (Table XX).

Table XX : Willenegger and Roth classification of FRI and outcome

Variable	Label	Bad outcome (N=54)	Good outcome (N=50)	p- value
Willenegger and Roth	Early	35 (50.72%)	34 (49.28%)	0.04
	Delayed	7 (50%)	7 (50%)	
	Late	12 (57.14%)	9 (42.86%)	

The Cierny-mader classification (anatomic and physiologic host) was related to outcome of FRI; patients classified stage 3 (81.25%) had a higher rate of bad outcome compared to those classified normal (44.247%) ($p = 0.01$) (Table XXI).

Table XXI : Cierny-mader physiological host classification and outcome

Classification		Bad outcome	Good outcome	P - value
Cierny- Mader (Anatomic type)	Normal	31 (42.47%)	42 (57.53%)	0.01
	Type 1 (Medullary)	8 (72.73%)	3 (27.27%)	
	Type 2 (Superficial)	1 (100%)	0 (0.00%)	
	Type 3 (Localised)	13 (81.25%)	3 (18.75%)	
Cierny- Mader (Physiologic host)	Type 4 (Diffused)	1 (100%)	0 (0.00%)	0.02
	A host (Normal)	49 (53.26%)	43 (46.74%)	
	B host; Bs	4 (36.36%)	7 (63.64%)	
	C host	1 (100%)	0 (0.00%)	

Relationship between type of surgery and outcome

There was an association between type of initial surgery and outcome; Patients managed by closed surgery (85.71%) had a higher risk of good outcome than those managed by open surgery (45.08%) ($p = 0.04$). A significant association was also found between type of initial fixation and outcome ($p = 0.01$). Patients with an internal fixation at the onset of infection had a higher risk of bad outcome (63.33%) than those with an external fixation (47.29%) as seen below.

Table XXII : Relationship between type of initial surgery, type of surgery and outcome

Variable	Label	Bad outcome (N=54)	Good outcome (N=50)	p- value
Type of fixation	External	35 (47.29%)	39 (52.71%)	0.01
	Internal	19 (63.33%)	11 (36.67%)	
Type of initial surgery	Closed	1 (14.29%)	6 (85.71%)	0.04
	open	53 (54.64%)	44 (45.36%)	

To conclude with the FRI classifications, there was no association between the BACH classification and outcome ($p = 0.62$) (Figure 27).

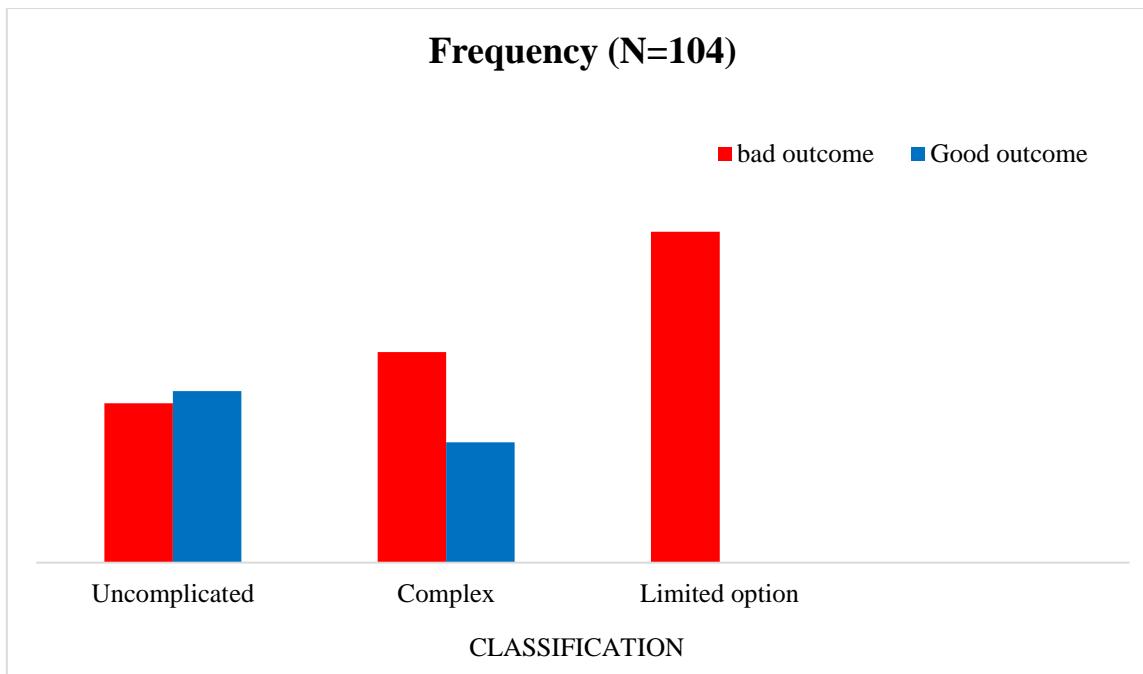


Figure 25 : Relationship between BACH classification and outcome

Relationship between respect of international guidelines and Outcome

In the course of our study, there was no association between the respect of international guidelines and outcome ($p= 0.54$). Also. 61.29% of participants that were not treated with respect to international guidelines had a bad outcome, while 38.71% treated according to international guidelines had a good outcome as seen below.

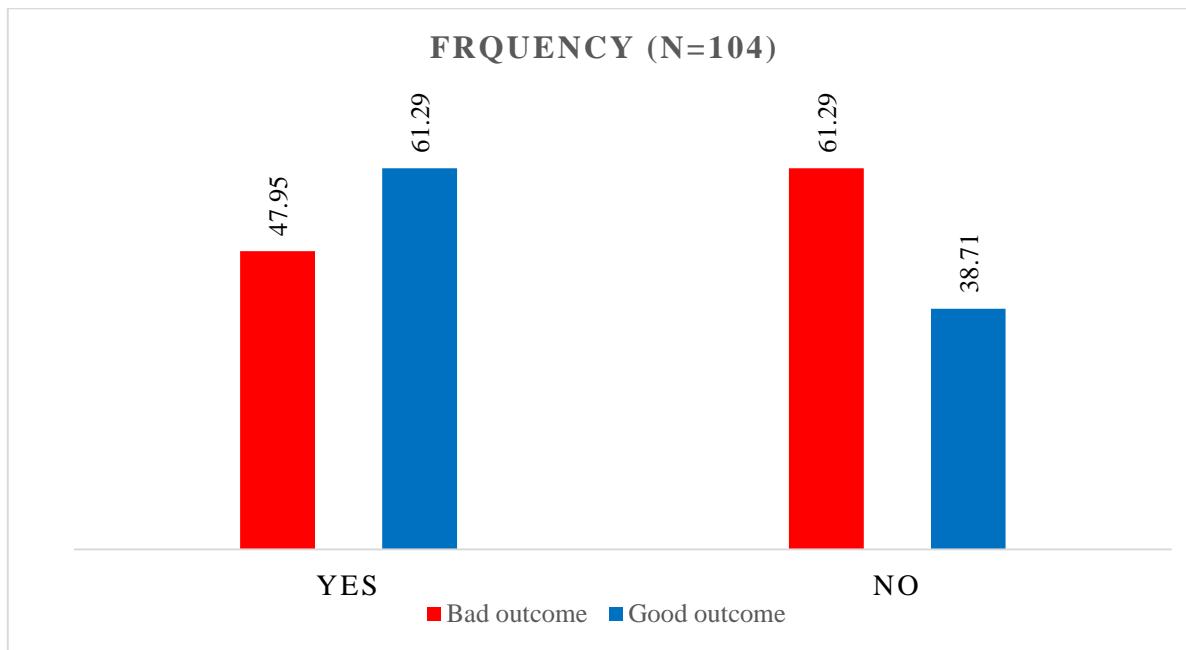


Figure 26: Respect of international guidelines and outcome

11.2 Multivariate analysis

.Concerning the factors affecting the prognosis of FRI, positive coefficients for significant modalities meant that patients with these modalities had higher chances of good outcome. On the other hand, significant modalities with negative coefficients meant that patients with these modalities were less likely to have a good outcome (The coefficients are interpreted at the 5% significance level).

In multivariate analysis using binary logistic regression, the only independent prognostic factors were grouped into; patient's related factors and treatment related factors

➤ Patients - related factors

Tobacco smoking was an independent factor of outcome ($OR = 0.87$. $p = 0.03$). The risk of having a bad outcome increased by 13% when the patient was a smoker. Outcome was not dependent on age. BMI or other comorbidities such as diabetes. HIV and Hypertension.

The delay of surgery had positive influence on outcome ($p = 0.04$). The OR being 0.96 indicated that for each additional day of surgery delay. The risk of having a bad outcome increased by approximately 4% when all other variables remained constant.

The delay of first wash or debridement had a negative influence on outcome ($p < 0.001$). An OR of 0.98 indicated that for each additional day of first wash of delay. The risk of having a bad outcome increased by roughly 2% all things being equal.

➤ Treatment – related factors

The duration of antibiotic treatment had a negative influence on outcome ($p < 0.001$). The OR being 0.89 indicated that for a single additional day on antibiotics. The risk of having a bad outcome increased by around 11% all things being equal.

Concerning the type of initial fixation, there is a 4% increase in the risk of having a bad outcome when a patient had an internal fixator compared to external fixator ($OR = 0.96$, $p = 0.04$) as seen below.

According to the Cierny-mader classification, those at stage 3 (Localised osteomyelitis) had a 20% risk of a bad outcome ($OR = 0.80$, $p = 0.04$). Those that were systemically compromised were 1.11 times more likely to have a bad outcome ($OR = 1.11$, $p = 0.02$)

Patient that were managed by suppression therapy had an 86% reduction in chances of having a good outcome ($OR = 0.14$, $p = <0.001$). Whereas those who were managed by Masquelet technique were 1.15 times more likely to have a good outcome ($OR = 1.15$, $p = 0.04$).

Table XXIII : Results of multivariate logistic regression identifying factors affecting the outcome of FRI

Variable	Coefficient	p- value	OR [95% CI]
Age	-2.30	1.00	0.61 [0.23 – 1.89]
Male gender	-1.54	0.71	1.33 [0.41 – 4.26]
Smoking	-3.51	0.03	0.87 [0.34 – 2.14]
Diabetes	-2.34	0.54	0.80 [0.22 – 2.92]
BMI	-3.74	0.31	3.04 [1.40 – 6.57]
Delay of surgery (in days)	-0.02	0.04	0.61 [0.30 – 1.43]
Delay of first (in hours)	-0.35	0.00	0.98 [0.05 – 5.72]
Antibiotic duration (in days)	-0.01	0.00	0.89 [0.43 -2.92]
About onset of infection	3.47	0.20	1.12 [0.31 – 5.57]
Internal fixation as primary management	-4.16	0.04	0.96 [0.37 – 2.97]
External fixation as primary management	2.45	0.05	3.04 [1.40 – 6.57]
Open surgery	-2.86	0.02	0.78 [056 – 2.75]
Cierny-mader stage 3 classification	-1.71	0.04	0.96 [0.48 – 4.06]
Willenegger and Roth classification	-1.56	0.65	0.25 [0.07 – 1.98]
Suppression therapy	-0.44	0.00	0.14 [0.05 – 0.78]
Debridement Antibiotics internal fixation	1.79	0.38	6.08 [2.48 – 9.33]
DAIEX	0.87	0.75	0.42 [0.13 – 2.33]
DAIR	-1.56	0.64	0.15 [0.03 – 1.45]
DAExFIX	-0.56	0.77	0.42 [0.21 – 0.91]
Debridement Antibiotics implant removal	2.17	0.49	14.50[11.43 – 17.3]
Masquelet therapy	2.07	0.04	1.15 [0.72 – 6.43]

DISCUSSION

Fracture-related infections is a devastating and challenging complication in the management of traumatic patients in orthopedics. Which can result in delay on soft tissue and bone healing. permanent loss of function affecting the patients quality of life .The aim of our study was to determine the outcome of fracture-related infections and to identify the factors affecting its prognosis in Yaoundé since there have been no reports on this topic in our setting. Following a 1 year 7 months prospective cohort study. A total of 146 confirmed fracture-related infections were included out of which 33 were lost to follow-up and 9 died. Hence 104 participants were retained from whom we collected and analysed data that will be discussed below.

Our study found out that the incidence of FRI in Yaoundé was 27.65%. Fifty-four (51.92%) participants had a negative result following treatment and 50 (48.08%) participants were treated successfully. The main factors that affected the prognosis of FRI negatively were: Past history of smoking ($p= 0.03$), management of initial injury by open surgery ($p=0.02$), delay of initial surgery ($p=0.04$), delay of first wash or debridement ($p=0.00$), the presence of an internal fixation at onset of infection ($p=0.04$), Cierny-mader anatomical and physiologic classification ($p=0.04$. $p=0.02$), treatment by suppression therapy ($p=0.00$) and prolonged long term antibiotic intake ($p=0.00$). Meanwhile the factor affecting the prognosis of FRI positively according to our study was; treatment by the Induced membrane technique ($p=0.04$).

Incidence of FRI

The prevalence data on FRI vary in the literature. In our study the incidence of FRI was 27.65% whereas Baisheng *et all* in Northeast China found an infection rate of 1.5% in a 10 year retrospective study of 48.186 patients treated surgically for a fracture[98]. Also, a study carried out in India by Doshi *et all* including 787 cases with tibia fractures. estimated the incidence of infection as 8.0% for open fractures and 1.6% for closed fractures [99]. Several factors account for this discrepancy, among which includes; the delay of fracture management and fixation. The high cost involving the management of FRI, the standards of our operating rooms, the methods of sterilisation and storage of surgical material, patient compliance to antibiotics and the inclination of patients to bone setters for traditional treatment.

Patient demographic

The mean age of participants was 40.46 years, predominantly in males (73.08%). This high predominance of the male gender and the youthful age group could be attributable to the greater likelihood of trauma and compound fractures in this population group in relation with their daily activities to join both ends. Our results were similar to those reported in Canada, Benin and Cameroon with a median age of 39.6, 39 and 37.1 respectively and a male predominance of 72% and 69% [14.32.35]. This similarity can be explained by the fact that, in both developed and developing countries. The young adult male in apparent good health represents the active sector of society. The most represented occupation were traders and most of the participants had a fair socio-economic status (monthly income ranging from minimum wage – 150,000fcfa). This could explain the higher incidence of FRI in these individuals as their financial constraint delays surgical management of fractures and also risks incompliance to antibiotic therapy as the patients may be unable to afford the drugs usually taken for a long period.

Clinical presentation

As described, young adults are more active and they are prone to road traffic accidents (RTA) during transportation. Where motorcycles are the most common means of transport, traffic regulations are not respected drivers and passengers have no protective equipment so in the course of our study, we found RTAs to be the cause of initial injury in 75% of cases. These results are lower than those found in Togo and Cameroon in 2023. Where we had RTAs at rates of 95.4% and 85.2% respectively [35.93]. Other causes such as domestic accidents, work accidents and ballistic accidents accounted for approximately 25% both in our study and of the above-mentioned authors. However, these results are contradictory to those found by Scharfenberger *et al.*[101] in Canada in 2017, where RTAs represented 45% of causes and work related accidents 41%. This could be explained by the fact that in highly industrialized countries, work-related accidents may predominate over RTAs. Observance of the Highway Code contribute to a decline in RTAs.

The mean duration between the accident and admission was 8.88 (± 22.56) hours. Meanwhile the mean time delay between the accident and first washing/debridement for open fractures was 10.26 (± 23.23) hours and the delay between initial trauma and the onset of antibiotic administration was 11.87 (± 26.98) hours. These results differs from those reported by José *et al* where the mean delay of admission was 1.5 hours. This difference could be explained by the fact that our population

seems much more reluctant to consultation. However in our study, there was no significant association between delay of admission, delay of antibiotic administration and the outcome of FRI. But the delay of debridement or first wash in the case of FRI treatment had a negative influence on outcome of FRI ($p=0.00$. OR=0.98). The mean delay to surgery was 30.3 ± 64.8 hours. and could be a risk factor for bad outcome as illustrated by Scharfenbergers [101] *et al* during a prospective study in 2017 on the timing of ankle fracture surgery and the risk of complications. Which showed that a delay of more than 1 day following trauma day is a risk factor for treatment failure. This delay to surgery could be explained by financial constrain of patients, absence of health insurance and ignorance on the path of some patients who chose traditional bone setters over medical treatment.

Open fractures accounted for 66.35% of the fractures with Gustilo-Anderson type III fractures being the most represented type of open fractures. Most of the infections were located on the Tibia (26.92%). These results are similar to those of Niebuhr *et al* [71] who had 67% of open fractures and 47.6% of tibial fractures which were infected in their study and also. ED *et al* [41] whose results presented open fractures to represent 76% and tibial fractures to represent 48.5% of FRI. Open fractures are more predisposed to infection as the protective skin barrier has been broken and contaminants from the environment have direct access to the bone. The tibia being the location most predisposed to infection can be explained by its thin muscular coverage. Hence, a break in the skin permits direct contact of the external environment with the bone.

The most prevalent clinical symptom presented by patients with FRI in Yaoundé was purulent drainage at the fracture site which occurred in 96.2% of cases. These results were similar to that of Lu *et al* [36] who carried out a retrospective study in the UK in 2022. Their results showed that 86.5% of cases with FRI presented with purulent wound. Also. 34.62% of cases presented with pre-operative infection (infection prior to fracture fixation). Open fractures which were not managed early predisposed to this condition. Pre-op FRI is not well defined in recent literature and is not taken into account with the consensus criteria [16]. Meanwhile 65.38% were post-op infections which is far greater than the results of Niraj *et all* who had only 5% post-op infections after ankle fracture management [102]. This could be accounted by high rate of open surgery (87.45%) in our setting.

Concerning the radiological signs, there is lack of information and the incidence of these signs as concerned with FRI but our study recorded that 25% of patients presenting with FRI had a radiologic sign of infection. The most common sign was bone lysis (83%) followed by periosteal reaction (72%).

4. MANAGEMENT

The patients' therapeutic pathway was dominated by surgery. We found out that 19% of patients opted for traditional massage, the reasons being traditional beliefs and lower cost similarly described by Yao *et al* [76] in 2021 in Côte d'Ivoire, who found financial problems and belief in traditional treatment in 58.5% and 39.6% of cases respectively. Successful principles for management of FRI include; fracture consolidation, restoration of the soft tissue envelope, return to function, prevention of residual chronic infection and eradication of infection.

The most commonly used implant was the external fixator in 52.5% of cases. as corroborated by Banza et al [100] in the Democratic Republic of Congo and Mertens et al. [36] in Cameroon. Our results are far superior to those found by Scharfenberger et al. [101]. In Canada in 2017.participants who had external fixation had rates of 2%, compared with 88% for IMN. This difference can be explained by difference in treatment times which are shorter in developed countries.

Treatment options for FRI include DAIR. DAIEX and DAI removal, depending on whether or not there is fracture consolidation [89]. There is no agreed upon consensus for the treatment modalities of FRI but several studies have shown a better outcome of DAIR in early onset FRI (<3 weeks) [38.89]. In that case infection after this time frame with no fracture consolidation were managed by suppressive therapy while awaiting fracture consolidation for implant removal or implant exchange to be done. Contrary to the consensus definition, 25% of early onset post-op FRI was managed by suppression therapy, preferably because it is less costly. This does not match the methods adopted by the international community for management of FRI. The management of pre-op FRI in our study consisted of debridement antibiotics and external fixation (13.35%) which is not defined in the literature also and has to be adapted to our context given the high prevalence of pre-op FRI.

For the cierny-mader classification of FRI, those at stage 1 were managed by DAIR (27.27%). Participants at stage 2 were managed only by DAExFix while participants at stage 3 by the induced membrane technique (43.75%) and stage 4 by debridement antibiotics implant removal. This differs from the treatment recoded by Jason in 2019 where stage 1 cases were by debridement including bone grafting and soft tissue coverage and antibiotics, stage 2 by debridement of the bone cortex + antibiotics while stage 3 or 4 by debridement. antibiotics + bone reconstruction and external fixation [55].

CLINICAL AND FUNCTIONAL OUTCOME OF FRI

For our study duration, participants were followed up for at least 3 months and up to 12 months which is in line with the minimum duration (12 months) of follow-up recommended by the FRI consensus. A total of one hundred and four patients were present at final evaluation. Out of which 48.08% had a good outcome defined by the clinical absence of infection and bone union and 51.92% had a bad outcome. In addition, out of the 69 patients followed for a period of 1 year 34.61% had a bad outcome. These results vary from those obtained by McNally *et al* [74] in 2022 where eradication of infection and bone union was achieved in 86.0%. Chadayammuri *et al* [35] in 2017 reported the adverse clinical and functional outcome to be 38.7% and Lu *et al* [42] in 2022 reported treatment failure rate to be 23.5%. This can be accounted for by the low socio-economic level of patients who delay the period for the onset of management due to financial constraint inhibiting them from purchasing medication and surgical material necessary for their management as recommended by international guidelines.

We also noticed that there was no significant difference on the outcome of participants who had their infection before or after surgery. This is because in our setting, treatment strategies usually very costly were mostly guided by the available resources and not the onset of infection. Up to 33.66% were managed by a suppressive therapy yielding a success rate of 22.12% and failure rate of 11.54%. On the other hand, Chadayammuri *et al* [35] in 2017 used suppressive therapy as an initial treatment awaiting bone union before implant removal. Participants managed by DAIR had a success rate of 27.28%. While various clinical studies reported excellent results with success rates of 90%

and more for implant retention in acute or early onset FRIs occurring within 3 weeks after fracture fixation. 70% in FRIs manifesting up to 6 weeks after osteosynthesis and if a DAIR was applied more than 10 weeks after fracture fixation the success rate decreased to 51–67%. Future studies have to be done in our setting to understand why there is a big gap on the awaited results of DAIR [18]. 80% and 60% of participants managed by Debridement Antibiotics and implant removal and DAIEX respectively in our study responded positively to treatment which is similar to the results of Sliepan *et al* in 2023 [92] where all patients treated by DAI removal and DAIEX respectively had a treatment success rate of 100% and 92.10% [92]. In addition there was no significant difference on the outcome of participants managed by DAExFIX. This result cannot be compared with other studies because it is not well defined in literature and had to be adapted to our context given the high prevalence of pre-op FRI. Considering the induced membrane technique

(Masquelet technique). 83.33% cases were treated successfully similar to the results of shen *et al* in 2023 who had a success rate of 92% [76]. This can be accounted by the fact that the Masquelet technique is a standardized surgical procedure that can be applied by qualified surgeons and the resources needed for the procedure is available in both settings. We also remarked that only 2% of the study population was amputated. The recurrence rate of infection was 25.96% and the rate of infection persistence after treatment was 29.5%. These results are similar to those recorded by McNally *et al* in 2022 [74] where the amputation rate was 3.3% and recurrence 6.65%.

Talking about the functional outcome. the mean SF-12 score for 1-year follow-up was 39.73 (SD 7.87) regarding the physical health component and 49.42 (SD 8.95) regarding the mental health component and the mean compared to USA nominative values of 56.58 (SD 6.58) for PCS and 60.76 (SD 10.76) for MCS [14]. Patients who suffered with FRI scored significantly lower than USA reference population. This demonstrates the large negative impact of FRI on both the mental and physical state of patients. This results are similar to those obtained Walter *et al* in 2020 [76]. In general, studies assessing patient-related outcome measures after FRI treatments are scarce. This could be explained by the fact that both in developed and developing countries. the burden of FRI is high and it has the same impact on the patients' health state [14]. The mean LEFS and UEFS at last follow-up was 42 points (40 to 80) and 46 points (41 to 80) respectively implying with respect to outcome. Participants had mild to moderate functional limitations 1-year after diagnosis and treatment of FRI. Comparing nominative score of LEFS 77 [85] and UEFS 72.9287 ± 8.57932 [13] to our results, we could see that patients suffering from FRI scored significantly lower than the nominative values. This shows the negative impact of FRI on limb functional outcome.

FACTORS AFFECTING THE OUTCOME OF FRI

This study employed the FRI consensus definition to assess therapy success or failure. We hypothesized that if the confirmatory criteria for FRI were met at any point after the infection treatment was completed it would be considered a failure because the initial indication for therapy remained. The criteria were simple and provided an objective endpoint for therapy failure, making it effective. Using the multivariable logistic regression analysis method, many factors were identified that can determine the outcome for patients with FRI. Some of these may be modifiable prior to surgery. These factors are grouped into patient's related factors, surgery and treatment related factors.

Concerning patient's related factors, our results suggested that smoking ($p=0.03$. OR=0.87) had a negative impact on the participant's outcome. Smoking has been shown to impair wound healing and increase the risk of postoperative complications. including infections. This complicates the already delicate process of managing FRI and significantly hampers the potential for successful outcomes. Meanwhile outcome was not dependent on age. BMI or other comorbidities such as diabetes. HIV and Hypertension. These results can be mapped to those obtained by McNally *et al*[74] in 2022 were tobacco smoking at the time of surgery increased the chance of failure by three times and outcome was not dependent on age. BMI and diabetes. But this varies from the results obtained by Lu *et al* in Switzerland where obesity, diabetes and smoking had a negative impact on treatment outcome. Moreover in our study participants' classified stage 3 according to cierny-mader had a 20% risk of treatment failure. This is in line with Lu *et al* in 2022 were patients at stage 3 had unexpectedly the highest odds for FRI treatment failure on both univariable and multivariable models. Bacterial colonization also had an impact on outcome. Patients who developed a FRI with *Enterobacter cloacae* ($P=0.004$. OR=1.67) in culture isolate only had better chances of recovery than those with polymicrobes or other bacteria. This was not the case in Switzerland in 2022 where the most common bacterium isolate was *Staph aureus* very sensitive to Beta lactamine.

In our series, time to first wash or debridement and delay of surgery had a negative influence on outcome ($P=0.00$. OR= 0.98 and $p=0.05$. OR=0.61 respectively). This was different from the results of Hull *et al* [93] in the USA who found no association between delay to debridement. Gustilo and Anderson type, age or comorbidities. Similarly. Hendrickson *et al* [74] found no significant difference between outcome and a 12-hour delay in debridement: 4.5% vs. 5.6%. Lu et al [84]in

2022 found that the difference in time between fracture and first debridement was not related to infection outcome. However. Smoking, diabetes, duration of surgery and Gustilo and Anderson fracture classification were independent factors of outcome. Participants with an internal fixation at onset of infection had higher risk of bad outcome than those with external fixation ($P= 0.04$. $OR=0.96$). Lu *et al* [84] in 2022 and Sliepan *et al* [92] in 2023 had different results. Type of fixation at initial management had no influence on outcome of FRI. This difference is due to the fact that in our setting, post-op FRI was mainly managed by suppression therapy or Debridement + antibiotics. In our study, there was no relationship between management of FRI by DAIR, DAIEX; DAI removal. Debridement = antibiotics and outcome. McNally *et al* [74] also found out that DAIR was associated with an overall lower success rate. compared to implant removal or conversion to an external fixation [74]. Nevertheless, some studies report no effect of implant removal or retention on FRI treatment efficacy, whilst some report the opposite. with implant removal being a significant risk factor for FRI treatment failure [93].This could be due to selection bias since surgeons could have removed more implants in patients who had more severe infections. The induced membrane technique had a positive impact on outcome ($P=0.04$. $OR= 1.15$). Shen *et al* in 2023[77] had similar results, this technique was effective for treating infected bone defects. Che *et al*[103] in China in 2022 had a primary success rate at 2 years of 75% . Antibiotic Duration had a negative influence on outcome. The OR being 0.89 indicated that for a single additional day on Antibiotics.The risk of having a bad outcome increased by around 11%. Several studies in the western world found out that duration of antibiotics was not associated with FRI [84]. The large heterogeneity in prescribing patterns and absence of any evident benefit for longer antibiotics provides an opportunity to study the benefits of a standardized short course of antibiotics.

STRENGTHS AND LIMITATIONS OF THIS STUDY

Strengths

Nonetheless, this is one of the first prospective studies on outcome and factors affecting the prognosis of FRI in our setting since the consensus on the diagnosis of FRI to properly understand how FRI is being managed in our context in order to determine its prognostic factors proper to LMIC's. This study explains the variations or the loopholes FRI management in our context to international guidelines. Hence will go a long way to improve the standard and outcome in our context.

Limitations

Although the study had limitations due to the variability of the cases, it accurately represented the diverse spectrum of patients with FRI. We used numerous analysis techniques to identify key therapy factors that have been discussed above. However this only offered an overview of the issue. We were unable to provide insight into how each treatment component impacted outcomes. Our findings suggest potential areas for future research. Also in the course of our study, not all cases could do a standard X-ray necessary for primary outcome due to lack of resources and more than 30% of the registered population was lost to follow-up this hindered our initial population sample and thereby affecting our results.

CONCLUSION AND RECOMMENDATIONS

CONCLUSION

At the end of our study, following our objectives and results we were able to draw the following conclusions;

The treatment of Fracture-Related Infections (FRI) in Yaoundé is multifaceted, encompassing various medical and surgical approaches. The most common treatments included suppression therapy (antibiotic therapy and wound dressing) for early post-operative infections and the DAExFIX procedure for pre-operative infections. Other treatment modalities such as DAIR and the Masquelet technique were also employed, depending on the classification of the onset of infection (early, delayed, or late) according to Willenegger and Roth. The diversity in treatment methods reflects the complexity of managing FRIs in LMIC's and the necessity of tailoring interventions to the specific circumstances of each patient.

When analyzing the adequacy of FRI treatments in Yaoundé against international guidelines, it is evident that there is a significant gap. The study revealed that only 29.81% of patients were treated in accordance with these guidelines, indicating a 70.19% rate of non-compliance.

Evaluating the outcomes of FRI treatments in Yaoundé shows a mixed picture. Of the 104 participants followed up, 48.08% achieved a good outcome defined by infection control and bone union, while 40.38% still had active infections. Additionally, 59.62% had their infections controlled, yet only 55.76% showed bone consolidation. No relationship was found between the respect of international guidelines and outcome while the use of DAIR had a negative impact on outcome with up to 68.42% of bad outcome.

The findings of this study underscore the complex interplay between various factors influencing the outcomes of fracture-related infections (FRI). Closed surgeries were associated with better outcomes compared to open surgeries, and external fixations were found to be more favorable than internal fixations. Tobacco smoking emerged as a significant predictor of poor outcomes. Additionally, delays in surgical interventions and the first wash or debridement were also associated with higher risks of negative outcomes. Prolonged antibiotic treatment duration was linked to worse outcomes, suggesting a need for optimized antibiotic regimens to prevent complications. Moreover, the Masquelet technique had a positive influence in patient's outcomes. Future efforts should focus on addressing these predictors to improve the overall management of FRIs in Yaoundé.

RECOMMENDATIONS

At the end of our study and following our results, we humbly make the following recommendations

1. To the international scientific community

- To standardized treatment protocols for fracture-related infections (FRIs) that can be easily adapted and implemented in resource-limited settings like Yaoundé. These protocols should include guidelines on the use of antibiotics, surgical interventions, and follow-up procedures to ensure consistent and effective treatment outcomes.

2. To the local scientific community

- To carry out more value-based prospective studies and large database research in other regions on the topic.
- To enhance training programs for orthopedic surgeons and healthcare providers, focusing on the latest techniques and best practices in FRI management. Ensure continuous professional development through regular workshops and seminars.

3. To the trauma/orthopedic surgeons

- To continually monitor factors contributing to poor outcomes in patients presenting with fracture-related infections (FRI) in order to enhance positive results.
- In cases of late infections, consider the Masquelet technique, which showed positive results.

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APPENDIX

Appendix 1: The Lower Extremity Functional Scale**THE LOWER EXTREMITY FUNCTIONAL SCALE**

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb Problem for which you are currently seeking attention. Please provide an answer for **each** activity.

Today, do you or would you have any difficulty at all with:

	Activities	Extreme Difficulty or Unable to Perform Activity	Quite a Bit of Difficulty	Moderate Difficulty	A Little Bit of Difficulty	No Difficulty
1	Any of your usual work, housework, or school activities.	0	1	2	3	4
2	Your usual hobbies, recreational or sporting activities.	0	1	2	3	4
3	Getting into or out of the bath.	0	1	2	3	4
4	Walking between rooms.	0	1	2	3	4
5	Putting on your shoes or socks.	0	1	2	3	4
6	Squatting.	0	1	2	3	4
7	Lifting an object, like a bag of groceries from the floor.	0	1	2	3	4
8	Performing light activities around your home.	0	1	2	3	4
9	Performing heavy activities around your home.	0	1	2	3	4
10	Getting into or out of a car.	0	1	2	3	4
11	Walking 2 blocks.	0	1	2	3	4
12	Walking a mile.	0	1	2	3	4
13	Going up or down 10 stairs (about 1 flight of stairs).	0	1	2	3	4
14	Standing for 1 hour.	0	1	2	3	4
15	Sitting for 1 hour.	0	1	2	3	4
16	Running on even ground.	0	1	2	3	4
17	Running on uneven ground.	0	1	2	3	4
18	Making sharp turns while running fast.	0	1	2	3	4
19	Hopping.	0	1	2	3	4
20	Rolling over in bed.	0	1	2	3	4
Column Totals:						

Minimum Level of Detectable Change (90% Confidence): 9 points

SCORE: _____ / 80

Appendix 2: The Upper Extremity Functional Index

THE UPPER EXTREMITY FUNCTIONAL INDEX (UEFI)

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your upper limb problem for which you are currently seeking attention. Please provide an answer for **each** activity.

Today, do you or would you have any difficulty at all with:

(Circle one number on each line)

	Activities	Extreme Difficulty or Unable to Perform Activity	Quite a Bit of Difficulty	Moderate Difficulty	A Little Bit of Difficulty	No Difficulty
1	Any of your usual work, housework, or school activities	0	1	2	3	4
2	Your usual hobbies, recreational or sporting activities	0	1	2	3	4
3	Lifting a bag of groceries to waist level	0	1	2	3	4
4	Lifting a bag of groceries above your head	0	1	2	3	4
5	Grooming your hair	0	1	2	3	4
6	Pushing up on your hands (eg from bathtub or chair)	0	1	2	3	4
7	Preparing food (eg peeling, cutting)	0	1	2	3	4
8	Driving	0	1	2	3	4
9	Vacuuming, sweeping or raking	0	1	2	3	4
10	Dressing	0	1	2	3	4
11	Doing up buttons	0	1	2	3	4
12	Using tools or appliances	0	1	2	3	4
13	Opening doors	0	1	2	3	4
14	Cleaning	0	1	2	3	4
15	Tying or lacing shoes	0	1	2	3	4
16	Sleeping	0	1	2	3	4
17	Laundering clothes (eg washing, ironing, folding)	0	1	2	3	4
18	Opening a jar	0	1	2	3	4
19	Throwing a ball	0	1	2	3	4
20	Carrying a small suitcase with your affected limb	0	1	2	3	4
Column Totals:						

Minimum Level of Detectable Change (90% Confidence): 9 points

SCORE: _____ / 80 = _____ % impairment

NAME: _____

DATE: _____

Appendix 3: The Short Form-12 score

Scales	Items		Response categories
	No.	Contents (abridged)	
PCS-12	1	General health	Excellent/Very good/Good/Fair/Poor
	2	Moderate activities	Limited a lot/Limited a little/Not limited at all
	3	Climb several flights of stairs	Limited a lot/Limited a little/Not limited at all
	4	Accomplished less (physical)	Yes/No
	5	Limited in kind of work	Yes/No
	8	Pain - interference	Not at all/A little bit/Moderately/Quite a bit/Extremely
	6	Accomplished less (emotional)	Yes/No
	7	Did work less careful	Yes/No
MCS-12	9	Calm and peaceful	All of the time/Most of the time/A good bit of the time/Some of the time/A little of the time/None of the time
	10	Energy	All of the time/Most of the time/A good bit of the time/Some of the time/A little of the time/None of the time
	11	Downhearted and blue	All of the time/Most of the time/A good bit of the time/Some of the time/A little of the time/None of the time
	12	Social limitations - time	All of the time/Most of the time/Some of the time/A little of the time/None of the time

Appendix 4: The BACH classification

	<u>Bone involvement</u>	<u>Antimicrobial options</u>	<u>Coverage by soft tissue</u>	<u>Host status</u>
Uncomplicated	<i>B₁</i> Cavitory infection without joint involvement (including cortical, medullary and non-segmental cortico-medullary)	<i>A_x</i> Unknown / culture negative osteomyelitis	<i>C₁</i> Direct closure possible: Plastic surgery expertise not required	<i>H₁</i> Well-controlled disease or Patient is fit and well
		<i>A₁</i> All isolates: • Sensitive to ≥ 80% of susceptibility tests and resistant to ≤ 3 susceptibility tests		
Complex	<i>B₂</i> Segmental infection without joint involvement	<i>A₂</i> Any isolate: • Sensitive to < 80% of all susceptibility tests performed or • Resistant to ≥ 4 susceptibility tests or • Resistant to antibiotic film antibiotics in the presence of an implant	<i>C₂</i> Direct closure not possible: Plastic surgery expertise required	<i>H₂</i> Patient with poorly controlled comorbidity or Severe comorbidity (with evidence of end-organ damage) or Recurrent osteomyelitis after previous debridement
	<i>B₃</i> Any bone infection with associated joint involvement	<i>A₃</i> Any isolate: • Sensitive to 0 or 1 susceptibility test performed		
Limited options				<i>H₃</i> Unfit for definitive surgery despite specialist intervention or Patient declines surgery

Appendix 5: Information sheet

Title: Outcome of fracture related infection and prognostics factors in Yaoundé

Investigator: I am SIME DJEBACHE Jasmine Grace. Final year medical student at the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. Cameroon.

Supervisor: Professor BAHEBECK Jean Professor of Orthopaedics and traumatology

Co-supervisors:

- ▶ Dr. FONKOUÉ Loic. senior lecturer of orthopedics and traumatology
- ▶ Dr. MULUEM Kennedy. lecturer of orthopedics and traumatology

Subject: An invitation to take part in the study

Study aim: Fracture-related infection (FRI) is a serious complication in orthopedics and trauma that impacts care costs, quality of life and patient function. According to the international guidelines, the treatment of FRI should always be surgical but this is not always applied in our daily practise due to its high cost. Our aim is to evaluate the results of FRI treatment in Yaoundé and to identify the prognostic factors specific to our environment.

Study sites: Yaoundé Central Hospital, Yaoundé General Hospital, University Teaching Hospital of Yaoundé. Military hospital of Yaoundé and the Yaoundé Emergency Center

Duration: December 2023 to June 2024

Procedure: A daily visit to the surgical emergency department, the orthopaedic trauma and paediatric surgery in-patient units and during consultation will be conducted. We will identify patients likely to be included in the study. These patients will be re-evaluated to ensure that they meet the inclusion criteria. We will collect data through a written questionnaire (appendix III). During their hospitalization patients will be examined at 6 weeks. 3-month, 6-month, 1 year looking for; signs of infection and bone union.

Benefits: You will receive free evaluation of your quality of life. If you do not live in Yaoundé, we will cover your transportation cost to return to your home town.

Risks and inconveniences: There are no major risks associated with this study other than the inconvenience of having to move to the fore mentioned hospitals for evaluation.

Cost: Evaluation will be done free of charge. You will not be given any material or financial incentives to participate in the study. Participation will be your free will.

Ethical considerations: Permission has been obtained from the appropriate persons in charge of the study sites and authorization gotten from the National Ethics Committee. An encryption code shall be used rather than your name on all documents containing data collected. The data will be handled with the greatest confidentiality. You can opt out of the study at any point and refusal to participate or opting out will involve no penalties nor alter the relationship between you and your attending physician, hospitals, study investigators or your employers.

Contacts: For more information or further clarification about the study you can contact the investigator through the following telephone number (655568043) and email address:
jasmunesims237@gmail.com

Fiche de Renseignement

Titre : Résultat du traitement et facteurs pronostic des infections liées à la fracture à Yaoundé

Investigateur : Je suis SIME DJEBACHE Jasmine Grace. Étudiante en 7^{ème} année de médecine à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I. Cameroun.

Superviseur : Professeur BAHEBECK Jean. Professeur titulaire de Chirurgie orthopédique.

Co-superviseurs:

- ▶ Dr. FONKOUÉ Loic. chargée de cours en chirurgie orthopédique
- ▶ Dr. MULEUM Kennedy. assistant en Chirurgie orthopédique

Objet : Invitation à participer à l'étude

But de l'étude : Les infections liées à la fracture (FRI) est une complication grave en chirurgie orthopédique qui a un impact sur les coûts des soins, la qualité de vie et la fonction du patient. Selon les recommandations internationales, le traitement des FRI devrait toujours être chirurgical. Mais cela n'est pas toujours appliqué dans notre pratique quotidienne en raison de son coût élevé. Notre but est d'évaluer le résultat du traitement de la FRI à Yaoundé et d'en déduire les facteurs pronostiques spécifiques à notre environnement.

Sites d'étude : Hôpital Central de Yaoundé. Hôpital Général de Yaoundé. Centre Hospitalier et Universitaire de Yaoundé. Hôpital militaire de Yaoundé. Centre des Urgences de Yaoundé.

Durée : Décembre 2023 à Juin 2024

Procédure : Une visite quotidienne au service des urgences chirurgicales, aux unités d'hospitalisation en traumatologie orthopédique et en chirurgie pédiatrique et lors des consultations sera effectuée. Nous identifierons les patients susceptibles d'être inclus dans l'étude. Ces patients seront réévalués pour s'assurer qu'ils répondent aux critères d'inclusion. Nous recueillerons les données à l'aide d'un questionnaire écrit (annexe III). Au cours de leur hospitalisation, les patients seront examinés à 6 semaines, 3 mois, 6 mois et 1 an à la recherche de signes d'infection et de consolidation osseuse.

Avantages : Vous recevrez gratuitement une évaluation de votre qualité de vie et de l'intensité de la douleur. Si vous ne résidez pas à Yaoundé, nous prendrons en charge vos frais de transport pour retourner dans votre ville d'origine.

Risques et inconvénients : Il n'y a pas de risques majeurs associés à cette étude, si ce n'est le désagrément de devoir se déplacer dans les hôpitaux susmentionnés pour l'évaluation.

Coût : Vous ne recevrez aucune incitation matérielle ou financière pour participer à l'étude. La participation sera de votre libre arbitre.

Considérations éthiques : La permission a été obtenue auprès des responsables des sites d'étude et l'autorisation a été obtenue auprès du Comité National d'Ethique. Un code de cryptage sera utilisé plutôt que votre nom sur tous les documents contenant des données collectées. Les données seront traitées avec la plus grande confidentialité. Vous pouvez vous retirer de l'étude à tout moment et le refus de participer ou le retrait n'entraînera aucune sanction et ne modifiera pas les relations entre vous et votre médecin traitant, les hôpitaux, les investigateurs de l'étude ou vos employeurs.

Contacts : Pour plus d'informations ou de précisions sur l'étude, vous pouvez contacter l'investigateur au numéro de téléphone (655568043) et à l'adresse électronique suivante : jasmunesims237@gmail.com

Appendix 6 : Administrative Authorisations

UNIVERSITÉ DE YAOUNDÉ I
FACULTÉ DE MÉDECINE ET DES
SCIENCES BIOMÉDICALES
COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE
Tel/ fax : 22 31-05-86 22 311224
Email: dekanatfmsb@hotmail.com



THE UNIVERSITY OF YAOUNDE I
FACULTY OF MEDICINE AND BIOMEDICAL
SCIENCES
INSTITUTIONAL ETHICAL REVIEW BOARD

Ref. : N° D953 /UY1/FMSB/VDRE/DASR/CSD

CLAIRANCE ÉTHIQUE 10 JUIN 2024

Le COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE (CIER) de la FMSB a examiné

La demande de la clairance éthique soumise par :

M.Mme : SIME DJEBACHE JASMINE GRACE

Matricule: 17M010

Travaillant sous la direction de :

- Pr BAHEBECK Jean
- Dr FONKOUÉ Loïc
- Dr MULUEM Olivier Kennedy

Concernant le projet de recherche intitulé :

Outcome and prognostic factors-related
infections in Yaoundé

Les principales observations sont les suivantes

Evaluation scientifique	
Evaluation de la convenance institutionnelle/valeur sociale	
Équilibre des risques et des bénéfices	
Respect du consentement libre et éclairé	
Respect de la vie privée et des renseignements personnels (confidentialité) :	
Respect de la justice dans le choix des sujets	
Respect des personnes vulnérables :	
Réduction des inconvénients/optimalisation des avantages	
Gestion des compensations financières des sujets	
Gestion des conflits d'intérêt impliquant le chercheur	

Pour toutes ces raisons, le CIER émet un avis favorable sous réserve des modifications recommandées dans la grille d'évaluation scientifique.

L'équipe de recherche est responsable du respect du protocole approuvé et ne devra pas y apporter d'amendement sans avis favorable du CIER. Elle devra collaborer avec le CIER lorsque nécessaire, pour le suivi de la mise en œuvre dudit protocole. La clairance éthique peut être retirée en cas de non-respect de la réglementation ou des recommandations sus évoquées. En foi de quoi la présente clairance éthique est délivrée pour servir et valoir ce que de droit

LE PRÉSIDENT DU COMITÉ ETHIQUE



REPUBLIC DU CAMEROUN
Paix-Travail-Patrie

MINISTERE DE LA SANTE PUBLIQUE

SECRETARIAT GENERAL

CENTRE DES URGENCES DE YAOUNDÉ

SERVICE ADMINISTRATIF ET FINANCIER

SERVICE DES AFFAIRES GENERALES ET DES
RESSOURCES HUMAINES

BUREAU DES RESSOURCES HUMAINES



REPUBLIC OF CAMEROON
Peace-Work-Fatherland

MINISTRY OF PUBLIC HEALTH

SECRETARIAT GENERAL

YAOUNDÉ EMERGENCY CENTER

ADMINISTRATIVE AND FINANCIAL
OFFICE'S

HUMAN RESSOURCES AND GENERAL
AFFAIRS-SERVICE

HUMAN RESSOURCES OFFICE

BP: 3911

E-mail : cury_minsante@yahoo.fr

Tél : 222 22 25 25/222 22 25 24/222 22 25 22

N° CCG/AR/MINSANTE/SG/DCURY/SAF/SAG-RH/CB-RH

Yaoundé, le

30 JAN 2024

AUTORISATION DE RECHERCHE

Je soussigné Dr Louis Joss BITANG à MAFOK, Directeur du Centre des Urgences de Yaoundé, autorise Madame SIME DJEBACHE Jasmine Grace, Etudiante à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I, à mener une enquête dans notre institution hospitalière sur le thème <<Outcome and prognostic factors of fracture-related infections in Yaoundé. >>, Pendant la période allant du 08 Janvier au 08 Février 2024, sous la direction de Dr. FONKOUÉ Loïc, Médecin Chirurgien Orthopédiste-Traumatologue.

En foi de quoi la présente autorisation lui est délivrée pour servir et faire valoir ce que de droit. /-

Copies :

- CM/CMA ;
- Chef SAG-RH ;
- Chef SAF ;
- Intéressée ;
- Chrono/archive,



REPUBLIQUE DU CAMEROUN

Pax - Travail - Patrie

MINISTÈRE DE LA SANTE PUBLIQUE

HOPITAL GENERAL DE YAOUNDE

DIRECTION GENERALE

BP 5408 YAOUNDE - CAMEROUN
TEL : (237) 22 21 31 81 FAX : (237) 22 21 20 15.



REPUBLIC OF CAMEROON

Peace - Work - Fatherland

MINISTRY OF PUBLIC HEALTH

YAOUNDE GENERAL HOSPITAL

GENERAL MANAGEMENT DEPARTMENT

N/Réf. 049-24 /HGY/DG/DPM/APM-TR.

Yaoundé, le 19 JAN 2024

Le Directeur Général

A/TO

Madame SIME DJEBACHE Jasmine Grace
Etudiante en 7^{ème} année d'Etudes Médicales
Tél : 655 568 043 Mle : 17M010
FMSB - UNIVERSITE DE YAOUNDE I

Objet/subject :

V/Demande d'autorisation de recherches.

Madame,

Faisant suite à votre correspondance du 10 janvier 2024 dont l'objet est porté en marge,

Nous avons l'honneur de marquer notre accord pour que vous effectuez vos travaux de recherches au service CHIRURGIE GENERALE ET VISCERALE, dans le cadre votre étude dont le thème s'intitule : « *Outcome and prognostic factors of fracture - related infections in Yaoundé* ».

Cette étude sera dirigée par le Docteur FONKOUÉ Loïc, chirurgien orthopédiste -Traumatologue.

Vous observerez la réglementation en vigueur à l'Hôpital Général de Yaoundé pendant la durée des recherches. Toutefois, les publications se rapportant à ce travail devraient inclure les médecins de l'Hôpital Général de Yaoundé.

Recevez, Madame, nos salutations distinguées. /-

Ampliations :

- DPM
- Chef Service Chirurgie Générale et Viscérale
- Docteur FONKOUÉ
- Chrono/archives.



Prof. EYENGA Victor

REPUBLIQUE DU CAMEROUN Paix - Travail - Patrie	REPUBLIC OF CAMEROON Peace - Work - Fatherland
PRESIDENCE DE LA REPUBLIQUE	PRESIDENCY OF THE REPUBLIC
MINISTERE DE LA DEFENSE	MINISTRY OF DEFENCE
DIRECTION DE LA SANTE MILITAIRE	DEPARTMENT OF MILITARY HEALTH
REGION DE SANTE MILITAIRE N°1	MILITARY HEALTH REGION N°1
HÔPITAL MILITAIRE DE REGION N°1	MILITARY REGION HOSPITAL N°1
Yaoundé le <u>25 JAN 2024</u>	N° <u>240036</u> /DV/MINDEF/DSM/RSM1/HMR1/12

AUTORISATION D'ACCES

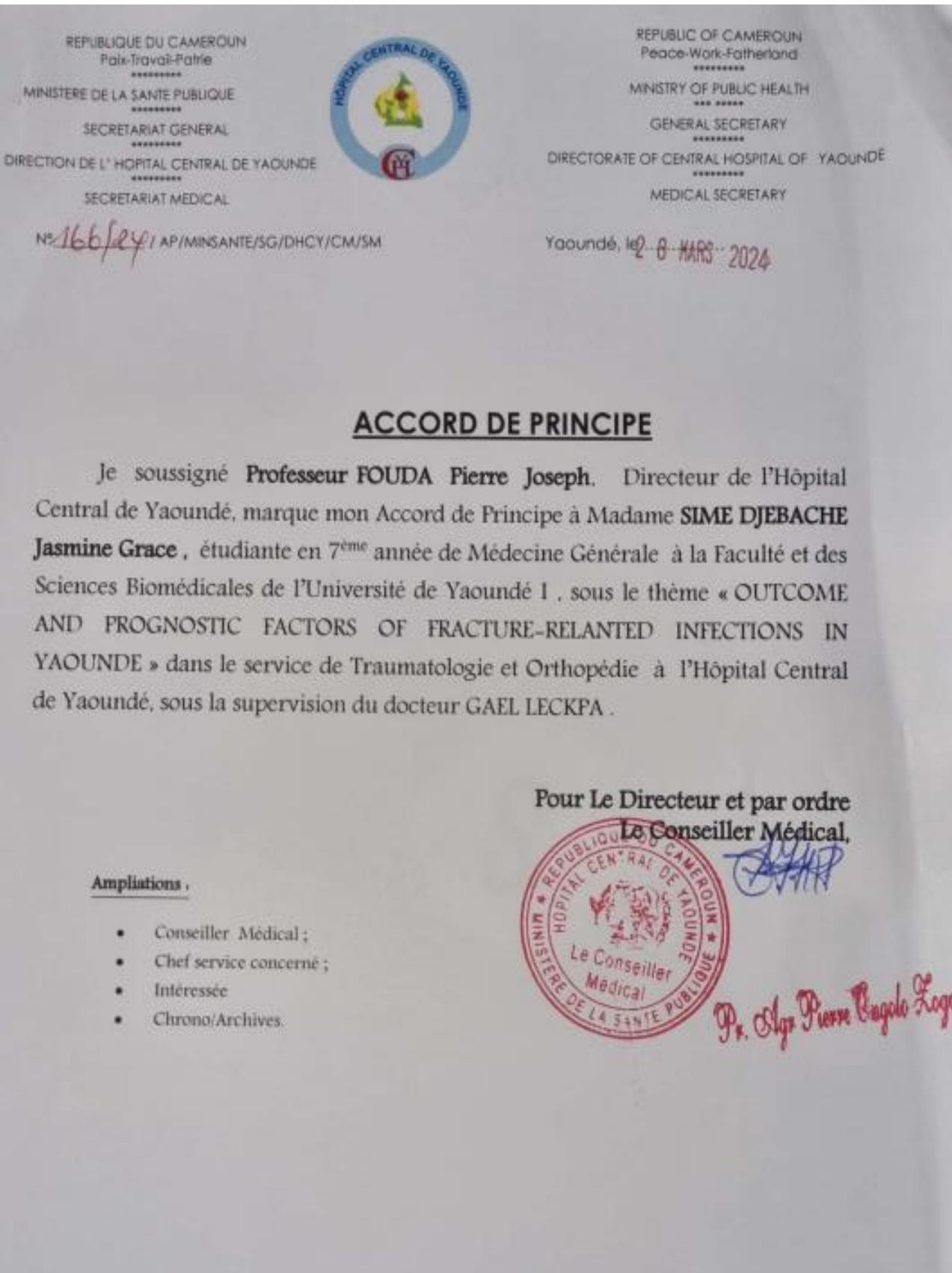
Je soussigné, Colonel-Médecin HAMADOU, Médecin-Chef de l'Hôpital Militaire de Région n°1 (HMR1),

Autorise Madame SIME DJEBACHE Jasmine Grace, étudiante en 7^{ème} année à la Faculté de Medecine et Sciences Biomédicales à l'Université de Yaoundé I, à accéder au Service Spécialisé de Chirurgie Orthopédie/Traumatologie de l'HMR1, en vue d'y effectuer une recherche dont le thème porte sur « *Outcome and prognostic factors of fracture-related infections in Yaounde* ».

En cas de publication de cet article, le Service d'accueil de l'HMR1 devrait être cité.

En foi de quoi la présente autorisation lui est délivrée pour servir et valoir ce que de droit. /-





Appendix 7 : Questionnaire

Site :Code : _____ Date:Name :Contact:

SECTION 1: SOCIODEMOGRAPHIC DATA

1.1	Age years	
1.2	Gender	1. Male 2. Female	<input type="checkbox"/>
1.3	Level of education	1. Primary 2. Secondary 3. University	<input type="checkbox"/>
1.4	Marital status	1. Single 2. Married 3. Divorced 4. Widow(er)	<input type="checkbox"/>
1.5	Profession	1. Manager 2. Armed force occupation 3. Elementary occupation 4. Plant and machine operators and assemblers 5. Craft and related traders workers 6. Skilled agricultural forestry and fishery workers 7. Technicians and associated professionals 8. Service and sales workers 9. Clerical support workers 10. Student 11. Retired worker	<input type="checkbox"/>
1.6	Social class	1. Class 1 (Receives less than base salary and or inadequate support) 2. Class 2 (base salary- 150 000F and/or average family support) 3. Class 3 (150 000F- 250 000F and/or good family support) 4. Class 4 (250 000F and/or good family support) 5. Class 5 (more than 500 000F and/or wealthy family and/or insurance)	<input type="checkbox"/>

SECTION 2: CLINICAL DATA AND WORK-UP

2.1	Weight (kg) kg	
	Height (m) m	
	Body mass index (kg/m ²) kg/m ²	
2.2	Comorbidities	1. Yes 0. No	<input type="checkbox"/>
		If yes, precise: Diabetes: 1. Yes 0. No	<input type="checkbox"/>
		Hypertension: 1. Yes 0. No	<input type="checkbox"/>

	<p>Smoking: 1. Yes 0. No If Yes; For how long have you been smoking (in Years) How many sticks do you smoke per day</p>	<input type="checkbox"/>
	Cardiovascular Disease 1. Yes 0. No	<input type="checkbox"/>
	Human Immune Virus (HIV) 1. Yes 0. No	<input type="checkbox"/>
	Rheumatologic disease: 1. Yes 0. No	<input type="checkbox"/>
	Kidney disease: 1. Yes 0. No	<input type="checkbox"/>
	Cancer 1. Yes 0. No	<input type="checkbox"/>
	Peripheral vascular disease 1. Yes 0. No	<input type="checkbox"/>
	Mental Issues 1. Yes 0. No	<input type="checkbox"/>
	Others	<input type="checkbox"/> <hr/>
2.3	<p>Initial Injury</p> <p>What caused the initial injury</p> <ol style="list-style-type: none"> 1. Road accident 2. Work accident 3. Domestic accident 4. Low energy trauma 5. High energy trauma 6. Pathological fracture 	<input type="checkbox"/>
	<p>What was the initial injury</p> <ol style="list-style-type: none"> 1. Open fracture 2. Closed fracture 	<input type="checkbox"/>
	<p>What was the affected side</p> <ol style="list-style-type: none"> 1. Left 2. Right 3. Both 	
	<p>Where was it located</p> <ol style="list-style-type: none"> 1. Tibia 2. Fibula 3. Humerus 4. Femur 5. Radius 6. Ulna 7. Femur + Tibia 8. Tibia + Fibulla 9. Humerus + Radius + Ulna 10. Pelvis 11. Radius + Ulna 12. Foot 13. Patella 14. Tibia + Humerus 	

	<p>If it was an open fracture. what was the Gustilo- Anderson Classification</p> <ol style="list-style-type: none"> 1. GA-1 2. GA-2 3. GA-3A 4. GA-3B 5. GA-3C 	
	Delay of admission (in hours)	
	Delay of first wash (in hours)	
	Delay of Antibiotics (in hours)	
	Type of initial surgery	
	<ol style="list-style-type: none"> 1. Open Surgery 2. Closed surgery 	
	What was done during the initial surgery	
	<ol style="list-style-type: none"> 1. External fixator 2. Intra-medullary nailing 3. Pins and screws 4. Rods 5. Wires 6. Plates 7. Others 	
	Delay of surgery (in days)	
2.4	<p>Clinical symptoms</p> <p>1. Yes 0. No</p>	<input type="checkbox"/>
	Fever ($\geq 38^{\circ}\text{C}$) 1.Yes 0.No	<input type="checkbox"/> <input type="checkbox"/>
	Localised pain 1.Yes 0.No	<input type="checkbox"/> <input type="checkbox"/>
2.5	<p>Clinical signs</p> <p>1.Yes 0.No</p>	<input type="checkbox"/>
	Fistula 1.Yes 0.No	<input type="checkbox"/>
	Sinus tract 1.Yes 0.No	<input type="checkbox"/>
	Wound breakdown 1.Yes 0.No	<input type="checkbox"/>
	Purulent drainage or pus 1.Yes 0.No	<input type="checkbox"/> <input type="checkbox"/>
	New onset of joint effusion 1.Yes 0.No	<input type="checkbox"/> <input type="checkbox"/>
	Signs of inflammation (redness. fever. swelling) 1.Yes 0.No	<input type="checkbox"/>
	Persistent or increasing or new onset wound drainage beyond a few days post-op without alternative explanation 1. Yes 0. No	<input type="checkbox"/>
	Others	
2.6	<p>About the Infection</p> <p>1 Pre-op 2. post-op infection</p> <p>If pre-op. how long after the accident did the symptoms present (in days)</p> <p>If post-op. how long after initial surgery did your symptoms present (in days)</p>	<input type="checkbox"/>
2.7	Radiologic findings	1.Yes 0.No <input type="checkbox"/>

		Lysis 1.Yes 0.No	
		Periosteal reaction 1.Yes 0.No	<input type="checkbox"/>
		Sclerosis 1.Yes 0.No	<input type="checkbox"/>
		Hyperemia demineralization 1.Yes 0.No	<input type="checkbox"/>
		Implant loosening 1.Yes 0.No	<input type="checkbox"/>
		Bone sequestration 1.Yes 0.No	<input type="checkbox"/>
		Copy of X-ray 1.Yes 0.No	<input type="checkbox"/>
2.8	Diagnostic biomarkers	1.Yes 0.No	<input type="checkbox"/>
		Elevated ERS 1.Yes 0.No	<input type="checkbox"/>
		Elevated WBC count 1.Yes 0.No	<input type="checkbox"/>
		Elevated CRP 1.Yes 0.No	<input type="checkbox"/>
2.9	Histology	1.Yes 0.No	<input type="checkbox"/>
		≥ 5PMNs / HPF ; 1. Yes 2. No	<input type="checkbox"/>
2.10	Microbiology culture	1.Yes 0.No	<input type="checkbox"/>
	- Sampling	1.Swab	<input type="checkbox"/>
		2.Pus aspiration	<input type="checkbox"/>
		3.Inta operatory deep biopsy	<input type="checkbox"/>
	Nº of samples		
	Culture results	1. Positive 2. Negative	<input type="checkbox"/>
	Number of bacteria present	1. 1 2. 2 3. 3	<input type="checkbox"/>
	Bacteria 1- 3	1. Enterobacter cloacea 2. Enterobacter hormaechei 3. Staph aureus 4. E. coli 5. Klebsiella spp 6. Staph coagulase negative 7. Staph lugdunesis 8. Pseudomonas aeruginosa 9. Enterococcus spp 10. Proteus mirabilis 11. Citrobacter sedlakii 12. Citrobacter freudi 13. Klebsiella pneumonia 14. Providencia staurtii 15. Pseudomonas spp 16. Enterococcus faeculis 17. Enterococcus avium	

	18.Enterococcus faecium 19.Staph saprophyticus 20.Acinobacter baumannii 21.Aeromonas hydrophilic 22.Morganella morganii 23.Salmonella 24.Staph epidermidis 25.Staph xylosus 26.Staph hemolyticus 27.Streptococcus group b 28.Peptoniphilus asaccharolyticus 29.Enterococcus hirae 30.Citrobacter koserii 31.Proteus sp 32.Cornyebacterium striatum	
Culture criteria for diagnosis	1. Yes 0. No	
Copy of bacteriology results	1.Yes 2.No	<input type="checkbox"/>

SECTION 3: CLASSIFICATION OF FRI

3.1	Willeneger and Roth	1. Early 2. Delayed 3. Late	<input type="checkbox"/>
3.2	BACH	1. Uncomplicated 2. Complex 3. Limited option	<input type="checkbox"/>
3.3	Cierny - Mader	Physiologic Host 1. A Host (Normal) 2. B Host ; Bs (Systemic compromise) 3. B Host ; B1 (localised compromise) 4. C Host (Treatment worse than disease)	<input type="checkbox"/>

	Anatomic Type 1. Type 1 (Medullary osteomyelitis) 2. Type 2 (Superficial osteomyelitis) 3. Type 3 (Localised osteomyelitis) 4. Type 4 (Diffused osteomyelitis)	<input type="checkbox"/>
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SECTION 4: MANAGEMENT OF THE FRI

	Initial treatment	Planned treatment	
		1. DAIR	<input type="checkbox"/>
		2. DAIEX	<input type="checkbox"/>
		0. Debridement Antibiotics Internal Fixation	<input type="checkbox"/>
		1. Debridement Antibiotics Implant Removal	<input type="checkbox"/>
		2. Masquelet technique	<input type="checkbox"/>
		3. Debridement + Antibiotics	<input type="checkbox"/>
		4. Masquelet + Implanr change	<input type="checkbox"/>
	Actual treatment	5. Papinaux technique	<input type="checkbox"/>
		6. Suppression therapy	<input type="checkbox"/>
		7. Amputation	<input type="checkbox"/>
		1. DAIR	<input type="checkbox"/>
		2. DAIEX	<input type="checkbox"/>
		8. DAExFIX	<input type="checkbox"/>
		9. Debridement Antibiotics Internal Fixation	<input type="checkbox"/>
		10. Debridement Antibiotics Implant Removal	<input type="checkbox"/>
	Experience of surgeon	11. Masquelet technique	<input type="checkbox"/>
		12. Debridement + Antibiotics	<input type="checkbox"/>
		13. Masquelet + Implanr change	<input type="checkbox"/>
		14. Papinaux technique	<input type="checkbox"/>
		15. Suppression therapy	<input type="checkbox"/>
		16. Amputation	<input type="checkbox"/>
		1. Resident	<input type="checkbox"/>
		2. 1-5yrs	<input type="checkbox"/>
	Local Antibiotics 1.Yes 0.Non	3. 5-10yrs	<input type="checkbox"/>
		4. >10yrs	<input type="checkbox"/>
		If Yes	<input type="checkbox"/>
		1. Powder	<input type="checkbox"/>
		2. Cement + Antibiotics	<input type="checkbox"/>
		3. Injection	<input type="checkbox"/>
		4. AIBG	<input type="checkbox"/>
		Delay of surgery (in days)days
4.2	Systemic Antimicrobial therapy	Exacyl 1.Yes 0.No	<input type="checkbox"/>
		Drain 1.Yes 0.No	<input type="checkbox"/>
	Antibiotic 1-3	1. Tazobactam + piperacilline
		2. Amoxiclav
		3. Ofloxacine	
		4. Metronidazole	

	<p>5. Gentamicine 6. Ciprofloxacin 7. Cefuroxime 8. Levofloxine 9. Amikacine 10. Fosfomycine 11. Clindamycine 12. Lincocine 13. Rifampicine 14. Fusidine 15. Vancomycine 16. Imipenem 17. Thiobactin 18. Nitrofurantoin 19. Doxycycline 20. Bactrim 21. Cotrimoxazole 22. Meropenem Duration</p>	
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SECTION 5: EVOLUTION AND FOLLOW-UP

Period: 3 months

5.1	Primary criteria	mRUST criteria 1. 0-4 2. 5-7 3. 8-9 4. 10-12 5. 13-16 Bone union 1.Yes 0.No	/16
		<input type="checkbox"/>	
		<input type="checkbox"/>	
		<input type="checkbox"/>	
		Radiological signs of infection 1.Yes 2.No	<input type="checkbox"/>
		If Yes Lysis 1.Yes 0.No Periosteal reaction 1.Yes 0.No Cortical irregularity 1.Yes 0.No Demineralization 1.Yes 0.No Bone sequestration 1. Yes 0.No Implant loosening 1. Yes 0.No Sclerosis 1.Yes 0.No	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
		Clinical signs and symptoms 1.Yes 0.No	<input type="checkbox"/>
		If Yes	<input type="checkbox"/>

	<p>Fistula 1. Yes 0. No</p> <p>Sinus 1. Yes 0. No</p> <p>Wound breakdown 1. Yes 0. No</p> <p>Local signs of inflammation (swelling, redness) 1. Yes 0. No</p> <p>Fever ($\geq 38.5^{\circ}\text{C}$) 1. Yes 0. No</p> <p>Pus / Purulent drainage 1. Yes 0. No</p> <p>Persistent or increasing or new onset wound drainage beyond a few days post-op without alternative explanation. 1. Yes 0. No</p> <p>New onset of joint effusion 1. Yes 0. No</p> <p>Recurrence of infection 1. Yes 0. No</p>	
Primary criteria	<p>Lab results:</p> <p>Elevated CRP 1. Yes 0. No</p> <p>Elevated ESR 1. Yes 0. No</p> <p>Elevated WBC 1. Yes 0. No</p>
Secondary criteria	<p>Backt to work 1. Yes 0. No</p> <p>S-F 12</p> <p>LEFS (If fracture located on lower limbs) 1. 0-20: Severe functional limitation 9. 21-40: Moderate functional limitation 10. 41-60: Mild to moderate functional limitation 11. 61-80: Minimal functional limitation or normal function</p> <p>UEFS (If fracture located on Upper limb) 1. 0-20: Severe functional limitation 2. 21-40: Moderate functional limitation 3. 41-60: Mild to moderate functional limitation 4. 61-80: Minimal functional limitation or normal function</p>

Outcome and prognostic factors of fracture-related infections in Yaoundé

5.3	Complications	1. Yes 0.No If Yes: 1. Deep vein thrombosis 2. Amputation 3. Pulmonary embolism 4. Bone deformity 5. Persistent of infection	<input type="checkbox"/>
5.4	Treatment changed	1. Yes 0.No 1. DAIR 2. DAIEX 3. DAExFIX 4. Debridement Antibiotics Implant Removal 5. Masquelet 6. Masquelette + Implant change 7. Debridement + Antibiotics 8. Debridement Antibiotics Internal fixation 9. Suppression therapy 10. Amputation 11. Papinaux technique	<input type="checkbox"/> <input type="checkbox"/>

Period: 6 months

5.1	Primary criteria	mRUST criteria 1. 0-4 2. 5-7 3. 8-9 4. 10-12 5. 13-16 Bone union 1.Yes 0.No	/16
		Radiological signs of infection 1.Yes 2.No	
		If Yes	<input type="checkbox"/>
		Lysis 1.Yes 0. No	<input type="checkbox"/>
		Periosteal reaction 1.Yes 0.No	<input type="checkbox"/>
		Cortical irregularity 1.Yes 0.No	<input type="checkbox"/>
		Demineralization 1.Yes 0.No	<input type="checkbox"/>
		Bone sequestration 1. Yes 0.No	<input type="checkbox"/>
		Implant loosening 1. Yes 0.No	<input type="checkbox"/>
		Sclerosis 1.Yes 0.No	
		Clinical signs and symptoms 1.Yes 0.No	<input type="checkbox"/>
		If Yes	<input type="checkbox"/>
		Fistula 1. Yes 0. No	<input type="checkbox"/>

	<p>Sinus 1.Yes 0.No</p> <p>Wound breakdown 1.Yes 0.No</p> <p>Local signs of inflammation (swelling, redness) 1.Yes 0.No</p> <p>Fever ($\geq 38.5^{\circ}\text{C}$) 1.Yes 0.No</p> <p>Pus / Purulent drainage 1.Yes 0.No</p> <p>Persistent or increasing or new onset wound drainage beyond a few days post-op without alternative explanation. 1. Yes 0. No</p> <p>New onset of joint effusion 1.Yes 0. No</p> <p>Recurrence of infection 1.Yes 0.No</p>	
Primary criteria	<p>Lab results:</p> <p>Elevated CRP 1.Yes 0.No</p> <p>Elevated ESR 1.Yes 0.No</p> <p>Elevated WBC 1.Yes 0.No</p>
Secondary criteria	<p>Backt to work 1. Yes 0. No</p> <p>S-F 12</p> <p>LEFS (If fracture located on lower limbs)</p> <ul style="list-style-type: none"> 12. 0-20: Severe functional limitation 13. 21-40: Moderate functional limitation 14. 41-60: Mild to moderate functional limitation 15. 61-80: Minimal functional limitation or normal function <p>UEFS (If fracture located on Upper limb)</p> <ul style="list-style-type: none"> 5. 0-20: Severe functional limitation 6. 21-40: Moderate functional limitation 7. 41-60: Mild to moderate functional limitation 8. 61-80: Minimal functional limitation or normal function

Outcome and prognostic factors of fracture-related infections in Yaoundé

5.3	Complications	<p>2. Yes 0.No If Yes;</p> <ul style="list-style-type: none"> - Deep vein thrombosis - Amputation - Pulmonary embolism - Bone deformity - Persistent of infection 	<input type="checkbox"/>
5.4	Treatment changed	<p>1. Yes 0.No</p> <ol style="list-style-type: none"> 1. DAIR 2. DAIEX 3. DAExFIX 4. Debridement Antibiotics Implant Removal 5. Masquelet 6. Masquelette + Implant change 7. Debridement + Antibiotics 8. Debridement Antibiotics Internal fixation 9. Suppression therapy 10. Amputation 11. Papinaux technique 	<input type="checkbox"/> <input type="checkbox"/>

Period: 1 year

5.1	Primary criteria	mRUST criteria 1. 0-4 2. 5-7 3. 8-9 4. 10-12 5. 13-16 Bone union 1.Yes 0.No	/16 <input type="checkbox"/>
		Radiological signs of infection 1.Yes 2.No	<input type="checkbox"/>
		If Yes	<input type="checkbox"/>
		Lysis 1.Yes 0.No	<input type="checkbox"/>
		Periosteal reaction 1.Yes 0.No	<input type="checkbox"/>
		Cortical irregularity 1.Yes 0.No	<input type="checkbox"/>
		Demineralization 1.Yes 0.No	<input type="checkbox"/>
		Bone sequestration 1. Yes 0.No	<input type="checkbox"/>
		Implant loosening 1. Yes 0.No	<input type="checkbox"/>
		Sclerosis 1.Yes 0.No	<input type="checkbox"/>
		Clinical signs and symptoms 1.Yes 0.No	<input type="checkbox"/>
		If Yes	<input type="checkbox"/>
		Fistula 1. Yes 0. No	<input type="checkbox"/>

	<p>Sinus 1.Yes 0.No</p> <p>Wound breakdown 1.Yes 0.No</p> <p>Local signs of inflammation (swelling, redness) 1.Yes 0.No</p> <p>Fever ($\geq 38.5^{\circ}\text{C}$) 1.Yes 0.No</p> <p>Pus / Purulent drainage 1.Yes 0.No</p> <p>Persistent or increasing or new onset wound drainage beyond a few days post-op without alternative explanation. 1. Yes 0. No</p> <p>New onset of joint effusion 1.Yes 0. No</p> <p>Recurrence of infection 1.Yes 0.No</p>	<input type="checkbox"/>
Primary criteria	<p>Lab results:</p> <p>Elevated CRP 1.Yes 0.No</p> <p>Elevated ESR 1.Yes 0.No</p> <p>Elevated WBC 1.Yes 0.No</p>
Secondary criteria	<p>Backt to work 1. Yes 0. No</p> <p>S-F 12</p> <p>LEFS (If fracture located on lower limbs)</p> <p>12. 0-20: Severe functional limitation</p> <p>13. 21-40: Moderate functional limitation</p> <p>14. 41-60: Mild to moderate functional limitation</p> <p>15. 61-80: Minimal functional limitation or normal function</p>
	<p>UEFS (If fracture located on Upper limb)</p> <p>9. 0-20: Severe functional limitation</p> <p>10. 21-40: Moderate functional limitation</p> <p>11. 41-60: Mild to moderate functional limitation</p> <p>12. 61-80: Minimal functional limitation or normal function</p>	

Outcome and prognostic factors of fracture-related infections in Yaoundé

5.3	Complications	<p align="center">a. Yes 0.No</p> <p>If Yes;</p> <p align="center">16. Deep vein thrombosis 17. Amputation 18. Pulmonary embolism 19. Bone deformity 20. Persistent of infection</p>	<input type="checkbox"/>
5.4	Treatment changed	<p align="center">1.Yes 0.No</p> <p align="center">21. DAIR 22. DAIEX 23. DAExFIX 24. Debridement Antibiotics Implant Removal 25. Masquelet 26. Masquelette + Implant change 27. Debridement + Antibiotics 28. Debridement Antibiotics Internal fixation 29. Suppression therapy 30. Amputation 31. Papinaux technique</p>	<input type="checkbox"/> <input type="checkbox"/>
5.5	outcome	<p align="center">1. Good outcome 2. Bad outcome</p>	

Appendix 8 : Anti-plagiarism

Duplichecker

Dupli Checker Plagiarism Report

Originality Report

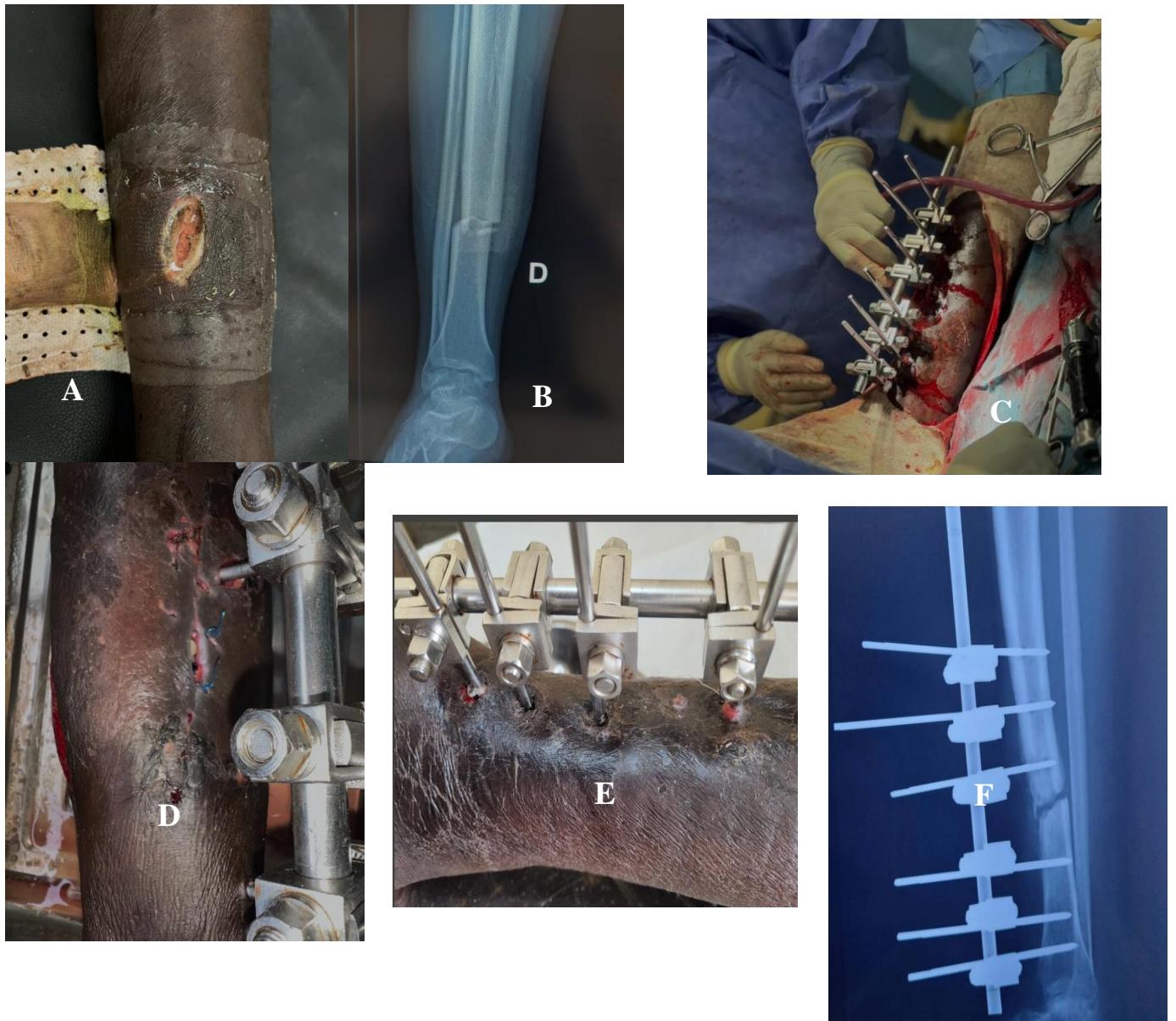
 7.5%	 92.5%	10158 Words	68620 Characters
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Primary Sources

1	https://www.ncbi.nlm.nih.gov/pmc... Bone and Joint Infections: The Role of Imaging in Tailoring	 0.14%
2	WEB · This includes early infection a- WEB · This includes early infection around fracture implants; infected non-unions; hematogenous infections arising after fracture healing, and infections in fractures-	 0.14%
3	https://books.google.com/books?i... War and Peace in the Religious Conflicts of the Long ...	 0.14%
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5	https://www.ncbi.nlm.nih.gov/pmc... try M McNally - 2020 - Cited by 31 — The FRI Consensus Group published the initial definition criteria in 2018 and the term 'fracture-related infection' was adopted by ...	 0.14%
6	https://journals.sagepub.com/doi/... ... management in addressing multiple facets including patient factors, fracture considerations of mechanical stability and biological viability, and ...	 0.14%
7	https://www.ncbi.nlm.nih.gov/pmc... try O Olakosunbo da Costa - 2016 - Cited by 26 — This study was carried out over a period of 2 years comprising all patients in mixed dentition that presented at the...	 0.14%

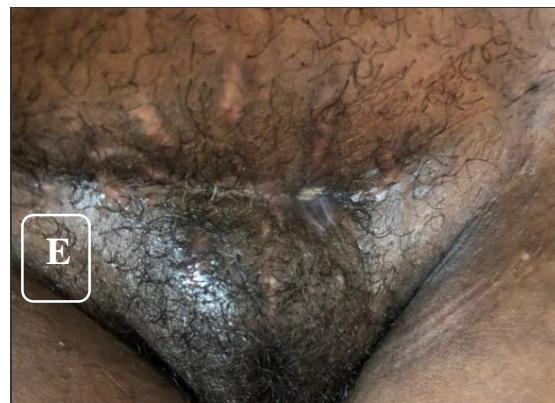
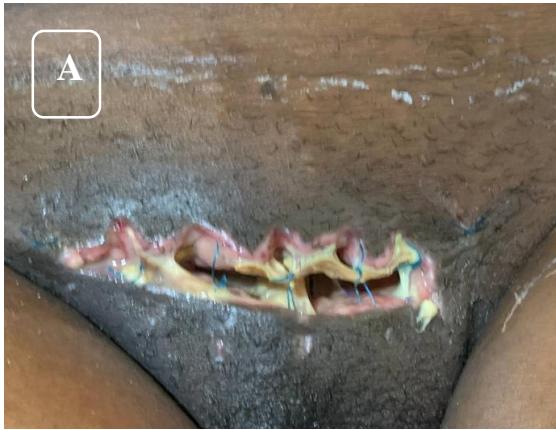
Appendix 9: Picture gallery

CASE 1



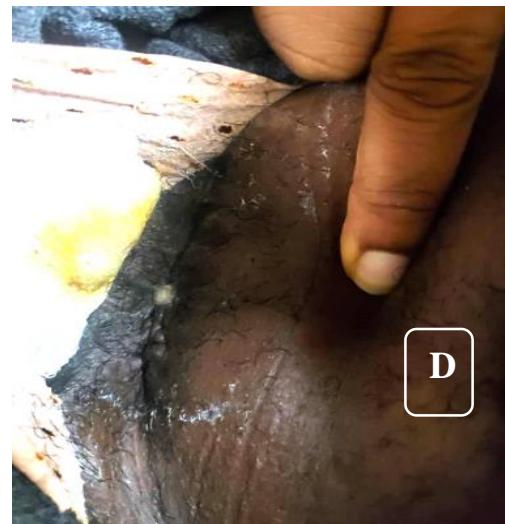
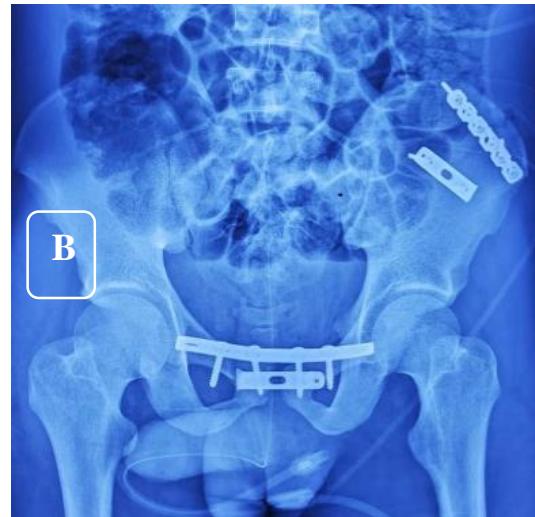
A= 40 year old male living with HIV presented with pre-operative FRI of the tibia B= No radiological signs of infection C= Management by DAExFIX D= Delayed FRI on day 15 post-op with visible clinical signs (purulent drainage) managed by Suppression therapy rather than DAIR. E= 12 months after persistence of infection. F= Stage 3 classification of Cierny-mader.(Localised osteomyelitis).

Case 2



A=34 year old female presented with early post-op FRI following internal fixation after a hip fracture (Tile C), clinical signs purulent wound drainage. Management was by suppression therapy. B= no sign of infection C= 3 months after persistence of infection. Treatment was DAI Removal D=6 months after, bone non-union E= persistence of purulent wound drainage:

Case 3



A= 22 year old male, presented with early FRI (purulent drainage), following internal fixation of a hip fracture. Management was by suppression therapy. C=12 months later non-union D= 12 months later, recurrence of infection.

Case 4



A= 43 year old male who developed delayed FRI (purulent drainage, wound breakdown). Management was by suppression therapy. Persistence of infection = DAIR 6months after C=12 months after; bone sequestration, bone union D=infection control.

Case 5



A



B



C



D



E

A= 47year old male with recurrent FRI following internal fixation with plates and screws after an open forearm fracture. Clinical, he presented with purulent wound drainage, B= nonunion of radius and ulna C= Treatment was DAI removal and dead space management was done by the masquelet technique, as recommended. E=12 months later, infection control and bone union.