**Implant-related Sepsis in Lower Limb Fractures following Gunshot Injuries in the Civilian Population: A systematic review**

**Authors**

Simon Matthew Graham1,2, MBChB, MRCS, MSc (Res), FRCS (Tr+Orth)

Maheshi P C Wijesekera3 , MBChB, MPhil

Maritz Laubscher2, MBChB (UFS), Dip PEC, FC Orth (SA), MMed Ortho (UCT);

Sithombo Maqungo2, MBChB, FC Ortho, MMed

William J Harrison4, MD, FRCS (Tr+Orth)

1. Liverpool School of Tropical Medicine, Liverpool, UK
2. Orthopaedic Research Unit, Department of Orthopaedic Surgery, Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa
3. East Lancashire Hospitals NHS Trust, UK
4. Countess of Chester Hospital, Chester, UK

**Abstract**

Purpose: The management of long bone lower limb fractures secondary to gunshot wounds (GSWs) in the civilian setting are complex and there is currently no consensus regarding the optimal approach to managing such fractures.  This study aims to address the relationship of implant related sepsis in fractures secondary to GSWs.

Methods: A systematic review of the literature was performed on both Pubmed and Scopus databases that look at fractures caused by GSWs in the lower limb. A total of 20 studies met the inclusion criteria set in this study, all of which were of level IV evidence.

Results: Current literature suggests that low and high velocity injuries managed with internal fixation, such as intramedullary nails, may carry a low risk of superficial and deep infection, with no obvious risk of osteomyelitis. However, infection was poorly defined across all studies and no study used a validated scoring system for infection making it difficult to draw any valid conclusion on the rate of infection following internal fixation of lower limb fractures following both high and low velocity GSWs.

Conclusion: There is no clear evidence to confirm or refute that internal fixation is the correct method of management in these complex injuries and guidance is needed due to the high and increasing proportion of patients presenting with these complex injuries worldwide.

**Key words: “Gunshot wounds” “GSW” “Lower limb” “fracture” “infection”**

**1.0 Introduction**

The number of gun and firearm related crimes, injuries and deaths continues to increase worldwide, with a reported rise in firearm offences of 23% in the United Kingdom (UK)[1] and 9% in the United States of America (USA)[2] both between 2015 to 2016. In total, gun-related violence kills over 1000 people and injures millions of others worldwide everyday[3–5]. Furthermore, with the recent gun related terrorist attacks across Europe[6], there is a need for Orthopaedic and Trauma Surgeons, who have no military training or experience, to understand the management of gunshot wounds (GSWs) in the civilian population.

There is a clear difference between civilian injuries and war zone injuries caused by GSWs. GSWs in war zones are generally the result of high velocity firearms and any trauma or fractures are commonly more complex than those sustained in the civilian population[7]. War zone injuries can also be complicated by other significant injuries, such as blast injuries. Furthermore, the level of contamination and associated destruction of tissues is often worse in war zone injuries[7]. These differences make it difficult to compare the outcomes of fracture following GSWs in war zone injuries, with civilian GSWs. However, due to the paucity of available literature on the treatment of civilian GSWs, treatment protocols are often based on military experience[8].

Our institute in Cape Town, South Africa manages over 240 gunshot injuries to the lower limb per year, more than 70 with associated fractures. These numbers are similar in other trauma centres throughout South Africa[8]. Our protocol, in two large tertiary referral trauma centres in South Africa, for the management of lower limb GSW fractures is to manage the wound with a simple dressing and administer a single dose of prophylactic intravenous antibiotic (first generation cephalosporin). Wounds are not routinely debrided and simple entry and exit wounds are treated with dressings alone. Bullets and fragments are only removed if retained intra-articular or if causing mechanical symptoms. The underlying fracture is treated on its merit and internal fixation is used in a high percentage of cases.

Lower limb GSW fractures represent a significant burden to the South African health care system and this is mirrored in many low and middle-income countries (LMIC) around the world. Currently there is no clear evidence based consensus on the best way to manage these complex injuries and the management varies from country to country. Therefore, it is not known if internal fixation is a safe method of fixation for these complex injuries[9][10].

The aim of this study is to undertake a systematic review to assess the frequency of implant-related sepsis in fractures of the femur and tibia caused by GSWs in the civilian population, in order to determine if internal fixation is a safe management option for these injuries. Additionally, we aim to address if there is a role for debridement of the bullet wound and track sustained following these complex injuries.

**2.0 Methods**

A systematic review of the literature was carried out to identify all relevant studies that evaluated lower limb fractures caused by gunshot injuries. This was carried out in accordance to the PRISMA guidance[11]. The search was carried out on the PubMed and Scopus databases. The Medical Subject Headings (MeSH) terms used are shown in table 1. A MeSH term from column 1 was used in combination with a Boolean operator with a MeSH term from the column 2. The terms were kept broad to maximise sensitivity.

The last search was carried out on the 08th June 2017.The search was restricted to studies in the English language, human studies and those that were produced from 1990 to present.

The inclusion and exclusion criteria of studies are shown in table 2.

The process of the literature search is shown in figure1. A total of 20 studies were included in this systematic review. Studies that met the inclusion criteria were summarised onto a spreadsheet so that data could be extracted. The summary consisted of type of injury, study results, methods and limitations. Each study was classified based on the circumstance of injury. This was classified as either civilian or war injuries, or mixed. Where there was no mention of the circumstance it was assumed to have taken place in a civilian setting. Only injuries occurred in a civilian setting were included in this study.

Articles were categorised according to high and low velocity injury based on the type of weapon. Injury caused by handguns were classified as low velocity as bullets fired by handguns travel under 2000 feet per second (the ballistic definition of low velocity gunshots)[8]. Those caused by shotguns were classified as intermediate velocity; whereas injury caused by military guns or hunting rifles were classified as high velocity.

**3.Results**

**3.1 Low velocity injuries**

We identified 8 studies that managed fractures of the lower limb with internal fixation caused by low velocity GSWs in the civilian population[12–20]. There was no study with a cohort of greater than 5 participants with low velocity tibial fractures that underwent internal fixation, as it did not meet the inclusion criteria of this review.

None of these studies reported wound infection using validated scores such as the ASEPSIS[21]or the Centres for Disease Control (CDC) score[22].A common theme among several of the studies was infection rates, such as superficial infection were reported without specifying the types and site of infection[15–17]. In addition, the fate of the bullets in general was poorly reported by all the studies reviewed, as most authors did not state if bullets or bullet fragments were removed during surgery. This was also true for high velocity firearms injuries.

**3.1.1Femur**

**a. Superficial wound infection**

The CDC define superficial wound infection as an infection that affects skin and subcutaneous tissue and occur with 30 days of an operative procedure. It may result in symptoms of pain, redness, heat, swelling or purulent drainage[22].

Dougherty et al[13] reported retrospectively results of 68 patients that underwent a mix of retrograde nailing (63%) and anterograde nailing (37%), following low velocity GSWs. Patients were treated with first-generation cephalosporins from presentation to the emergency department and for 48 hours post-operatively. The authors observed what they defined as a superficial wound infection in 2 patients (3%), around the bullet track in the retrograde nailing group. The author did not state if these patients had retained bullets fragments. Both were successfully treated with of antibiotics. Dougherty et al[13], confirmed that bullet fragments were removed if accessible however this was at the discretion of the surgeon and the number of patients who had this done was not reported[13], a similar approach to our units.

Cannada et al[14]reported equally encouraging results in a smaller cohort (n=35) of patients who underwent IM nailing. In this study, bullets were removed from only 3 patients and no patients developed superficial wound infections. All patients were on a first-generation cephalosporin preoperatively and postoperatively for 48 hours. Similar promising results have been reported by other researchers in smaller cohorts of patients[20].

Seng et al[12]described their experience of 7 femoral fractures that were managed with open reduction and internal fixation with plates and screws. All patients were treated with co-amoxiclav and gentamicin for 48 hours. No patients developed superficial infection[12].

Several study groups did not report superficial wound infection or did not provide enough information to determine if the study cohort developed superficial infection[15–19]. Furthermore, there were no studies that reported the results of superficial wound infection or pin site infection in femur fracture fixed with external fixators.

**b. Deep infection**

Deep infection as defined by the CDC as an infection one that involves the fascial or muscle layers and usually occurs between 30-90 days post-surgery. It presents with pain, fever, or tenderness and may result in an abscess, purulent drainage or spontaneous wound dehiscence[22].

Among the 68 cases Dougherty et al[13] retrospectively studied there was a 3%(n=2) rate of deep wound infection. Both patients had sustained large soft tissue injuries and had received first-generation cephalosporin for 48 hours post-operatively. They were successfully treated with antibiotics and one patient required debridement with irrigation and antibiotics but no removal of metal work was required in either patient. Patients were followed up for an average of 33.5 months (range 3-148)[13].

Further researchers, Wiss et al[19] (n=56), Nowotarski et al[15] (n=39),Tornetta et al[16] (n=38) and Wright et al[18] (n=18) reported retrospective studies that managed patients with IM nailing and demonstrated 0% rate of deep infection. All these patients were treated with a cephalosporin for at least 48 hours postoperatively.

**c. Septic arthritis**

Two authors evaluated septic arthritis in patients managed with intra-medullary nailing of the femur[13, 14]. Dougherty et al [13] defined septic arthritis as a positive culture on an aspirate or if a patient had to returned to theatre for irrigation and debridement of the joint. This was the primary outcome of this study, which compared retrograde nailing, and antegrade nailing of the femur. There were no cases of septic arthritis of the knee or hip in either group over the average follow up of 33.5 months[13].

Cannada et al[14] reported a 0% rate of septic arthritis of the knee or hip, in the cohort of patients (n=35) that underwent retrograde nailing of the femur. Patients were followed up for 7 months. However, the diagnosis of septic arthritis was not defined by authors[14].

**d. Osteomyelitis**

Osteomyelitis was reported in four studies[15, 18–20] although the definition of osteomyelitis was not provided by any author. Nowotarski et al[15] reported one case of osteomyelitis (3%) among the 39 patients who underwent IM nailing in a retrospective study. The patient that developed osteomyelitis had a Winquist-Hansen grade IV femoral fracture. This patient was initially started on oral antibiotics, and underwent exchange nailing, which led to fracture union. This patient was classified as a deep infection by the authors, however the description given suggests it was in fact osteomyelitis or late implant infection, using the CDC definition for deep infection.

Additional research groups report 0% rates of osteomyelitis in study cohort sizes between 18–56, with a minimum average follow-up of 12 months (total range 4-39 months)[18–20].

**3.2 High Velocity injuries**

There was only one study[23]that evaluated management of civilian gunshot injuries to the lower limb as the result of high velocity injuries. No studies reported results in tibia fractures. Again, none of the studies used a validated method to describe wound infection. Deep wound infection and septic arthritis were not reported as complications by the authors.

**3.2.1. Femur**

**a. Superficial wound infection**

Ali et al[23] studied 68 patients who sustained high velocity GSW, that underwent interlocking nailing. Ninety-four per cent of patients were managed with closed interlocking nailing while 6% patients required open nailing as the guide wire could not be passed across the fracture. There was a 4%(n=3) rate of superficial infection, all occurring in the bullet track and were treated with antibiotics and daily dressings. All patients were given first generation cephalosporin and aminoglycosides intravenously for 72 hours. Authors did not state at what time interval the antibiotics were administered[23].

1. **Osteomyelitis**

Ali et al[23] reported a 6% (n=4) rate of osteomyelitis in their cohort of 68 patients, but failed to give a clear definition of osteomyelitis. Two patients resolved with the administration of antituberculosis drugs. The other two patients with chronic discharge and signs of delayed union underwent excision of the infection track with curettage of fracture site, bone grafting and dynamisation at an average of 34 weeks post operatively. The source of infection was the bullet track in all cases. The fate of the bullet was not described. The follow-up period for this cohort was between 18-30 months[23].

**3.3 Ambiguous studies**

Four studies reviewed did not clarify if the patients’ fractures were caused by low or high velocity firearms[24–27].Two studies[24, 25]did not present the type of weapon that caused the injury. Nicholas et al [26]and Bergman et al[27]did not map the complications to the firearm velocity. None of these studies commented on the rate of septic arthritis, osteomyelitis or late implant sepsis.

Ferraro et al[24] managed 90 tibial fractures by casting (64%), external fixation (18%) and unreamed intramedullary locking nail (16%). There were 5 cases with vascular injuries and all patients were given intravenous antibiotics where the type, length and interval was not stated. Eight patients (with 6 in the casting group) underwent extensive irrigation and debridement and were admitted for 72 hours of intravenous cephalosporin. The rest were discharged on oral antibiotics. Among those that underwent nailing, there was a 0% rate of deep infection[24].

Perry et al[25] studied 29 tibial, and 29 femoral fractures following gunshot injuries. Eight femoral fractures underwent ORIF and 4 tibial fractures were managed with ORIF or fine wire external fixation (distribution not described by authors). All other fractures were conservatively managed. Thirty six patients required irrigation and debridement. Since there were 9 patella fractures included in the original sample, the bone distribution of irrigation and debridement could not be accurately determined. In addition, the number of procedures did not add up to the sample size and the use of antibiotics was not detailed by the authors. The rate of superficial infection was 13%(n=1) which was in a internally fixed femur and this patient underwent multiple debridement with IV antibiotics. The rate of superficial infection among the tibial fractures was 0%. The rate of deep infection in the tibial and femoral fractures were 0%[25].

Nicholas et al[26] studied a cohort of 14 femoral fractures that were managed with closed intramedullary nails that was caused by a mixed velocity. All patients were started unspecified intravenous antibiotics on admission and were continued for 120 hours. There were 3 cases with arterial injuries two required grafts and the other underwent a below the knee amputation. There were 2 superficial infections (14%) that resolved with antibiotics, and no deep infections[26].

Bergman et al[27] studied a cohort of mixed velocity GSWs of 65 femoral fractures however, the distribution of velocity of the fractures was determined in only 10 patients. Two patients had a low velocity injury, 4 patients each sustained intermediate and high velocity injuries. Patients were treated with statically locked intramedullary nailing 95% (n=62) and statically locked reconstruction nail 5%(n=3). One patient required vascular repair. All patients were given intravenous cephazolin on admission and 31% had an aminoglycoside. The antibiotics were continued for 48hours postoperatively and patients were on antibiotics for an average of 96 hours. There were no cases of infection (acute or chronic as stated by the authors). However, authors did report a persistent serous discharge from 2 bullet wounds that halted after further antibiotic administration. This was not classified as an infection as it did not meet any of the CDC criteria for wound infection[27].

**Discussion**

Only four researchers [13, 19, 23, 27] reported studies with large sample sizes (N>55) that evaluated the management of fractures of the lower limb caused by GSWs. The general trend of management was intramedullary nailing of low energy GSWs and external fixation for high-energy injuries.

All researchers treated patients with a course of antibiotics for between 48-72 hours, except Nicholas et al[26] who treated patients with antibiotics from admission and was continued for 120 hours. There was no clear consensus on the optimal duration or type of antibiotic across the studies making it difficult to draw a clear conclusion on the best duration of antibiotic use. There are no studies that do not use antibiotics, or use a single dose, to compare these results against. However, low rate of deep infection amongst low velocity injuries are shown with the use of postoperative IV antibiotics, as seen amongst the femoral fractures that required IM nailing. The synergistic use of gram negative cover has no effect on reducing infection rates. This has been confirmed in a systematic review by Papasoulis et al[28].

A survey based study[29] that looked into antibiotic preference among surgeons in the Orthopaedic Trauma Association(OTA) showed that 86% surgeons administered antibiotics for those with fractures caused by low velocity GSWs. This decision was not guided by institutional protocol. However, this survey did not specify if the fractures were treated non-operatively or operatively[29].

The evidence for the use of open reduction and internal fixation with plates are lacking, as only one report of this has been described[12].

In high-energy GSWs, the superficial and deep infection rate was high in femoral fractures treated with intramedullary nails[23]. This was regardless if patients were treated in synergy with first generation cephalosporin and aminoglycoside. Evidence for this comes from only one study each antibiotic regime. Miric et al[30] managed 17 femoral fractures with pelvi-femoral external fixators and reported a 6%(n=1) rate of deep pin track infection and a 12%(n=2) rate of chronic osteomyelitis. All patients received perioperative antibiotics with a cephalosporin and gentamicin. To our knowledge, there is no comparative study comparing the use of external fixators for femur fractures following GSWs.

None of the studies produce information regarding late implant sepsis in the lower limb. Low energy carries no risk of osteomyelitis or chronic infection, with the evidence base predominantly supporting femurs treated with intramedullary nailing[18–20]. In high energy injuries, there remains a low level of osteomyelitis[23]with nailed femurs.

Overall, infection was poorly defined across all studies and no study used a validated scoring system for infection. Additionally, late implant sepsis was not looked into by any study. As a result, it is difficult to draw any valid conclusion on the rate of infection following internal fixation of lower limb fractures following GSW.

**Limitations of the literature**

There are a number of limitations in the study design, length of follow-up and outcome measures used to assess infection in the majority of studies reviewed. Additionally, it is possible that some studies may have misclassified complications in instances where a definition of the outcome was not stated. This is evident in one study[15] where osteomyelitis was misclassified as a deep infection. Most studies were carried out in developed nations such as USA and the UK, except the one study that looked in to high velocity injuries that was carried out in Pakistan. With reference to individual studies, individual risk factors for infection were not explored by authors. Additionally, the fate of the bullets was not adequately described in most studies.

**Conclusions**

With the number of gun and firearm related crimes, injuries and deaths continuing to increase worldwide,[3–5] there is a genuine need to undertake a prospective study investigating the rate of implant sepsis in lower limb fractures following GSWs. Currently there is no clear evidence to confirm or refute that internal fixation is the correct method of management in these complex injuries and guidance is needed due to the high and increasing proportion of patients presenting with these complex injuries worldwide.

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