

REVIEW ARTICLE

Salvage Procedures for Management of Prosthetic Joint Infection After Hip and Knee Replacements

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Abstract:

Background:

The increasing load placed by joint replacement surgery on health care systems makes infection, even with the lowest rates, a serious concern that needs to be thoroughly studied and addressed using all possible measures.

Methods:

A comprehensive review of the current literature on salvage procedures for recurrent PJIs using PubMed, EMBASE and CINAHL has been conducted.

Results:

Prolonged suppressive antibiotic therapy (PSAT), resection arthroplasty and arthrodesis were the most common procedures performed. Suppressive antibiotic therapy is based on the use of well tolerated long term antibiotics in controlling sensitive organisms. Resection arthroplasty which should be reserved as a last resort provided more predictable outcomes in the hip whereas arthrodesis was associated with better outcomes in the knee. Various methods for arthrodesis including internal and external fixation have been described.

Conclusion:

Despite good union and infection control rates, all methods were associated with complications occasionally requiring further surgical interventions.

Keywords: Antibiotics, Arthrodesis, Fusion, Girdlestone, Infection, Joint, Replacement, Resection.

INTRODUCTION

Health services are experiencing an exponential global rise in numbers of lower limb arthroplasty procedures

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performed for an ageing population. Over the last 5 years, the UK National Health Service witnessed a growth of hip and knee arthroplasty procedures to 4000-5000 cases/year [1]. Subsequently, even a minimal prosthetic joint infection (PJI) rate of 0.57% constitutes a major concern [2] especially with the financial burden of a single revision procedure for sepsis exceeding £21, 000 [3]. The picture is further complicated by the continuous metamorphosis and emergence of new resistant bacterial strains as well as infections with rare organisms [4 - 7].

Upon diagnosis of PJI, patients with less comorbidities and adequate bone mass usually receive the optimum treatment of a single or two-stage revision procedure [8]. The remaining patients together with those who fail the above treatments or refuse further surgery constitute a major challenge for the treating surgeon. Salvage options for such cases include implant retention and administration of suppressive antibiotics, resection arthroplasty or arthrodesis of the infected joint (single or two stages). This has driven the healthcare providers to try and devise algorithms and strategies to optimize PJI management [9 - 12].

We carried out this review to explore salvage options in the current literature and present a patient, organism and joint matched guidance to selection of the appropriate strategy.

PROLONGED SUPPRESSIVE ANTIBIOTIC THERAPY (PSAT)

PSAT has limited applications in the management of PJIs including:

- Exhaustion of all operative treatment options in a surgically fit patient
- Elderly patient or poor general condition precluding surgical intervention
- Patients unwilling to undergo surgery

PREREQUISITES FOR PSAT

- Infective pathogen sensitive to a well-tolerated oral antibiotic [13]
- Antibiotic that can be safely administered for prolonged suppression
- Baseline adequate renal and liver function tests
- Feasible regular tests and follow ups to ensure safety and effectiveness of the treatment regimen (*e.g.* antibiotic levels, renal and liver function tests and regular C-reactive protein (CRP), Erythrocyte Sedimentation Rate (ESR) and Full Blood Count (FBC) monitoring).

CONTRAINDICATIONS

Factors quoted in the literature as absolute contraindications to PSAT include:

- Radiological signs of implant loosening
- Radiological signs of osteomyelitis [14]

In fact, Brandt et al. [15] considered the above factors as indications for a 2 stage revision procedure.

MICROORGANISMS

Some of the most common microorganisms accounting for PJI and can potentially be controlled with PSAT include:

Staphylococcus Group (Aureus and Epidermidis)

Methicillin sensitivity is the main predictive factor for infection control in Staphylococcal infections. Methicillin Sensitive Staphylococcus aureus (MSSA) infections can be controlled using penicillins whereas for Methicillin resistant cases, PSAT has never been associated with good infection control rates [13].

Streptococcus

Streptococcus strains of bacteria account for around 20% of PJIs. In a case series of 18 patients, Everts *et al.* [16] successfully controlled Streptococcus PJIs in more than half of their cohort (10/18) using long-term antimicrobial therapy. Strains included Streptococcus Viridans, Streptococcus Pneumoniae, Group A, B, G and D streptococci.

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Gram-negative (GN) Organisms

Jaen *et al.* [17] demonstrated that the main predictor for successful PSAT in patients with GN organisms was their susceptibility to fluoroquinolones.

Salmonella Species

Previous reports recommended ciprofloxacin as the most effective agent against Salmonella PJIs [18]. However, with the increased virulence of the organism and the emergence of new resistant strains, it became important to perform *in vitro* sensitivity testing for each individual case. Studies have shown that various antimicrobial agents, including ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole and third-generation cephalosporins, are valid options for treatment of different strains [18].

ANTIMICROBIALS

Treatment of PJIs should be guided by *in vitro* culture and sensitivity testing after synovial fluid sampling. The only exception is sepsis secondary to PJI where immediate administration of broad-spectrum antibiotics is necessary until culture results are available. Antibiotic combinations may be necessary for PJI control, particularly in cases complicated by biofilm formation [19, 20]. PSAT is preferably given orally. However, it is not uncommon that intravenous or intramuscular (*e.g.* teicoplanin) routes are also utilized. Some of the common antibiotics used for PSAT include:

Ciprofloxacin

A member of the fluoroquinolones family of antibiotics which was previously used as the main treatment for Salmonella PJIs [18]. However, this has changed with the emergence of more resistant strains [21].

Teicoplanin

This is a semi-synthetic broad spectrum glycopeptide similar to the vancomycin-ristocetin group of antibiotics [22]. Besides being as effective as vancomycin against Methicillin Resistant Staphylococcus Aureus (MRSA), teicoplanin can also be administered *via* the intramuscular route in three weekly doses without compromising its bioavailability. This makes it an important option for outpatient long term antibiotic therapy. Nevertheless, baseline and routine check of the patient's renal function are mandatory as it may result in renal function impairment [23].

Rifampin

Rifampin is an antimicrobial agent from the rifampicin family and is bactericidal due to the inhibition of bacterial RNA polymerase [24]. Rifampin has been shown to be effective in antibiotic combinations used to control staphylococcal biofilms [19]. However, long-term dosage of rifampin for PJI treatment has only recently been published by the Infectious Disease Society of America which recommends 300-450 mgs twice daily [25].

Linezolid

Linezolid is a bacteriostatic antimicrobial and a member of the oxazolidinone class of drugs that acts by inhibiting bacterial protein synthesis [26]. It is effective against most virulent Gram-positive pathogens [27]. However, it is more expensive than vancomycin as a home-infusion therapy. Hence, it is preferable to preserve it for vancomycin resistant cases [28].

SIDE EFFECTS

Regular monitoring of the patient is essential to ensure safe treatment with suppressive antibiotics. This includes routine examination and tests to rule out predictable side effects of relevant antibiotics. Renal dysfunction was the most commonly reported adverse effect (AE) in one study especially with teicoplanin administration [23].

In a series of 393 patients with osteoarticular infections, Schindler *et al.* reported AEs related to prolonged antibiotic therapy in 29% of cases. Most commonly encountered AEs were gastro-intestinal which represented 78% of all AEs (mostly diarrhea followed by nausea and vomiting). Fourteen patients developed C. difficile induced diarrhea (14/393, 3.6%). Other significant AEs included renal insufficiency (9%), drug induced hepatic dysfunction (8%) and blood dyscrasias (5%) [29]. In addition to AEs, emergence of resistant strains of microorganisms is a significant risk to be considered. This may influence the hospital population not only the individual undergoing treatment. Recent studies also found increasing resistance among Salmonella species. Therefore, treatment should always be guided by

susceptibility studies [30].

RESECTION ARTHROPLASTY

Resection arthroplasty was first described by Girdlestone as a salvage procedure for complex hip pathologies and for patients with tuberculosis affecting the hip joint [31]. Nowadays, indications for a permanent girdlestone procedure include severe bone loss precluding revision total hip replacement (THR), high risk of recurrent infection with any further metalwork insertion and when patients have significant comorbidities preventing major surgical intervention. Resection arthroplasty in total knee replacement (TKR) has not been as popular and in fact has been largely abandoned because of the poor and unpredictable functional outcomes. For example, Lettin *et al.* [32] reported variable functional outcomes after excision arthroplasty of infected constrained TKRs and persistent pain in 20% of patients. Falahee *et al.* [33] reported resolution of infection in up to 89% of the patients but with only 50% of patients independently mobilizing after the operation. Hence, the outcomes of the procedure were deemed satisfactory only to those who were severely disabled by their infected knees pre-operatively [33]. Accordingly, resection arthroplasty of infected TKRs is only indicated for severe bone loss precluding other interventions, or as a temporary measure preceding a second stage revision TKR or arthrodesis [34 - 37]. Therefore, we will only be focusing on the girdlestone procedure as a salvage option for infected THRs in the following sections.

Indications

A girdlestone procedure is indicated as a salvage procedure when alternative hip reconstructions could not promise better outcome for the patient. Wroblewski [38] outlined the following indications:

- Inadequate bone stock for component fixation (whether missing or unhealthy residual bone)
- Extensive residual and resistant soft tissue infection
- Gross abductor muscle weakness and soft tissue scarring
- Patient unfit for major surgical intervention in the form of revision surgery
- Patient unwilling to undergo further replacement surgery

Technique

When first described by Girdlestone in 1926, the aim of the resection procedure was to excise infected native bone or treat ankylosed painful hip joints. This involved resection of the head and neck of femur through an intertrochanteric osteotomy [39]. Currently, utilizing the same principles to salvage an infected THR requires more complex surgery that involves extraction of the hip implant and scrapping off as much as possible of the residual bone cement in order to control infection. This increases the incidence of complications such as blood loss, neurovascular injuries and especially peri-prosthetic fractures. As a result, some authors recommend fashioning a window or a gutter in the proximal femur to facilitate extraction of the femoral component [40]. Others prefer to perform the resection as a two staged procedure where the second stage involves further debridement and insertion of Gentamicin cement beads filling the defect [41].

Outcomes

For resistant organisms and recurrent infections, a Girdlestone procedure remains an ideal option for controlling infection with rates reaching as high as 97% [42, 43]. However, utilization of such a procedure nowadays is also declining due to the variable functional outcomes and patient satisfaction post surgery [44]. In a case series of 39 patients who underwent 41 resection arthroplasties for infected THRs, Kantor *et al.* reported only two patients being able to mobilize without assistive devices after the procedure and 93% had residual hip pain at the last follow up [45]. This study also showed increased oxygen consumption and energy expenditure in comparison to above knee amputees. On the other hand, McElwaine *et al.* [46] showed significant post-operative pain relief despite overall poor functional results. Another study of Girdlestone procedures performed for gram-negative PJI in 10 patients reported that infection resolved in all cases and that patients were fully ambulatory and fully satisfied with their functional outcomes. Of note is that only one patient in this case series complained of chronic pain at 5 years follow-up [47]. Manjon-Cabeza *et al.* investigated the functional outcomes after a Girdlestone procedure in 48 elderly patients (>65 years of age). They found that 42.8% of patients were wheelchair bound and that 23.8% had residual moderate pain at a mean follow up of one year postoperatively. Authors concluded that a Girdlestone procedure is very damaging to functional outcome in elderly patients [48]. On the other hand, Bourne *et al.* [43] followed 33 Girdlestones performed for PJI at a mean of 6.2 years

and reported satisfactory pain relief in 91% of patients, control of infection in 97% and satisfactory functional outcomes in 79% of patients. Authors concluded that a Girdlestone procedure provides a reasonable salvage option and that the results seem to improve with time [43]. Similarly, another mid-term follow up study suggested improvement in functional outcomes over time with 59.3% of patients being satisfied at a mean follow up of 7.1 years and two patients only using a wheelchair [49].

Factors Influencing Outcomes

Studies have also reported on factors which may influence outcomes of a Girdlestone procedure. For example, despite Bourne *et al.* [45] reporting that patients with Gram-negative PJIs developed more postoperative wound complications, Castellanos *et al.* [40] found no correlation between the type of organisms and persistence of infection, nor between limb shortening and the functional results. Of note is that patients achieved 83% satisfactory pain levels and 86% resolution of infection in this study [40]. Kantor *et al.* [45] found that adequate soft tissues with healed wounds and signs of heterotopic ossification on plain radiographs correlated well with good functional outcomes and reduced pain levels postoperatively. On the other hand, poor outcomes have been reported with elderly patients [48], diabetics and patients with multiple comorbidities [46, 50]. Established osteoarthritis of the contralateral hip also predisposed to poor mobility and subsequent lower function after a Girdlestone procedure [46]. Poor prognosis has also been associated with retained cement in the femoral canal as this may act as a nidus for persistent infection [43, 50]. Bourne *et al.* [43] also suggested a relationship between the retained cement and resultant bony sequestra and prolonged postoperative wound discharge.

Complications

Besides the risks that may complicate any hip surgery, a girdlestone procedure performed for PJI carries specific risks being a revision surgery performed on unhealthy tissues. Recurrence of infection is the most common and challenging of those complications [51]. Additionally, the risk of neurovascular injuries is increased with extraction of mal-positioned implants or implants that have migrated from their original position [52]. A case of a colo-articular fistula has also been reported after a Girdlestone procedure in an intravenous drug abuser with no previous bowel pathology [53].

SECONDARY PROCEDURES

Conversion to THR

Garcia-Rey *et al.* [54] compared the outcomes of THR following a Girdlestone procedure to those of revision THR performed for aseptic loosening. They found that post-operative clinical outcomes were similar in both groups despite significantly worse limb length discrepancy (LLD) affecting the girdlestone group. For both groups, older age (>70 years) and large acetabular bone defects were associated with higher LLD, worse post-operative function and range of movement [54]. Despite various reports confirming improved outcomes post conversion to a THR [55], the number of potential complications renders this procedure a challenge for both the surgeon and the patient. In one study, such complications included 11.4% dislocation, 2.3% recurrence of infection, 9.1% trochanteric non-union and 4.5% wound complications [56].

Muscle Flap for Persistent or Recurrent Infection

In 119 patients with recurrent infections following a Girdlestone procedure, Suda *et al.* [57] demonstrated 100% infection control using a vastus lateralis interposition flap implanted into the acetabular cavity using Mitek anchors. The acetabular cavity was deemed the source of recurrent infection after the Girdlestone procedure.

Arthrodesis

Joint fusion has always been considered as one of the main limb salvage procedures for PJI. In contrast to resection arthroplasty, arthrodesis offered more predictable outcomes and better function in the knee as opposed to the hip joint. In fact, the literature contains contradicting results and views on hip arthrodesis. For example, Kostuik *et al.* [58] suggested that an arthrodesis for failed THR may provide better functional results than a Girdlestone procedure. However, Courpied *et al.* [59] reported that hip arthrodesis is a potential source for persistent back and knee pain. Moreover, Barnhardt *et al.* [60] concluded that despite an overall 66.6% satisfaction rates, sexual dysfunction affected 83% of patients and only 50% would consider undergoing the procedure again.

Knee arthrodesis on the other hand stands out as a salvage procedure with better functional outcomes and patient satisfaction. In fact, a recent systematic review proved that arthrodesis is the procedure of choice, when compared to suppressive antibiotics, two-stage reimplantation and amputation, for management of persistent infection after a failed two-stage reimplantation procedure [61].

Knee arthrodesis for PJI can be performed as a single or two-stage procedure following resection arthroplasty. Some authors prefer the later as it allows eradication of infection and build up of bone mass after explanation of the infected prosthesis [34].

METHODS

Our literature search showed that knee arthrodesis for PJI can be carried out by various methods according to patient factors and surgeon skills. We identified 28 articles describing different methods which broadly fell under four categories: intramedullary nailing (IMN), external fixation (EF), cannulated screws and plating (Table 1).

Table 1. Various methods of knee arthrodesis described in	the literature.
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	Reference	Arthrodesis Method	Publication	Ν	Complications	Outcomes
1	Rothacker 1983 [72]	Hoffman External Fixator (Multiplanar pin insertion)	Retrospective	50	Pin site infection (1/50, 0.5%)	Union 86.2%
2	Kinik 2009 [73]	Ilizarov bone transport	Case reports	3	Need for posteromedial release for equinovarus deformity (2/3, 66%)	Union 100% Acceptable alignment Bone transport of up to 22cm (mean=17.3)
3	Eralp 2008 [77]	Unilateral External Fixator	Retrospective	11	LLD 1.4cm (range 1-3) Pin tract infection (5/11, 45.4%)	Union 100% Eradication of infection 100% Walk independently 100%
4	Kutscha-Lissberg 2006 [79]	Hybrid External Fixator	Prospective	17	Superficial pin tract infection (2/17, 11.76%) Painful wire, exchanged (1/17, 5.9%) Failed union (2/17, 11.76%)	Eradication of infection (14/17, 82.3%) Independently mobile without walking aids in patients with isolated knee disorders (9/9, 100%) Pain Relief (17/17, 100%)
5	Oostenbroek 2001 [74]	Ilizarov External Fixation	Retrospective	15	Complications 80% Non-union (1/15, 6.66%) LLD 4cm (range 2 - 6) Pin tract infection (15/15, 100%) Pin tract infection requiring IV antibiotics and removal of infected pin (3/15, 20%) Peri-prosthetic fracture at time of implant removal (2/15, 13.33%)	Union (14/15, 93.33%) Eradication of infection 100%
6	Gunes 2005 [75]	Circular External Fixator	Case report	1	Pin tract infection requiring oral antibiotics	Union 100% Complete eradication of infection 100% Independent weight bearing and walking without crutches
7	Ulstrup 2007 [76]	Sheffield Ring Fixator	Retrospective	10	Nonunion (4/10, 40%) Pin tract infection (7/10, 70%)	Union (6/10, 60%) Eradication of infection 100%
8	Corona 2013 [78]	Monolateral External Fixator	Retrospective	21	Pain scores significantly higher in nonunion cases	Union (17/21, 81%) Eradication of infection (18/21, 86%) Worse functional outcomes in patients > 75 years.
9	Riouallon 2009 [80]	Combination of external fixator and Steinman pin	Retrospective	6	Complications (3/6, 50%) Hematoma requiring surgical evacuation (1/6, 16%) Peri-prosthetic fracture (1/6, 16%) Osteitis managed by surgical curettage (1/6, 16.66%)	Union 100% Eradication of infection (5/6, 83%) Weight bearing at 2 - 3 months

(Table	e 3) contd					
10	De Vil 2008 [62]	Intramedullary nail	Retrospective	15	Persistent infection and nonunion (4/15, 26%) Amputation (3/15, 20%) Aseptic non-union (1/15, 6.66%) LLD 4.5cm (range 2.8 - 6.2)	Union (11/15, 73%) Return to work (50%)
12	Putman 2013 [64]	Customized Modular Intramedullary Nail	Retrospective	31	Persistent infection requiring nail removal (3) and long term suppressive antibiotics (3) (6/31, 19.4%) LLD 1cm (range 0.5-3.4)	
13	Rao 2009 [66]	Modular Cemented Intramedullary Nail	Retrospective	7	Recurrent infection requiring revision procedure (2/7, 28.6%)	Significant improvement of pain scores
14	Waldman 1999 [65]	Modular Intramedullary nail	Retrospective	21	Nonunion requiring repeat bone grafting (1/21, 4.7%)	Union (20/21, 95%)
15	Ellingsen 1994 [63]	Intramedullary nail	Retrospective	18	Complications (10/18, 55%) Nonunion (2/18, 11%) Prolonged operation (6 hours) Average blood replacement 2975 ml	
16	Bargiotas 2006	Intramedullary Nail	Retrospective	12	Nonunion (2/12, 16%) Recurrence of infection (2/12, 16%) AKA (1/12, 8.33%) LLD 5.5 cm	Union (10/12, 83.33%)
17	Talmo 2007 [91]	Long Intramedullary Fusion Nail	Retrospective	29	Pain following complete fusion 62% Metal failure and implant breakage (2/29, 6.9%) Recurrent infection (3/29, 10.34%)	Union (24/29, 83%) Independent mobility requiring a single walking aid (17/29, 58.6%)
18	Lai 1998 [69]	Short Huckstep Nail	Retrospective	33	Recurrent infection (1/33, 3%)	Union (30/33, 91%)
19	Lee 2012 [70]	Distraction with Huckstep Intramedullary Nail and Bone Graft (Autologous + Allograft)	Retrospective	8	LLD 1.1 cm	Union (8/8, 100%) Eradication of infection (8/8, 100%)
20	Fern 1989 [67]	Curved Kuntscher Nail	Prospective	13	Metalwork failure requiring removal and repeat fixation (1/13, 7.7%) Persistent wound discharge requiring metal removal (1/13, 7.7%)	Not recorded
21	Iacono 2013 [85].	Press-fit Modular Intramedullary Nail with Antibiotic Loaded Cement	Retrospective	22	LLD <1 cm Recurrent infection (3/22, 4.5%)	Significant improvement in pain and function
22	Barsoum 2008 [71]	Wichita Fusion Nail	Retrospective	7	Complication rate 57% Persistent infection requiring rod removal (2/7, 28.5%) Atrophic nonunion (1/7, 14%) Permanent peroneal nerve palsy (1/7, 14%)	Union (6/7, 86%) Pain Relief (5/7, 71%) Ambulation (6/7, 86%)
23	Nichols 1991 [88]	Dual Compression Plates	Retrospective	11	Femoral stress fracture (1/22, 4.5%) Persistent infection (1/22, 4.5%)	Union (11/11, 100%)
24	Kuo 2005 [89]	Dual Plating with Locking Compression Plate (LCP)	Case reports	3	None reported	Union (3/3, 100%) Independent mobility using a single crutch (1) or walker (2)
25	Lim 2009 [90]	Cannulated Screws	Retrospective	8	Delayed union requiring bone graft (1/8, 12.5%) Wound necrosis requiring skin graft (1/8, 12.5%) LLD 3.1cm (range 1.1 - 6.5cm)	Union (7/8, 87.5%) Eradication of infection (8/8, 100%) Independent mobility Pain and function improved
26	Bartlett 2011 [81]	Stanmore Knee Arthrodesis Prosthesis	Retrospective	9	Uncontrolled infection (1/9, 11%) Prosthetic fracture (1/9, 11%)	Implant survivorship 90% Independent mobility 100%
27	Jung 2009 [83]	Computer Assisted Navigation and Ilizarov fixation	Case report	1	Not recorded	Not recorded
28	Bigliani 1983 [82]	Pulsing Electromagnetic Field with Various Methods of Fixation	Prospective	20	Not recorded	Union (85%)

IMN is a popular method of arthrodesis and can be performed as a single [62 - 67] or two-stage revision procedure following debridement, cement spacer insertion and a period of intravenous antibiotics [68, 69] with or without the addition of bone grafts [70].

Bargiotas *et al.* used IMN arthrodesis in a two-staged approach. First stage involved implant removal and application of a cement spacer. After eradication of infection, the second stage included creation of large bleeding convex-to-concave bone surfaces and then inserting the nail. The authors reported 83.3% fusion rates following this strategy [68]. Various implants have been used as an IMN device including the long arthrodesis IMN [62, 63], customized modular IMNs [64, 65], modular cemented IMNs [66], the Huckstep nail [69], [70], the curved Kuntscher nail [67] and the Wichita fusion nail [71]. Different designs have also been used for EF. These included the Hoffman EF with multiplanar pin insertion [72], the Ilizarov or circular ring fixators [73 - 76], unilateral EFs [77, 78], hybrid EFs [79] and a combination of EF and Steinmann pin application [80].

EF offered the advantage of bone transport and subsequent lengthening to compensate for large bony defects [73]. A single institution designed device (The Stanmore Knee arthrodesis prosthesis) has also been identified. The design of this implant included distal femoral and proximal tibial replacements that are coupled using a cam and post and locked using an axle and circlip. This was still considered a form of arthrodesis, as it is a locked device restricting movement in all directions [81].

Two adjunctive techniques have also been reported: one aimed at enhancing fusion across the joint using electromagnetic field alongside various methods of arthrodesis performed [82] and the other employed computer assisted navigation to improve the accuracy of the cuts and alignment after which an Ilizarov EF was applied [83].

Outcomes

Outcomes of arthrodesis for PJI are variable according to the method utilized. Four papers compared the outcomes of various methods of fixation. Mabry *et al.* [84] failed to show any significant difference between IMN and EF in relation to union, complication rates and infections. Iacono *et al.* [85] found that functional outcome scores and LLD were significantly better in the IMN group but with higher rates of persistent infection. There was no significant difference in pain scores between both groups [85]. Van Rensch *et al.* [86] showed that IMN resulted in higher union rates. However, they opted to use it only after eradication of infection. They recommended the use of the Ilizarov EF for persistent infections [86]. Yeoh *et al.* [87] investigated the outcomes of arthrodesis for infected TKR using the Mayday IMN and compared it to monolateral EFs. Their results showed that the IMN group achieved higher union rates and shorter hospital stay [87]. Overall union rates varied between 81 - 100% with EF methods and 83 - 100% with IMN. Two reports of dual plating for arthrodesis showed 100% union rates [88, 89] and one cohort of fusion using cannulated screws yielded 87.5% union rates [90].

Mean time interval required for complete bone union ranged from 3.5 - 10.3 months for EF and 5.2 - 9.8 months for IMN. This was reported to be 5.6 months for dual plating [88] and 6.1 months for cannulated screws [90].

Eradication of infection was achieved in 82.3 - 100% with EF, 71.4 - 100% with IMN, 85.5% with dual plating [88] and 100% with cannulated screws [90]. Independent mobility (with walking aids) reached 100% in all fixation methods. Pain relief reached 100% with EF [73, 79] whereas this was variable with IMN as reported rates of residual pain reached as high as 62% despite complete union [91]. Arthrodesis using cannulated screws produced significant improvement in pain scores [90].

Monolateral EF was associated with worse functional outcomes in patients older than 75 years of age [78]. Using pulsing electromagnetic field to enhance arthrodesis was found to promote union only in the early postoperative phase. Patients already diagnosed with delayed union did not benefit from this adjunct treatment [82]. Klinger *et al.* [92] investigated the long-term functional outcomes and pain scores in a cohort of twenty patients (18 EF and 2 IMN). They concluded that two-stage arthrodesis offered more predictable outcomes than a single-stage procedure. Persistent infection and deficient bone stock were also consistently associated with poor prognosis [92].

COMPLICATIONS

Current literature provides clear evidence that complications following such a complex procedure are inevitable. However, the complications vary considerably according to the method employed, surgical skills and patient factors. For example, only 2 reports (14 patients) in the literature used dual plating for arthrodesis in PJI. However, overall complications reported were minimal (9%) when compared to more widely used methods [88, 89] including IMNs (55 - 57%), EF (24 - 80%), cannulated screws (25%) [90] and the Stanmore prosthesis (22%) [81].

Recurrence of Infection

Although relatively unexpected, this is the most feared complication after a procedure aimed at eradication of persistent infection [93]. Of the most commonly used techniques, EF was associated with the lowest re-infection rates with no recurrence seen in 4 studies [73 - 75, 97] and recurrence rates ranging from 14 - 17.7% in 3 other studies [79, 78, 80]. On the other hand, re-infection rates ranged from 3 - 28.6% for IMNs. Open procedures were associated with less re-infections; 0% after cannulated screws fusion [90], 4.5% with dual plating [88] and 11% with the Stanmore prosthesis [81].

Nonunion and Failure of Fusion

There was no detectable difference between the incidence of nonunion following EF (range 11.7-40%) and IMN arthrodesis (range 11 - 33.3%). Plating techniques were not complicated by nonunion while the utilization of cannulated screws in isolation resulted in 12.5% delayed union requiring repeat bone grafting and fixation [90].

Limb Length Discrepancy

LLD is not uncommon following lower limb reconstruction surgery and worsens after revision and salvage procedures. Gurney *et al.* [94] found that 2-3 cm was the upper limit of acceptable LLD. Difference in leg length was in the range of 1.4 to 4 cm following EF arthrodesis, 1 to 5.5 cm following IMN and 3.1 cm with cannulated screws [90]. Kinik *et al.* [73] used the Ilizarov bone transport method to compensate for the expected length difference and managed to obtain up to 22 cm of bone transport.

Residual Pain

Talmo *et al.* [91] found pain persisting in 62% of their patients following IMN even after complete bony union. A painful wire that requires removal could cause residual pain following EF [79]. Residual pain was less noted in patients who received the Stanmore prosthesis for knee arthrodesis as they reported improvement of the mean pain scores from 7.9 to 3.3 [81].

Peri-prosthetic Fracture

This was reported as an intra-operative complication at the time of implant extraction before application of an EF in 13.3% and 16.6% of patients in 2 studies [74, 80]. Postoperative stress fracture complicated 4.5% of plate fusion procedures [88] and periprosthetic fracture was the reason for failure of 11% of the Stanmore arthrodesis implants [81]. Fractures at both sides of a modular nail have also been reported even after achieving complete union [95].

Further Intervention

Further surgical interventions were necessary in 5.9% - 66.6% of EF cases and included wire removal or exchange, posteromedial release for equinovarus deformity, hematoma evacuation and surgical curettage for osteitis [73, 79, 99, 80]. For IMN cases, 4.7% - 28.6% of the patients underwent further surgery in the form of implant removal for persistent or recurrent infection, nail exchange and repeat fixation for metal failure, and bone grafting for nonunion [64 - 67, 71]. Cannulated screws arthrodesis was complicated by 12.5% skin necrosis requiring debridement and skin graft coverage and 12.5% delayed union requiring bone grafting [90].

Procedure Related Complications

Specific complications were associated with different methods of arthrodesis. While implant failure and hardware breakage affected 6.9% and 7.7% of IMN cases in 2 studies [91, 67], pin site infections complicated 0.5-100% of EF arthrodesis. Mean operative time up to 6 hours with more than 2.9 L of blood replacement requirements has also been recorded following IMN arthrodesis for PJI [63].

SECONDARY PROCEDURES

Bone Transport for Failed Fusion

Kinik et al. [73] utilized bone transport techniques to gain a mean length of 17.3 cm (range 11 - 22 cm) in primary

and revision arthrodesis procedures for patients with large bone defects.

Salvage for Infected IMN Arthrodesis

Cavadas *et al.* [96] introduced a three stage salvage procedure which involved removal of the infected nail, debridement, cement spacer insertion and EF application followed by application of a vascularized free fibular bone graft after eradication of infection. The third stage included exchanging the EF to an internal fixation device. In addition to three major surgical interventions and the prolonged treatment course, two out of the five patients developed deep infection after the third stage and one patient developed a stress fracture at the fibular graft site [96].

Conversion to Arthroplasty

Jain *et al.* [97] carried out a systematic review on the outcomes of conversion of hip arthrodesis to THR. They found that this procedure results in "unacceptably high complication rates" when compared to arthrodesis. Complication rates reached 54% and included infection, mechanical failure and nerve palsy [97]. When converting knee arthrodesis to TKR, the main hurdle is soft tissue fibrosis and tension limiting the range of movement of the new implant. Hence, trials of two-staged approach have been implemented using a soft tissue expander in the first stage to enhance soft tissue flexibility and excursion. This was followed by conversion of the arthrodesis to arthroplasty using a fully constrained rotating hinge knee and a final range of movement of 95 degrees in flexion has been reported [98]. Kim *et al.* [99] used posterior stabilized knee prostheses for the conversion and they also stressed that integrity of soft tissue sleeves is a prerequisite for a successful operation.

CONCLUSION

All three salvage procedures for PJI require clear understanding of indications and applicability as they are associated with relatively high complication rates. An accurate diagnosis with sensitivity testing and close follow up of patients is a key for successful PSAT. Resection arthroplasty which should be reserved as a last resort provided more predictable outcomes in the hip whereas arthrodesis was associated with better outcomes in the knee. Despite good union and infection control rates, all methods for arthrodesis have been associated with complications occasionally requiring further surgical interventions.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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