The Egyptian Journal of Hospital Medicine (July 2017) Vol.68 (1), Page 1107-1116

Management of Chronic Osteomyelitis Following Gunshot Injuries: A Systematic Review of Literature

Esam E. Abuharba, Amr M. Abdelhady and Saleh G. Mansour
Orthopedic Department, Faculty of Medicine, Ain Shams University-Egypt.
Corresponding author: Esam E. Abuharba. Phone: 00201019480444. Email: esam702003@yahoo.com

ABSTRACT

Background: Chronic osteomyelitis of long bones are common in daily clinical practice, however, the treatment of these diseases has still been a challenge and difficult for orthopedic surgeons. Gunshot injuries lead to damage to bone and soft tissues that can complicate with bacterial invasion and cause bone infection. Many ways can overcome of bone infection, surgical debridement, bone fixation and antibiotic are used in management of chronic osteomyelitis. The objective of this systematic review was to review available studies reporting in management of chronic osteomyelitis following gunshot injuries and compare the methods used into the treatment.

Methods: A comprehensive literature search was performed from the electronic databases Medline, PubMed, Google scholar, and Cochrane collaboration between 1995 and 2016. References were analyzed from included studies, inclusion criteria included (1) English literatures, (2) Humans clinical trials, (3) Orthopedic Journals only, (3) Definitive treatment strategy for management chronic osteomyelitis. In total, 5 articles were included in the systematic review.

Results: A total of 278 patients from 5 studies were included in this systematic review. The mean age of the patients is all studies were 33.84 year, the ratio male to female is 6:1. The most of patients were classified as Gaustilio type lllB and CiernyMader type lllB. The result of all different studies shows a good outcome in 260 patients but 7 patients had poor outcome who were still had bone infection and one patient end by amputation. Radiographic X-ray did postoperative follow up every two weeks. The mean follow up duration was 40 months and all patients responsible for keep the fixator clean.

Conclusion: Our systematic review showed that the patients with chronic osteomyelitis were treated by surgical debridement and bone fixation had a good result. But, this research lost the randomized trials methods, risk factors of patients, compare control groups and good statistical analysis. Without any direct comparison of treatment modalities, it is difficult to determine which individual treatment option is the most efficacious.

Key words: Osteomyelitis, chronic infection, surgical treatment, gunshot injury, and radical debridement.

INTRODUCTION

The term osteomyelitis defined as an inflammatory process accompanied by bone destruction and infected by microorganism. The infection can be limited to a portion of the bone or can involve several regions, such as periosteum, cortex, marrow, and the surrounding soft tissue. Historically, osteomyelitis has been classified as acute, subacute, or chronic based on occurrence of infection or injury. The duration of symptoms of infection is associated with peculiar anatomo-pathological findings and clinical and diagnosis features [(1)]. Management of chronic osteomyelitis is challenging to the patient and physician at the same time. Treatment of chromic osteomyelitis consists of excision of the devitalized material, skeletal stabilization, obliteration of dead space, obtaining good soft tissue cover and reconstruction of the bone defects, all in conjunction with antibiotics [(2)].

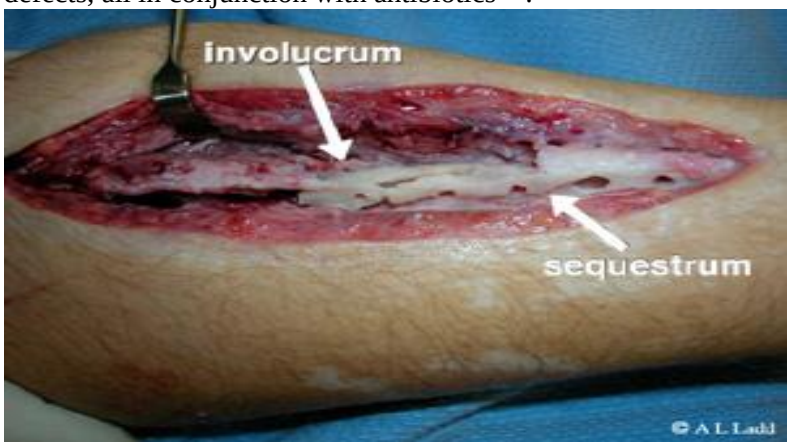

Figure-1: chronic bone infection.

Received: 01 / 04 /2017 DOI : 10.12816/0039037
Accepted: 10 / 04 /2017

Mechanism of Gunshot Injury:

Gunshot wounds caused by firearms represent damage to the body, whose features are large destruction of the tissue, primary contamination with polymorphic bacterial flora and contaminated organisms. Gunshot injuries are usually injuries to the extremities about 70%, out of which about 40% is accompanied with comminuted fractures. They occur due to the force of bullets from firearms or a piece of grenade, land mines, or other explosive devices [(2)].

Gunshot wounds cause open wounds, which are more suspected to expose to microorganisms. In addition, acute osteomyelitis will happen and over several days or weeks become as long standing infection, which is somewhat defined as chronic osteomyelitis that evolves over months or even years, characterized by the persistence of microorganisms, low grade inflammation, and the presence of dead bone (sequestrum) and fistulous tracts (Figure-2) [(3)].

Pathophysiology of Chronic Osteomyelitis:

Chronic osteomyelitis may result from inadequately treated acute osteomyelitis or more commonly from a contiguous source of infection. The contiguous spread may follow treatment of gunshot open fracture, internal fixation of fractures, or prosthetic replacements [(4)].

Many factors are responsible for chronic osteomyelitis. The presence of sequestra, as well as foreign bodies like metal implants or bullets, contributes to the chronicity of infection, together with factors related to the pathogenic microorganism and the host. The host factors that impact the healing are identified as smoking, obesity, diabetes, and peripheral vascular disease. Some pathogenic microorganisms have the ability to remain intracellular and not affected by antibiotics, while the others produce a protective biofilm glycocalyx and maintain a low metabolic rate. Biofilms develop on inactive surface like implant or dead tissue like sequestra of bone. These develop in steps consisting to adhesion of microbe to the surface followed by multiplication. In addition, some of the microorganisms are more virulent, causing further tissue destruction, which leads to pus and sinus formation [(5)].

The main causes of non-healing in chronic osteomyelitis, which are retained dead matter, persistent cavities in the bone, and chronic osteomyelitis [(6)]. Many cases were noted to have polymicrobial infection in contaminated wounds. Recently, the challenges have been infection with methicillin resistant staphylococcus aureus and multidrug resistant organisms. Chronic osteomyelitis due to P. areuginosa has a twofold increased chance of recurrence compared to S. aureus [(7)].

Diagnosis of Chronic Osteomyelitis:

The diagnostic problem in post gunshot osteomyelitis is that there is no single routine test available that can detect an infection with sufficiently high diagnostic accuracy. A combination of clinical, laboratory, microbiological, and medical imaging tests is performed [(8)].

Clinical features:

There are no specific symptoms or signs of chronic osteomyelitis. Chronic pain, persistent discharge from a wound, presence of sinus tracts, mild fever, and malaise are the most come symptoms of the patients [(9)].

Figure-2: Picture sinus tract.

Laboratory studies

Imaging procedures:

1- CBC
1- Plain X-ray film.
2- CRP.
2- Ultrasonography
3- ESR.
3- CT scan.
4- Blood Culture.
4- MRI.
5- Bone and tissue biopsy.
5- Bone Scintigraphy.

Classification of chronic osteomyelitis

There are many bone infection classifications such as:

1- **Waldvogel *et al.*** Classified according to duration [(10)].

2- **Kelly *et al*.** Classified according to etiopathogenesis [(10)].

3- **Cierny and Mader** classified according to anatomo-pathological [(10)].

4- **Gahter** classified according to bone defect [(10)]**.** However, the Cierny and **Mader** is widely used considering the extent of bone involvement and the physiologic class of the patients [(10)]**.**

Chronic osteomyelitis due to gunshot injury can classified as type 4 anatomic type and type B local physiology class of host of Cierny-Mader [(10)].

Preoperative Evaluation and Decision Making:

After diagnosis chronic osteomyelitis, careful evaluation of many factors is necessary to come with a detailed management plan. This evaluation should not include the involved bone only but also the soft tissue surrounding, vascular status, patient condition, and the infecting organism. This evaluation helps in developing the surgical approach, estimating the required debridement and the magnitude of resulting bone defects, and assessing the need for bone stabilization and further reconstructive procedures. Also, presence of any deformity should be observed and it is correction planned [(11)]**.**

Treatment of Chronic Osteomylitis:

The goal of treatment in chronic osteomyelitis is completed eradication of infection while preserving the soft tissue cover, healing of bone segment, preservation of limb length and function, and patient lives normal life [(12)]**.**

I. Surgical Treatment:

A. Surgical debridement:

The first step begins with radical debridement of all nonviable and infected tissues, including excision all sequestra along with any infected bone or soft tissue. To ensure that all foci of infection are removed, debridement proceeds until bleeding, viable tissue is present at the resection margins. Viable bone is characterized by punctuate bleeding (i.e. the paprika sign) [(12)]**.**

B. Dead space management:

The dead space created after debridement should be managed properly while the infection is being treated. Obliteration of the dead space is achieved with durable vascularized soft tissue that may be local flaps or distant flaps [(13)]**.**

C. Management of bone defects:

The dead space created after debridement should be managed properly while the infection is being treated. Obliteration of the dead space is achieved with durable vascularized soft tissue that may be local flaps or distant flaps [(13)]**.**

D. Distraction osteogenesis:

Distraction osteogenesis stills a method of choice for the management of bone defects in excess of 4 cm. The procedure offers several advantages in the cases of post osteomyelitis skeletal reconstruction, including the increase in regional blood flow for a period 4 months following the corticotomy, and depending on how much the bone loss is? [(14)]**.** Although bone transport can be achieved with various devices, circular external fixation in accordance with Ilizarov principle remains foremost due to its reliability, modularity and safety in the presence of infection [(15)]**.**

II. Systemic antibiotic:

A. Parenteral antibiotic agents: A management protocol is including up to one week intravenously followed by 6 weeks orally that shows great chance of eradicate of infection. Combined quinolones and rifampicin are usually the treatment of choice; because they have excellent bioavailability regarding staphylococcal infections related to implants and achieve high levels in soft tissue and bone [(16)]**.**

B. Oral antibiotics agents:

Recent studies demonstrate that oral antibiotics can achieve levels in bone that exceed MICs of targeted organisms. In particular, fluoroquinolones, linezolid, and trimethoprim have been found to achieve bone concentrations at 50% of serum. Although the sulfamethoxazole component of trimethoprim-sulfamethoxazole (TMP-SMX) has poorer penetration (10%-20%), it is serum concentrations are 20-fold higher than those of trimethoprim alone, so it is bone

concentrations generally exceed the MICs of susceptible organisms [17]. Other oral agents available in many communities associated strains of methicillin resistant staphylococcus aureus (MRSA) are susceptible are doxycycline and clindamycin. Those are achievable bone levels exceed the MICs of susceptible MRSA isolates [18].

Quality Appraisal

Methods:

The electronic databases Medline, PubMed, Google scholar, and Cochrane collaboration were systematically searched from 1995 to 2016. We conducted a systematic review and best evidence synthesis.

The researches were done on the following key words:

- Gunshot damage to bone and soft tissue.
- Pathogenesis of chronic osteomyelitis.
- Types of chronic osteomyelitis.
- Management of chronic osteomyelitis following gun shot.
- Bone defects following gun shot.
- Soft tissue coverage following gun shot.

Studies were screened according to pre defined inclusion and exclusion criteria.

Eligibility Criteria

Titles and abstracts were screened for eligibility according to the following inclusion and exclusion criteria.

Inclusion Criteria

- Languages: English articles only.
- Publication type: Published in peer-reviewed journals.
- Study design: Clinical Trials.
- Study population: Human studies.
- Orthopedic Journals only.

Exclusion Criteria

- In vitro studies.
- Duplicated articles by the same Authors unless with longer follow up studies.

Point of comparison:

- Patient demographics age and sex.
- Preoperative evaluation.
- Surgical technique used.
- Postoperative results.
- Postoperative complication.

After doing a search on websites Pubmed, Medline, Google scholar, and Cochrane we found 5 papers met our criteria about Management of chronic osteomyelitis following gunshot injuries.

Paper 1: Infected non-union of tibia and femur treated by bone transport [19].

Paper 2: treatment of the chronic war tibial osteomyelitis, gustilio type lllB and cierny-maderlllB, using various methods [20].

Paper 3: War related infected tibial non-union with bone and soft tissue loss treated with bone transport using the Ilizarov method [21].

Paper 4: Acute peg in hole docking in the management of infected non union of long bones [22].

Paper 5: Treatment of tibial bone defects with the Ilizarov circular external fixator in high velocity gunshot wounds [23].

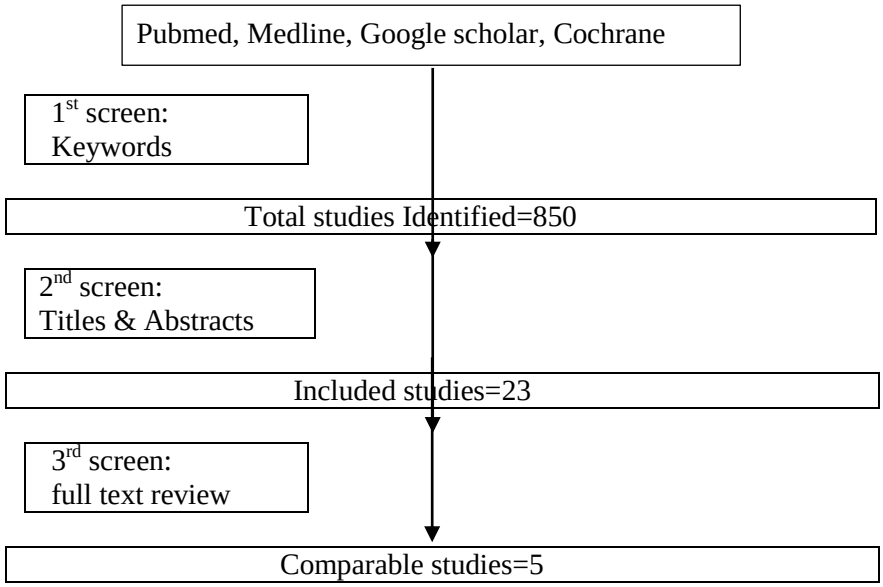

Figure-3: Schematic showing data of research.

Data Extraction

The data were collected from reviewed studies that evaluate the treatment of chronic osteomyelitis. The following data were extracted from each included study: first author, publication year, No. of patients, sex ratio, mean age, preoperative evaluation, method of treatment, outcome, postoperative complication, and follow up duration.

Table-1: Data Extraction.

Papers	Peng Yin 2015	Grubor P. 2014	Msarko B 2010	Shabir 2008	Atrsalp 1998
No. of pats	110	59	30	36	43
Male : female	92:18	57:2	29:1	22:14	All male
Average of age per year	38.9	38.2	34.4	37.3	24.4
Preoperative evaluation	Lab,	Lab,	Lab,	Lab,	Lab,
Clinical:	Radiographic & CT-scan	Radiographic& CT	Radiographic & CT	Radiographic & CT	Radiograghic &CT.
Main bone defect	6.15 cm	N/M	6.9cm	3.6cm	9.7cm
Soft tissue loss	39pts	26pts	28pts	7pts	7pts
Method of treatment	Debridement, Ilizarov, Fix, antibiotics & bone graft	Debridement Ex. Fix, Antibiotics, & Bone graft	Debridement, &Ilizarov	Debridement Ab, Ilizarov	Debridement Ab, Ilizarov.
One stage operation	86pts	53pts	29pts	33pts	42pts
Two stage operation	14pts	6pts	1pts	3pts	1pts
Bone graft Bone	12pts	5pts	1pts	13pts	0pts
transport by distraction	100pts	26pts	30pts	23pts	41pts
Soft tissue coverage	14pts	26pts	6pts	3pts	16pts
Outcome	100 union 10l ost FU.	55 union 3 non-union	29 union 1 non-union	35 union 1 non-union	40 union 1 non-union
Postoperative complication	70 Patients PTI, 2 patients refracture.	3 still infected 1 amputated	8 PTI 3 odema joint stiffness	23 PTI 5odema 1RSOD Sequestrum	8 PTI joint stiffiness 1 mal-union
Mean Follow up duration	23 months	23 months	99 months	6.4 months	50 months

Ab= antibiotics, CT= Computed Tomography, Ex. Fix= external fixation, FU= follow up, Lab= laboratory, pts=patients, RSOD= reflex sympathetic dystrophy, PTI=Pin track infection,

Data Analysis and Results

Studies were selected based on the title and abstract by the assessment of chronic osteomyelitis and gunshot injuries. A total of 850 studies of which 53 met our inclusion criteria after initial screening of titles and abstracts of these 53 studies 5 met the criteria for final review.

Study characteristics:

The total number of patients in these studies is 278.

10 of patients were lost the follow up as encountered by study of Ping Yin (2015).

The mean age of patients in all studies is 33.84 year.

The mean follow up period average is 40 months.

All patients had chronic osteomyelitis most of them post gunshot injuries.

Male to Female ratio:

Most of the patients are males (243) when you compare to females (35) in ratio male to female 6:1:

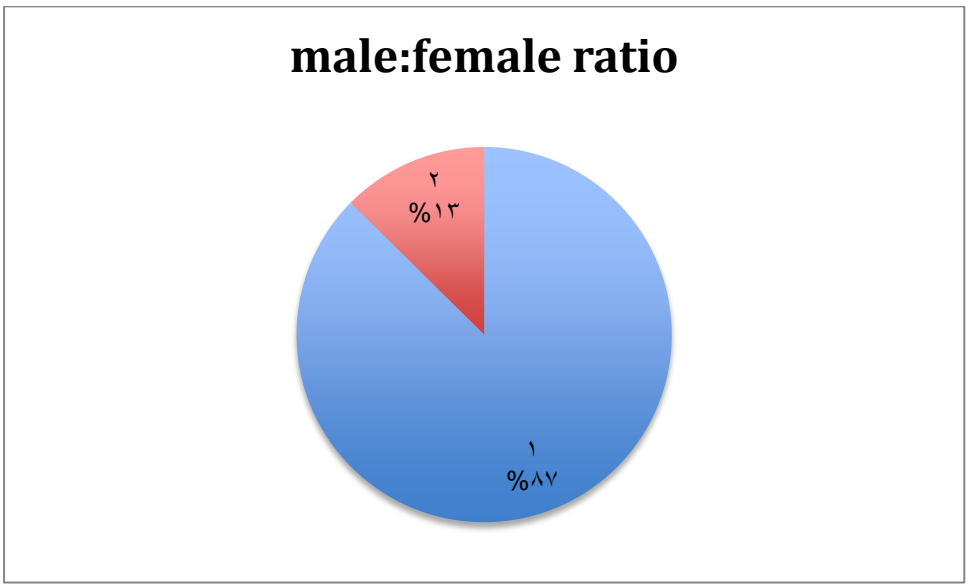

Chart-1: 1-male and 2-female.

Outcome:

The result of treatment of 278 patients is 259 of them fully union, 10 patients lost, and 6 patients still non-union.

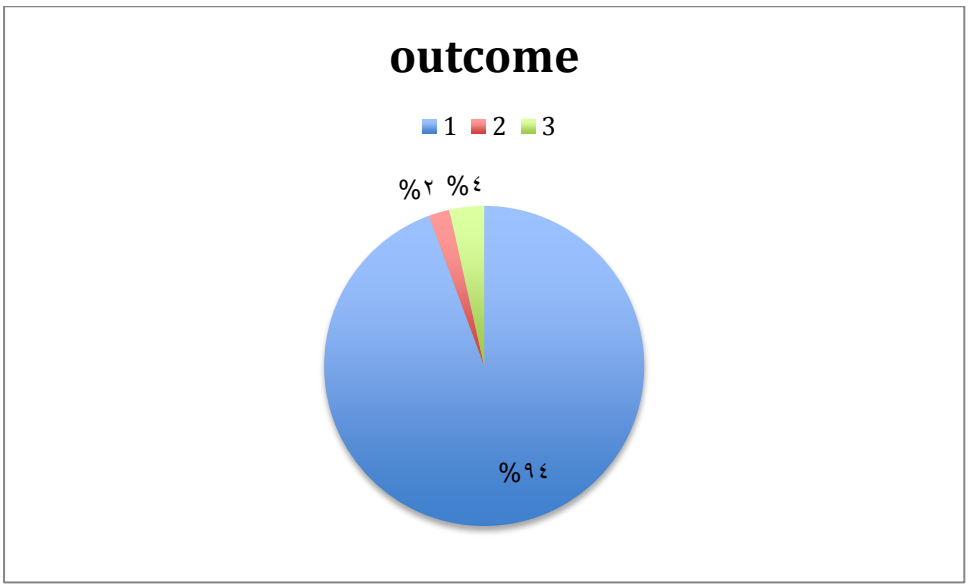

Chart-2: 1. Union, 2. Nonunion, 3. Lost.

One stage verses two stages operation:

253 of the patients are treated with one stage operation while 25 of the patient are treated with two stages operation.

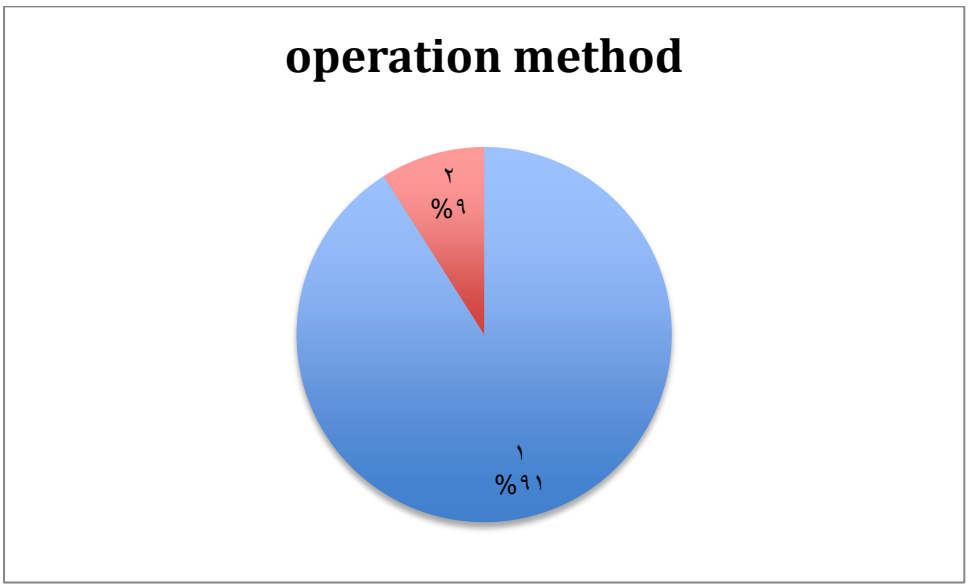

Chart-3: 1. One stage, 2. Two stages.

Used antibiotic verses not used antibiotic:

248 patients were treated by using antibiotic while 30 patients were not treated by using antibiotic.

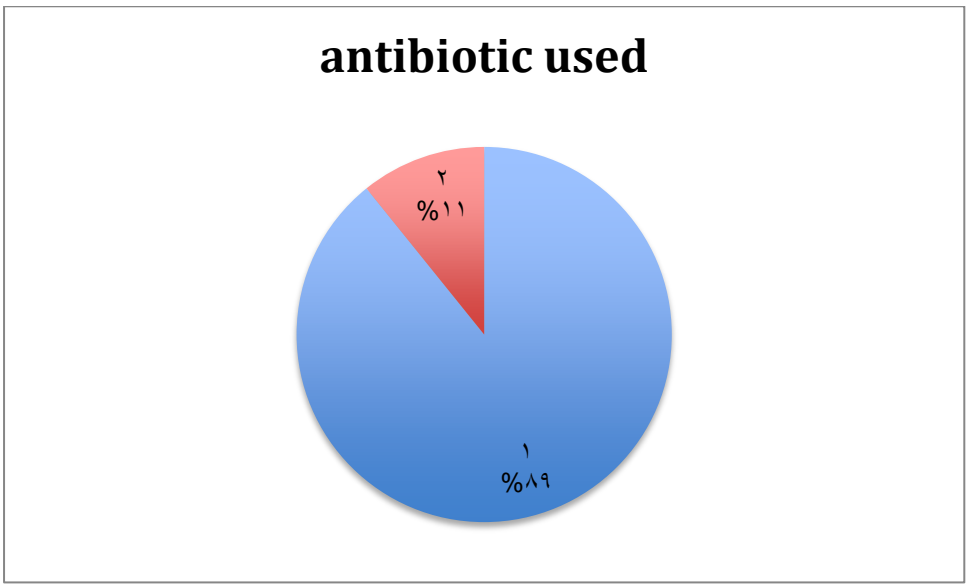

Chart-4: 1. Antibiotic used, 2. No antibiotic used.

Bone graft verses bone distraction:

26 of the patients were treated by bone graft versus 200 of the patients were treated by distraction osteogenesis.

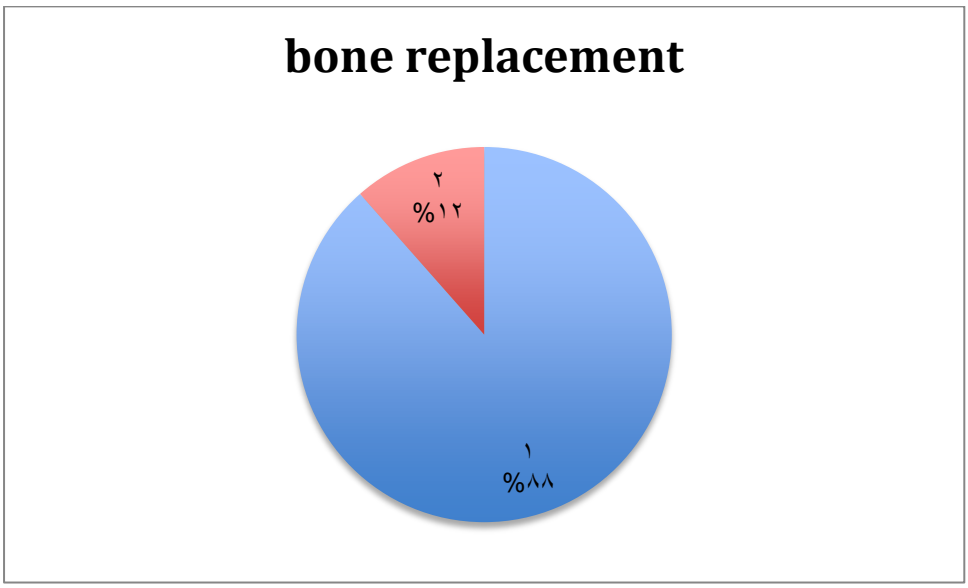

Chart-5: 1. Bone distraction. 2. Bone graft.

Soft tissue coverage verses no soft tissue coverage:

65 of the patient were needed soft tissue coverage while 213 of the patient were not needed soft tissue coverage.

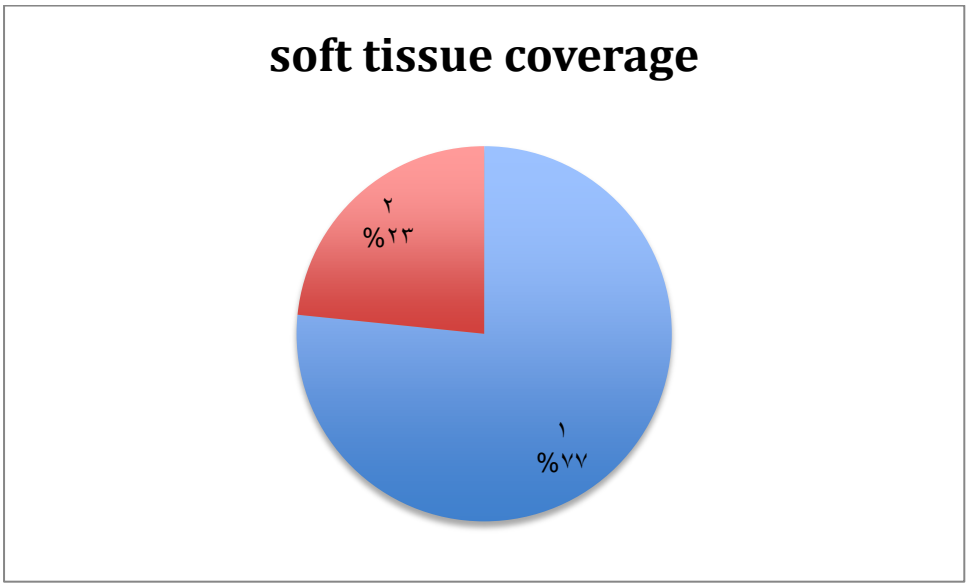

Chart-6: 1. No soft tissue coverage, 2. Soft tissue coverage.

Postoperative Complication:

Pain was the most common complication about 151 patients (68%), Pin truck infections were 117 patients (53%), angular deformities were 42 patients (19%), joint stiffness 54 patients (15%), delayed ossification docking 24 patients (11%), non-union 9 patients (3%), edema 7 patients (2.5%), re-fractures 5 patients (2%), lost follow up 10 patients (4.5%), 8 patients (2.8%) still had osteomyelitis, and 1 patients (0.3%) reflex sympathetic dystrophy which was managed by physiotherapy.

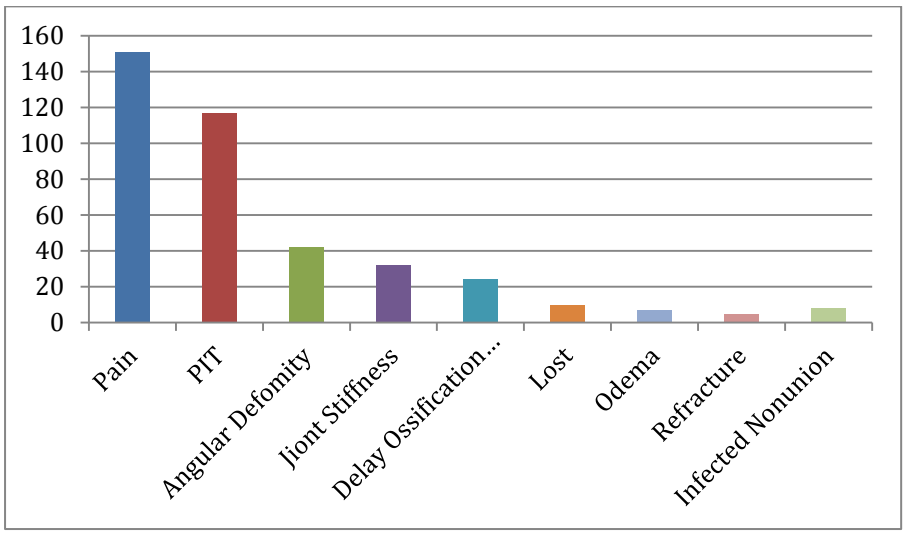

chart-7: postoperative complication.

INTERPRETATION OF RESULTS AND DISCUSSION

This systematic review of 5 studies was performed to assess the different ways to management chronic osteomyelitis following gunshot injuries. Three of them are retrospective and two are prospective without control group. All the patients were adult group and they had long bone chronic infection mainly femur and tibia. Most of the patients were diagnosed by laboratory, radiography, and tissue culture and sensitivity. Mixed bacterial organisms often cause the war osteomyelitis. In our system review, 130 patients (55%) were infected by staphylococcus aureus, 38 patients (16%) were infected by Mixed bacterial organisms and 57 patients (24%) were infected by other kinds of bacterial usually Pseudomonas.

Most of patients were classified as Gaustilio type lllB and CiernyMader type lllB. All the patients in our study were undergone radical surgical debridement before the fixations to eradicate the infection form the bone and soft tissue. 89% of patients treated by systemic and local antibiotics according to culture and sensitivity of infected bone combined with external fixation while 11% of patients treated without antibiotic. Systemic antibiotics were contained for 4 weeks intravenously and 4-6 weeks orally at home.10%of cases were treated with radical surgical debridement and external fixation without of antibiotics. 91% of patients were treated by one stage operation while 9% of patients were treated by two stages operation. Soft tissue coverage were done in 23% of patients and 77% were not needed soft tissue coverage.

Ilizarov external fixation were used in treatment most of our study with bone defects. The mean bone defect after debridement was 6.6 cm, which was treated by corticotomy and distraction osteogenesis to re-stable the limb length. Ilizarov is one of the main methods in replace bone defect more than 4cm but the main criticisms were lengthen treatment time and worn bulky frame. 88% of patient was treated through distraction osteogenesis while 23% of patient was treated with bone graft. The Ilizarov technique has ability to address all bone related issues such as large bone defect, angular deformities, joint stiffness and ability to start early weight bearing.

The result of all different studies shows a good outcome in 260 patients but 7 patients had poor outcome that were still had bone infection and one patient end by amputation. Postoperative follow up every two weeks by radiographic. The mean follow up duration was 40 months and all patients responsible for keep the fixator clean.

CONCLUSION

Chronic bone infection due to gunshot injuries is one of the most difficult treatments because of the multiple bacterial organisms that usually contaminate gunshot and war wounds. The results of the included studies imply that treatment of chronic osteomyelitis with antibiotic and external fixations with radical debridement were showed high success rates. Further work needs to be undertaken to determine whether the results shown in the included studies are as promising as they seem. The research of high methodological quality has to be performed. Randomized controlled

trials with higher numbers of patients, risk factors of patients, control groups and good statistical analysis could provide more definitive evidence for different methods of treatment of chronic osteomyelitis due gunshot injuries.

REFERENCES

1. **Romano CL, Romano D, Logoluso N, Drago L (2011):** Bone and joint infections in adults: A comprehensive proposal. Eur Orthop Traumatol., 1: 207-217.
2. **Grubor P, Milicevic S, Grubor M, Meccarillo L (2015):** Treatment of bone defects in war wounds: Retrospective Study. Med Arh., 69:260-264.
3. **Jowan G, Penn B, Kate V, Anton F (2015):** High Velocity Gunshot Injuries to the Extremities: Management on and off the Battlefield. Curr Rev Musculoskelet Med., 8 :312-317.
4. **Pande K, Putera J, Seri B (2015):** Optimal Management of Chronic Osteomyelitis: Currents perspectives. Orthopedic Research and Reviews, 7 :71-81.
5. **Tan Y, Wang X, Li H, Zheng Q, Li J (2011):** Arch Orthop Trauma Surg., 131: 255-259.
6. **Henderson W, Lauste L (1995):** Chronic osteomyelitis following gunshot wounds. JR Amy Med Corp., 141:42-44.
7. **Lew D, Waldvagel F (2004):** Osteomyelitis. The Lancet,364: 369-379.
8. **Ikpeme I, Ngim N, Ikpeme A (2010):** Diagnosis and treatment of pyogenic bone infections. African health sciences; 10 (1): 82-88.
9. **Govaert G, Glaudemans A (2016):** Nuclear Medicine Imaging of Posttraumatic Osteomyelitis. Eur J Trauma EmergSurg., 42: 397-410.
10. **Marais L, Ferreira N, Aldous C, Sastorius B (2015):** A modified staging system for chronic osteomyelitis. Journal of Orthopeadics, 12 : 184-192.
11. **Patzakis M, Zalavras C (2005):** Chronic Posttraumatic Osteomyelitis and Infected Nonunion of the Tibia. Current Management Concepts. J Am AcadOrthopSurg., 13:417-427.
12. **Haidar R, Boghossian A, Atiyeh B (2010):** Duration of post-surgical antibiotics in chronic osteomyelitis;empiric or evidence-based. International Journal of Infectious Diseases, 14: e752-e758.
13. **Fleiter N, Walter G, Bosebeck H, Vogt S, Buchner H, Hirschberger W, Hoffmann R (2014):** Clinical use and safety of A novel Gentamicin-releasing Resorbable Bone Graft Substitute in the Treatment of Osteomyelitis / osteitis. Bone Joint Res., 3:223-229.
14. **Dinh P, Hutchinson B, Zalavras C, Stevanovic M (2009):** Reconstruction of Osteomyelitis Defects. SeminPlastSurg.,23:108-118.
15. **Gubin A, Borzunov D, Marchenkova L, Malkova T, Smirnova I (2016):** Contribution of G.A. Ilizarov to Bone Reconstruction: Historical Achievements and State of the Art. StratTraum Limb Recon., 11:145-152.
16. **Marais L, Ferreira N (2015):** Bone Transport through an Induced Membrane in the Management of Tibial Bone Defects resulting from Chronic Osteomyelitis. StratTraum Limb Recon; 10:27-33.
17. **Mouzopoulos G, Kanatakis N, Kontakis G, Obakponovwe O, Townsend R, Giannoudis P (2011):** Management of Bone Infections in Adults: the surgeon's and microbiologist's perspectives. Injury. Int. J. Care Injured, 55:S18-S23.
18. **Spellberg B, Lipsky B (2012):** Systemic Antibiotic Therapy for Chronic Osteomyelitis in Adults. Clinical Infectious Diseases, 54(3):393-407.
19. **Yin P, Zhang L, Li T , Zhang L (2015):** Infected nonunion of tibia and femur treated by bone transport. Journal of Orthopeadic Surgery and Research, 10:49 DOI 10:1186/s 13018-015-0189-5.
20. **Grubor P, Falzarano G, Grubor M , Piscopo A (2014):** Treatment of the chronic war tibial osteomyelitis, Gustilio type lllB and CiernyMaderlllB, using various method, A retrospective study. Euromediterranean Biomedical Journal, 9(2): 7-18.
21. **Bunbasirevic M, Tomic S, Lesic A , Mmilosevic I (2010):** War related infected tibial nonunion with bone and soft tissue loss treated with bone transport using the Ilizarov method. Arch Orthop Trauma Surg.,130:739-749.
22. **Dhar S, Mir M, Molvi A, Afzal S (2008):** Acute peg in hole docking in the management of infected nonunion of long bones. International Orthopaedics (SICOT), 32:559-566.
23. **Atesalp A, basbozkurt M, Erler K , Sehirlioglu A (1998):** Treatment of tibial bone defects with the Ilizarov circular external fixator in high velocity gunshot wounds. International Orthopaedics (SICOT),22: 343-347.