**Review article**
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# Current concepts in the management of infected non-union of the femur: internal versus external fixation

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**Abstract**

**Introduction** The management of infected non-unions continues to be a herculean task for the orthopaedic surgeon due to the emergence of microbial resistance, failure of fixation, frequent re-fractures and resurgence of previously treated infection.

The **aim** of the paper was to structure the approach to the management of patients with infected femoral non-union based on the literature review and surgeons' experience.

**Material and methods** A detailed literature review, including current updates on the management of fracture-resistant infections (FRI) and non-union of the femur was conducted. Search words and phrases used for navigation in the international medical literature platforms were: osteomyelitis, non-union, diagnostic solutions, local antibiotics, biomechanical stability.

**Results and Discussion** The principles of surgical management of infected non-union of the femur remain the same: (a) adequate soft tissue sampling; (b) thorough debridement; (c) fracture stabilization; (d) dead space and defect management; (e) delivery of local antibiotics and (f) soft tissue coverage. The goal of surgery is to get rid of infection. There is no place for empirical treatment of suspected infection. Therapy should be initiated based upon microbial cultures of deep tissue specimens. While selecting the type of hardware for non-union of the femur, one often encounters a dilemma concerning the most appropriate surgical tool for stabilization. Internal fixation with bone grafting would depend on the size of the gap; commonly defects < 6 cm are treated with this modality. External fixation becomes indispensable in certain scenarios such as poor local skin and soft tissue conditions, associated limb length discrepancy > 2 cm, large defect gaps ⩾ 6 cm, concomitant deformity, small fragments or osteopenic bone.

**Conclusion** Based on this review of current concepts, the authors conclude that there is no ideal or universal approach for management of infected non-union of the femur, and the approach may vary depending on the technical expertise available and the institutional practices. Irrespective of the modality used, the golden rules of fixation remain the same, alignment, preservation of biology, contact of fragments, stability and early restoration of function.

**Keywords**: osteomyelitis, non-union, femur, diagnostic solutions, local antibiotics, biomechanical stability

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## INTRODUCTION

The term ‘infected non-union’ of long bones has now been largely replaced by the term ‘fracture related infection’ (FRI) based upon the research conducted by the FRI consensus group in 2018 [1]. The term ‘FRI’ encompasses: (a) all infections which occur in the presence of a fracture; (b) early infection around a fracture; (c) infected non-unions; (d) haematogenous infections following fracture healing and (e) infections in fractures with no internal fixation. The diagnostic criteria for FRI include serum inflammatory markers, medical imaging, microbiology, molecular biology, and histopathology [2]. Standard diagnostic aids are mandatory in all cases, such as total leukocyte count (TLC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), of which, CRP is the most useful serum inflammatory marker [2] with a sensitivity ranging between 60–100 % and specificity between 34.3 % and 85.7 %.Newer modalities which are useful in prosthetic joint infections, such as biomarkers in synovial fluid, namely interleukin 6 (IL-6), leukocyte esterase strips, alpha defensin and synovial fluid CRP, are yet to establish a role in FRI [3]. Conventional radiography may not give much information, but sinograms are extremely useful to indicate where the discharge leads to, superficial or deeper tissues. Computerized tomography (CT) can detect bone resorption, sequestration, periosteal or endosteal new bone formation, cortical irregularities, and atrophic non-union. Magnetic resonance imaging (MRI) can differentiate between bone and soft tissue infection. Bone scans have a high sensitivity but low specificity for infections [4]. The most recent diagnostic adjunct is 18-Fluorodeoxyglucose Positron Emission Tomography (FDG–PET), which can detect the extent of infection in remote locations, especially intramedullary, and in the presence of an implant. Many studies have reported a high sensitivity and positive predictive value in patients for whom clinical findings are inconclusive for a local infection [5].

## METHODS

A detailed analysis of literature, including current updates on the management of fracture related infections (FRI) and non-unions was conducted, with the objective of simplifying and putting together a structured approach in the management of infected non-unions of the femur. Search words and phrases used for navigation in the international medical literature platforms were: osteomyelitis, non-union, femur, diagnostic solutions, local antibiotics, biomechanical stability. Key points are enlisted below.

## RESULTS AND DISCUSSION

### A. Approach to surgical management

The principles of surgical management of infected non-unions remain the same, irrespective of the anatomical location, and these are: (a) adequate soft tissue sampling; (b) thorough debridement; (c) fracture stabilization; (d) dead space and defect management; (e) delivery of local antibiotics and (f) soft tissue coverage [6]. These are discussed as under.

a–b) *Debridement and sampling* One must have clarity on 'what' and 'how much' to take out, since all sclerotic bone is not necessarily dead bone. An MRI/PET scan can provide valuable information and aids in decision making [7]. The role of methylene blue is debatable, but can be a useful adjunct in determining the extent of inviable bone [8]. It is essential to administer antibiotics immediately *after* sampling [9]. If the patient was previously on antibiotics, an antibiotic free holiday of at least 1–2 weeks is mandatory [10]. Five or more deep tissue samples should be collected in separate containers, using un-used surgical instruments for each sample [2]. Samples should preferably be inoculated directly into the culture broth. Superficial, skin, or sinus tract, swabs should *not* to be used.

c) *Fracture stabilization* The peculiarities of the femur include large deforming muscular forces which tend to pull the proximal femur into flexion and abduction, thereby creating a varus and procurvatum deformity of the proximal femur. This is especially true when a subtrochanteric corticotomy is used for lengthening along with an external fixator [11]. The deforming forces can be overcome by using a sturdy construct consisting of 4–5 Shanz pins in the proximal segment in a 'delta' configuration, or by using commercially available clamp modifications (ALFA fixator, SH Pitkar, Pune, India), which can accommodate up to 5 pins in the same plane or in two planes at a variable angle, as highlighted in Figure 1.

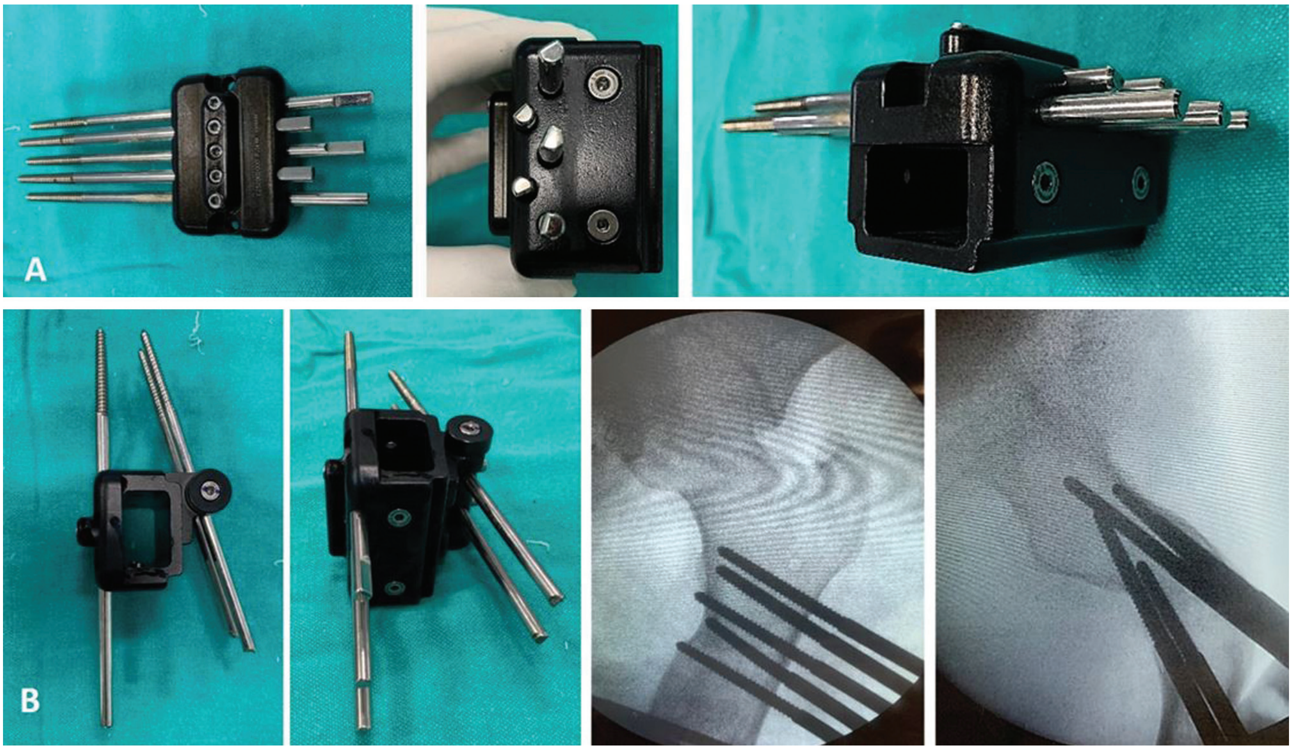


**Fig. 1** (A) Clamp with 5 pins in same direction; (B) Clamp with 5 pins with variable angle adjustment and its clinical application in the proximal femur

Large ring fixators in the femur are poorly tolerated by patients due to difficulty in maintaining personal hygiene, the need for a modified bed to accommodate the frame and the laboriousness in ambulation [12]. Possible remedies include the use of a monolateral rail fixator, with pins driven up into the neck for a stronger purchase, where the bone stock is better as compared to the trochanteric region. The swivel clamp of the rail fixator is very useful in this regard (Fig. 2). The rail fixator weighs less and is less cumbersome to the patient [12].

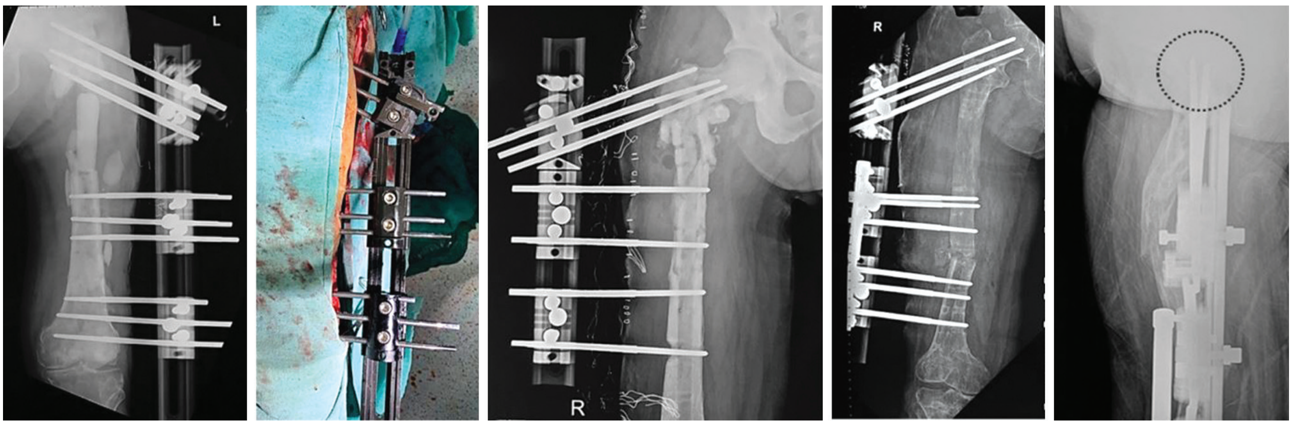


**Fig. 2** Swivel clamp of the rail fixator system with pins that can be angled upwards into the femoral neck; care is taken to ensure their central location in the lateral view

For small fragments, such as the distal femur condylar block, or osteopenic bone or those with pre-existing knee stifness, a knee-spanning construct is desirable to counterbalance undesirable movements at the non-union site, consequent to a long lever arm [13]. Spanning frames may be hinged (commercially available) or non-hinged and can be taken off after satisfactory union has been achieved to resume range of motion (ROM) exercises (Fig. 3). A quadriceps-plasty may be added at the end in cases of residual knee stiffness [14]. The use of olive wires can be extremely useful in tackling small coronal plane fragments [15], wherein the wires are placed perpendicular to the fracture plane and tensioned using a traction assembly to achieve interfragmentary compression and union (Fig. 4).


**Fig. 3** (A) Commercially available modular knee spanning frame with articulating knee hinge; (B) indigenous modification of the same using Ilizarov components

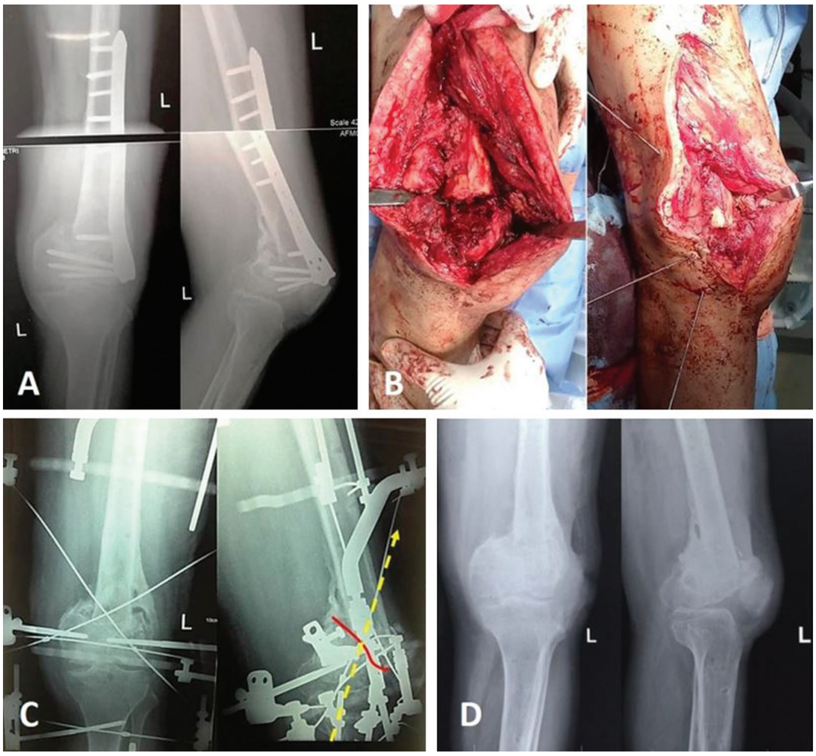


**Fig. 4** (A, B) Infected non-union Hoffa fracture with a small, osteopenic, condylar segment; (C) counter-opposed olive wires are driven from down upwards, perpendicular to fracture plane (in red), and tensioned using a traction assembly at the top to achieve interfragmentary compression, resulting in union (D)

d) *Defect management* Detailed description of defect management is beyond the scope of this study, hence, a generalised approach [1] to defect management is summarized as a flow chart in Figure 5.

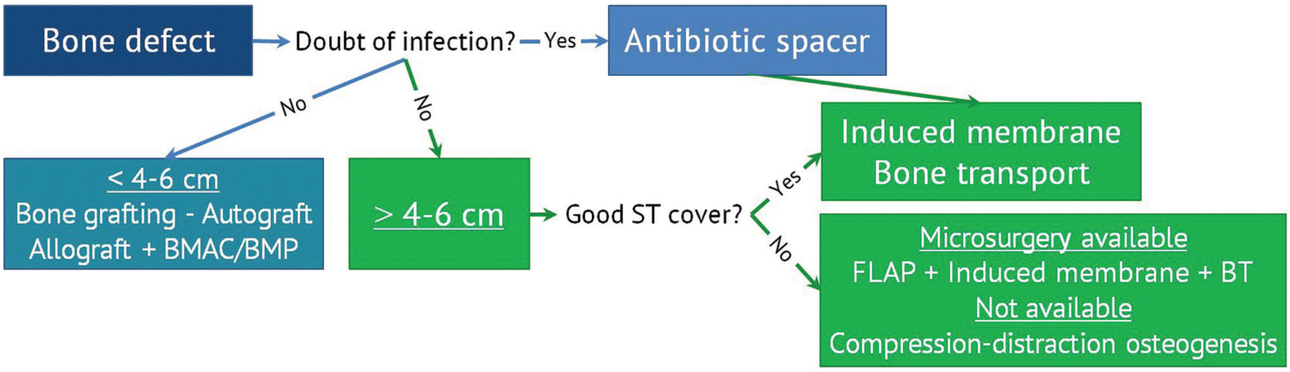


**Fig. 5** Approach for dead space and defect management

e) *Local antibiotic delivery* This is the crux of treatment. Commonly used vehicles for local antibiotic delivery include polymethyl methacrylate (PMMA) cement spacers or beads on a string, the 'bead pouch' technique [17], cement coated nails, antibiotic coated implants, and absorbable calcium sulphate-based carriers, and are selected depending upon the availability of resources and anatomical location of the infection [6]. The choice and duration of antibiotics is a topic of contention. General guidelines are as follows [6]; the antibiotic should be (a) heat stable, (b) be available in powder form, (c) should not be cytotoxic to host tissues, (d) have minimal systemic side effects and (e) released at concentrations exceeding several times the minimum inhibitory concentration (MIC). Note that cement can hold up to 8 g of antibiotics per 40 g of PMMA [18]. The combined duration of parenteral and oral antibiotics is generally 6–12 weeks, in consultation with the infectious diseases' specialist [19].

f) *Soft tissue coverage* Early flap cover for exposed bone or musculo-tendinous units should be performed as soon as possible, once the general condition of the patient stabilizes. For this, a close association between the orthopaedic and plastic surgeons is warranted, often referred as the 'ortho-plastic' approach [20]. For uncomplicated, discharging wounds, negative pressure wound therapy (NPWT) is an extremely rewarding modality, with several advantages [21] such as (a) enhancement of wound healing, (b) cyclic cleansing and dilution of wound debris, (c) disruption of biofilm, (d) accelerated granulation tissue formation and (e) earlier reduction in wound size.

*Rehabilitation phase* Bracing is highly recommended to protect the regenerated bone and the healed non-union site from re-fracture (Fig. 6) and should be continued for a period of 2–3 months following frame removal [22]. Early weight bearing with an appropriate walking aid and active ROM exercises are quintessential.

**B. Implant selection: internal versus external fixation**

While selecting the type of hardware for non-unions of the femur, one often encounters a dilemma concerning the *most* appropriate surgical tool for stabilization. The following guidelines have been drafted to help simplify the arduous task of decision making.

<u>Choice of internal fixation</u>

1. Bulky frames result in poor compliance. Long periods in a frame can cause tremendous psychiatric problems and considerable patient discomfort and dissatisfaction [11].


**Fig. 6** Customised thigh brace for post-operative rehabilitation in non-union of the distal femur

2. Due to closely spaced components, frames leave little space for future reconstructive surgery, such as flap cover and bone grafting.

<u>Pre-requisites to be fulfilled</u> Internal fixation with bone grafting would depend on the size of the gap; commonly defects < 6 cm are treated with this modality [23]. The distal fragment should be of sufficient size to hold screws. The plate should be a robust, locking plate and long enough for adequate stability [22]. It may be augmented with a medial plate or a plate can be augmented over a retained nail. Cortical auto- or allografts, such as a non-vascularised fibula, provide additional stability, in combination with locking plates [22]

The induced membrane technique, first described by AC Masquelet [24] in 1986, is based upon the principle that the cement spacer provokes a biological reaction resulting in a pseudo-synovial membrane formation, which is rich in BMPs and TGF Beta, VEG-F, angiotensin 2, vWF and prevents graft resorption at the second stage. The second step is performed 6–8 weeks later, in which bone grafting is done, and may be augmented with bone substitutes (in the ratio < 1:2), only *after* infection has been cleared. One must try to close the membrane over the graft, without packing it too tightly. Several studies have also reported satisfactory outcomes with a single stage protocol, consisting of debridement and internal fixation with bone grafting [25]. The choice ultimately depends upon the surgeon's preference and institutional practices. Disadvantages of internal fixation include a prolonged period of non-weight bearing ambulation and its limited application in large sized bone defects (> 6 cm) or small fragments [23].

<u>Choice of external fixation</u>:

External fixation becomes indispensable in certain scenarios such as:

1. Poor local skin and soft tissue conditions.
2. Associated limb length discrepancy > 2 cm [26].
3. Large gaps ⩾ 6 cm.
4. Concomitant deformity.
5. Small fragments or osteopenic bone.

Salvaging traumatised limbs with bone loss has always been a vexing challenge for orthopaedic surgeons across the globe. Initial attempts were often plagued by downright failure or unacceptable functionality. The introduction of the Ilizarov method instilled hope for many patients and physicians alike and produced remarkable results [27]. It has been adopted as the last resort in the management of segmental bone defects and non-unions of the lower extremities. Two Ilizarov techniques can be adopted for bone defects: (a) compression with approximation of fragments (resulting in shortening), and concomitant distraction through an osteotomy (for lengthening) *or* (b) bone transport and regeneration of the missing bone segment through distraction osteogenesis, with subsequent compression at the docking site to achieve union [28]. Either of these methods can be used to address the problems associated with bone defects, namely bone loss, soft tissue loss and infection, without the need for major reconstructive surgery [28]. The intrinsic biomechanical stability of the ring or rail fixators provides the requisite milieu to stimulate neo-histogenesis and promote bone union. Co-existing deformities can be corrected simultaneously and early weight-bearing is possible. Disadvantages of this method include tethering of soft tissues, potential risk of neurovascular injuries, regenerate-associated problems, pin-site infections, and joint stiffness [12, 29].

Choice of implant in proximal femur non-unions:

These are extremely vexing and challenging to treat because of a small sized fragment and difficulty in obtaining adequate purchase in this segment [30]. Ring fixators become cumbersome, especially when rings are used in upper thigh [12]. Monolateral fixators may improve patients' compliance and quality of life, but are delimited by the size and bone quality of the proximal fragment. Antibiotic-cement nails (Fig. 7, Fig. 8) are extremely useful in treating this variant, since they have adequate hold in the small proximal segment, and can address the intramedullary infection [32]. Antibiotic coated plates [33] have also been described, wherein the plate is retained following removal of the cement coating during the second stage, and the gap is bone grafted. Large volumes of bone graft can be obtained by the Reamer Irrigator Aspirator (RIA, De Puy Synthes) in cases of sizeable defects [32].

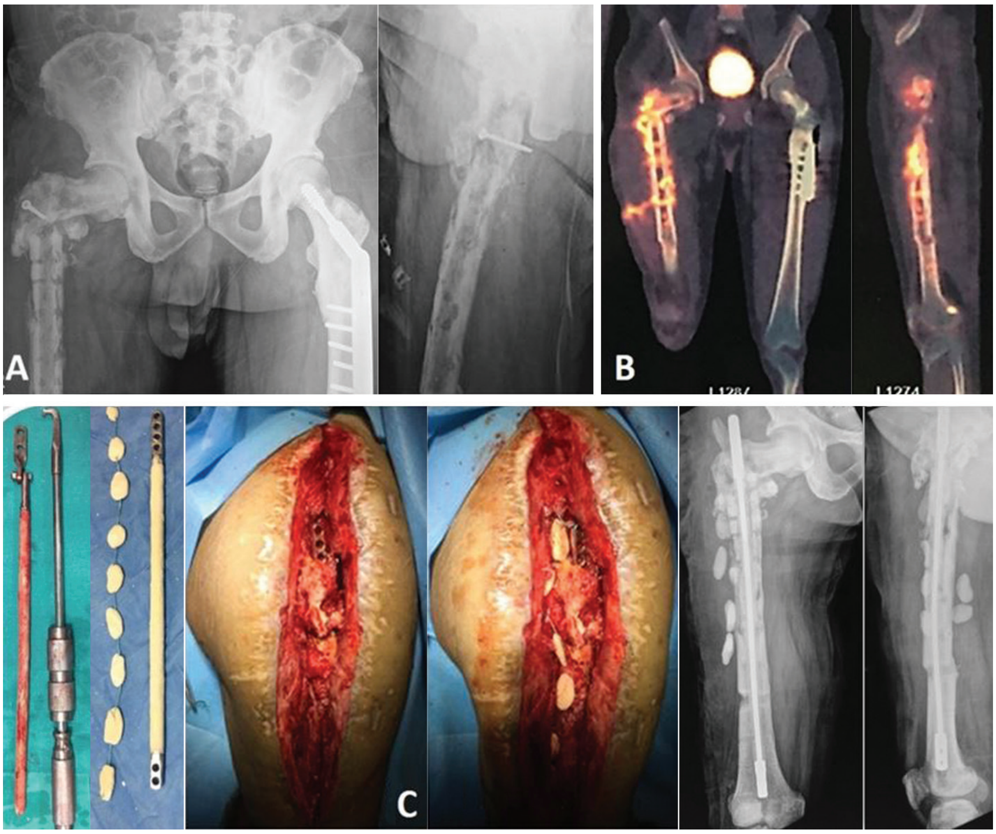


**Fig. 7** (A) Infected non-united subtrochanteric fracture in a 49-year male with multiple previous failed surgeries; (B) FDG-PET scan showing hot spots in the entire medullary canal and proximal femur; (C) custom made Ilizarov antibiotic nail, comprising of a threaded rod with posts at either end, coated uniformly with antibiotic impregnated cement (3 such nails were used), to control the medullary infection, until the discharge ceased


**Fig. 8** Rail fixator application followed with compression across the non-union (A) to achieve union in about 5 months (B)

## CONCLUSION

The authors concluded that there is no ideal or universal approach for management of infected non-unions of the femur, and the approach may vary depending on the technical expertise available and the institutional practices. In general, the following guidelines have been drafted to have a consensus on the modus operandi when dealing with bone infections, and to assist in implant selection for fracture stabilization. The goal of surgery, at the very least, is to get rid of the infection. There is *no place* for empirical treatment of suspected infection. Therapy should be initiated based upon microbial cultures of deep tissue specimens. Nuclear imaging with localizing scans is the newest refinement in diagnosis and planning. There are multiple ways of treating gaps; in general, small gaps with sizeable fragments are amenable to internal fixation, whereas larger gaps or small sized fragments are better managed with external fixation. The golden rules of fixation remain the same, irrespective of the modality used, and these can be abbreviated as 'ABCF' — restoring **A**lignment, preservation of **B**iology, achieving good **C**ontact (stability) and early restoration of **F**unction.

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