Injury xxx (xxxx) xxx

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Implant retention with serial debridement and use of antibiotic-loaded calcium sulfate beads in acute fracture-related infection (FRI) after pelvic ring or acetabular fractures: A retrospective case series of 7 cases ☆

Alessandro Casiraghi [a], Claudio Galante [a,*], Mohamed Rohayem [b], Giulio Vittone [c], Marco Domenicucci [a], Stefano Cattaneo [a], Marco Paderno [a], Giuseppe Grava [a], Evelyn Van Hauwermeiren [d], Giuseppe Milano [c]

[a] Department of Bone and Joint Surgery, ASST Spedali Civili, Brescia, Italy
[b] Orthopedic surgery department, Tanta University Hospitals, Egypt
[c] Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy
[d] Operative Unit of Infectious Disease, ASST Spedali Civili, Brescia, Italy

ARTICLE INFO

Article history:
Accepted 22 January 2023
Available online xxx

Keywords:
DAPRI
Antibiotic pearls
Local antibiotic therapy
Infection
Pelvic fracture
FRI
Fracture-related infection

ABSTRACT

Background: The development of a pelvic wound infection in the presence of hardware after open reduction and internal fixation presents a clinical dilemma and there is little literature to aid in decision-making. The purpose of this study was to describe the possibility of debridement, antibiotic pearls and retention of the implant (DAPRI) procedure to eradicate the infection.
Methods: Tumor-like debridement, antibiotic pearls and retention of the implant (DAPRI) aimed to remove the biofilm allowing a higher and prolonged local antibiotic concentration by using calcium sulfate antibiotic-added beads. Wound status, radiological signs of bone healing, gait and functional activity of the patient were evaluated.
Results: Seven patients underwent this technique. The mean follow up time was nine months (range: 6 -16 months). Complete wound healing was achieved in all the patients with no major complications. Average time of bony union was 4.3 months (range: 3–6 months) with no need for implant removal.
Conclusion: The DAPRI technique might represent a safe and more conservative treatment for management of early fracture-related infections (FRI) of the pelvis and acetabulum.

Introduction

Pelvic ring injuries are potentially life-threatening conditions associated with high incidence of morbidity and mortality ranging from 5 to 60% according to current literature [1]. Definitive operative intervention usually requires extensive surgical approaches, massive soft tissue dissection and lengthy procedures [2]. The prevalence of surgical site infection following fixation of pelvic ring injury is 2.1% [3]. The immunosuppressive state induced by trauma, open extremity associated injuries, massive blood loss, intensive care admission predispose to both local and systemic infections. Obesity, preoperative blood leukocytosis, perioperative fever, Morel-Lavallèe lesions, cell saver usage, subfascial drains and postoperative antibiotic may have also roles in the development of infection [4–6]. Indeed, the economic burden of postoperative infection is significant, with a potential increase in the cost of health care by 20% and length of hospital stay by 36% [7].

Limited literature exists about the treatment of postoperative pelvic fracture-related infections (FRI).

Qiu et al. [8]. treated 10 cases of infection in different bones with irrigation, debridement, and retention of the implant, using antibiotic. The bone union rate was 100%, there was recurrence of infection in one patient before bone healing, but the infection was eradicated after implant removal.

Berkes et al. [9]. analyzed the bone union rate in 121 patients (123 infections) with infection within 6 weeks after internal fixation of acute fractures: 87 (71%) obtained fracture union following debridement, hardware retention, and culture-specific antibiotic treatment, but 26 of them eventually underwent hardware removal after radiographic union due to recurrence of infection. Therefore, infection control rate shown was 50.4%.

☆ Level of evidence: 4

* Corresponding author.
E-mail address: claudio.galante@unibs.it (C. Galante).

https://doi.org/10.1016/j.injury.2023.01.045
0020-1383/

Rightmire et al. [10]. showed similar results on 69 patients with acute infection, with 68% (47 cases) of them achieving successful union; 28 of them required hardware removal because of persistent (18 patients) or recurrent infections (10 patients). Therefore, the success rate was 27%.

Implant-related infections are difficult to treat for different reasons. First, systemic antibiotics may not reach sufficiently high levels to eradicate biofilm due to local soft tissue damage. Second, inability of the defense mechanisms to eradicate these microorganisms, as these microorganisms are protected by a highly hydrated extracellular matrix. [11]

Most of the current knowledge and approaches are adapted from prosthetic infection management, but the ultimate goals in the two conditions are different [12]. In 2018, with the support of the Arbeitsgemeinschaft für Osteosynthesefragen (AO) Foundation, an international consensus has been reached on the definition of fracture-related infections (FRI). [13] This definition revolves around the establishment of diagnostic criteria to guide the decision-making process. Having a clear definition helped in establishing a stepwise approach in the treatment of FRI [12].

A novel surgical technique consisting of debridement, antibiotic pearls, and retention of the implant (DAPRI) has been developed to treat periprosthetic joint infection (PJI). It enhances the classical debridement, antibiotics, and implant retention (DAIR) procedure to improve the possibilities of retaining an infected implant [14,15]. According to the authors in the DAPRI procedure, eradication of infection is achieved through combined surgical and antibiotic treatment and by incorporating bioabsorbable antibiotic pearls, which can prolong the local antibiotic concentration [16]. The main cornerstone is eliminating the bacterial biofilm on the implant surfaces, on the bone and on the soft tissues. The goal is to disrupt the bacterial biofilm, which is the major culprit of antibiotic resistance and immune evasion. The other cornerstone is the high and prolonged local antibiotic concentration. Actually, there is little literature regarding standardized use of DAPRI in trauma patients and no definite algorithm exists for the treatment of early deep pelvic FRI [17].

The purpose of the present study was to report preliminary data on the treatment of postoperative pelvic infection by applying a modified DAPRI protocol to eradicate infection and allow bone consolidation in early deep pelvic FRI.

Methods

Study design

The study was designed as a retrospective case series of consecutive patients treated in a single level I trauma center from January 2019 and December 2021. Due to the nature of the study on a small number of cases, no Institutional Review Board approval was required at our institution.

Study population

Patients were considered eligible for treatment with DAPRI protocol based on the following inclusion criteria:

- previous osteosynthesis of pelvic ring or acetabulum fracture with plates and screws
- clinical signs of infection at the surgical site
- increase of serum inflammatory markers
- less than 4 weeks since osteosynthesis

Exclusion criteria were:

- unstable osteosynthetic construct (isolated screw loosening wasn't considered an exclusion criterion, while loosening of the whole plate constituted a contraindication for implant retention)
- absence of a vital soft tissue envelope allowing primary wound closure after debridement
- severely impaired patient physiology contraindicating urgent surgery [9,18].

Patient characteristics are detailed in Table 1.

Diagnosis of infection

Diagnosis of infection was performed according to FRI consensus group criteria [13]. Increasing or new onset pain, local redness, swelling, hotness and fever were considered early suggestive signs; as well as persistent, increasing or new-onset wound drainage, beyond the first few days postoperatively. Wound breakdown and purulent drainage were considered confirmatory criteria for infection. Laboratory investigations were performed on the first day postoperatively and subsequently every 48–72 h until discharge. An upward trend or secondary rise of serum inflammatory markers (erythrocyte sedimentation rate, white blood cell count, C-reactive protein) without solid alternative explanation was considered a suggestive sign. Once there was clinical suspicion of infection a CT scan was performed for detection of abscess collections and evaluation of implant loosening. Phenotypically indistinguishable pathogens identified by culture from at least two separate deep tissue/implant (including sonication-fluid) specimens taken during an operative intervention were considered confirmatory criteria as well as the presence of pus during surgery.

Surgical technique

The adopted surgical technique was somehow similar to the DAPRI proposed for the treatment of infected total hip replacement [15], the main difference is that we performed serial debridement surgeries.

During the administration of regional and general anesthesia, antibiotic prophylaxis was administered according to internal protocol at our institution (cefazoline 2 g preoperatively or clindamycin 600 mg if allergy to Beta-lactams has been reported) as the intraoperative cultures are not influenced by preoperative antibiotic therapy [19,20]. The first step was generous exposure through the original surgical approach. Several samples (at least 5 samples) from different deep tissues were taken for cultural examination. An adequate zone-by-zone debridement was performed to remove all the soft-tissues possibly contaminated by the infected biofilm. Differently from the original DAPRI protocol [14,15], methylene blue injection (for staining of the bacterial biofilm) or argon beam radiation (for detachment of the biofilm) were not used. Screws were checked and removed if loose.

A 4% chlorhexidine gluconate-added brush was used to scrub all the tissues and implants: this is performed to mechanically remove the preformed biofilm. Abundant pulse irrigation with 9 liters of povidone iodine added saline was performed. At this point, the contaminated instruments were removed from the surgical field. Clean redraping of the patient was done with new gowns and gloves for the operating team. A new back table with new instruments was brought in the surgical theater. Further irrigation of the wound was undertaken using 0.9% sodium chloride (saline). After irrigation a methodical zone by zone search for residual signs of infection was performed. If no residual signs of infection were detected a final step consisting of implantation of a local antibiotic carrier was carried out, otherwise closure of the wound was performed. A major difference between our technique and the traditional DAPRI was in fact the use of serial debridement procedures. Surgical procedures, similar to the one previously described,

Table 1
Characteristics of patients and treatments performed.

Patient	Sex	Age	Diagnosis	Implants	Surgical approach	Pathogen	Number of debridement surgeries	Interval ORIF-first debridement (days)	Time of bony union (months)	Complications
1	F	43	Combined pelvic-acetabulum fracture	Plates and screws	Ilioinguinal	Negative cultures	3	8	3	None
2	M	47	Two column acetabular fracture	Plates and screws	Modified Stoppa	Negative cultures	2	17	5	Subcutaneous fluid collection
3	M	46	T-shape acetabular fracture	Plates and screws	Modified Stoppa + Ilioinguinal first window	Finegoldia magna	2	16	3	None
4	F	41	Pelvic ring malunion	Plates and screws + posterior pelvic ring fixation	Bilateral Stoppa + posterior approach to the sacrum	Enterococcus faecalis	4	10	5	None
5	M	53	Anterior column with posterior hemi-transverse acetabular fracture	Plates and screws	Modified Stoppa	MSSA	2	19	4	None
6	F	16	Vertical shear pelvic fracture	Plates and screws	Pfannenstiel + first window	MSSA	2	8	3	Subcutaneous fluid collection
7	M	25	Pelvic ring malunion	Plates and screws + posterior pelvic ring fixation	Pfannenstiel + posterior approach to the sacrum	Klebsiella pneumoniae	5	8	6	None

were repeated until intraoperative conditions showed no macroscopic sign of infection. Two to four days was the average interval between sequential operations. Timing of intervention was determined according to local and systemic signs of infection; inflammatory markers trends were also taken into account.

When intraoperative conditions showed no gross sign of infection after the second irrigation, calcium sulfate beads loaded with antibiotics were implanted. We used commercially pure, synthetic physiological pH calcium sulfate powder - Stimulan (Biocomposites Ltd, Keele, United Kingdom) with the RapidCure kit which includes 10 cc (20 gr) of calcium sulfate hemihydrate powder, a pre-mixing solution bulb, pellet mold and spatula (see Fig. 1). The ingredients were combined, and antibiotics of choice were added (Stimulan is approved for use in combination with gentamicin, tobramycin and vancomycin). In all patients, we used 10 cc of calcium sulfate (Stimulan) with vancomycin 1000 mg and gentamicin 240 mg. the composite was then mixed for 30 s until “doughy”. The resulting paste was applied to the molds using the spatula and allowed to set for 10 to 15 min. The mold produced three sizes of bead (3, 4.8 and 6 mm in diameter). In pelvic fractures we used 4.8-mm and 6-mm beads. The prepared beads were placed at the site of infection and in close proximity of the implants, and the wound was then closed. Particular attention was given to the reconstruction and closure of the anatomical planes, in order to seal the compartment. This reduces the risk of wound drainage due to the progressive degradation of calcium sulfate.

After calcium sulfate beads implantation no further debridement procedure was performed.

Postoperative care

Postoperatively, empirical treatment with broad-spectrum antibiotics therapy was administered intravenously according to internal guidelines at our hospital after an infectious disease specialist evaluation. The antibiotic regimen consisted in Daptomycin 8 mg/kg/day + Piperacillin/Tazobactam 4,5 gr x 3–4 times a day or Cefepime 2 gr x 3 times a day. If an allergy to Beta-lactams was found Daptomycin was administered in combination with oral Ciprofloxacin 500 mg x 2 times a day.

Antibiotic therapy was modified in accordance with our institutional infectious disease service when antibiogram results of intraoperative culture samples were available. The DAPRI procedure was followed by a 2-week course of intravenous antibiotic therapy; after this period antiobiotic therapy was switched to oral administration when possible for another 10 weeks, completing a total of 12 weeks. When switch to an oral regimen took place, high dosage and high bioavailability antibiotics were used according to the pathogen antibiogram profile.

After discharge, once stable clinical conditions were achieved, our patients underwent a rehabilitation process and a clinical and radiological follow-up. Follow-up with the infectious disease specialist was scheduled at 4, 8 and 12 weeks from the start of antibiotic therapy. Blood tests for WBC, ESR, CRP and renal function markers were performed every two weeks. If the patients experienced any alteration of the local and or systemic conditions or an increase of serum inflammatory markers was detected, an urgent ambulatory evaluation was scheduled and the need for further testing was discussed. The procedure was considered successful when clinical presentation and serologic tests (erythrocyte sedimentation rate, C-reactive protein, and D-Dimer) remained normal after withdrawal of antibiotic treatment.

Orthopedic follow-up visits were scheduled at 1, 3, 6 and 12 months after surgery. At each step of the follow-up wound status, radiological signs of bone healing, gait and functional status of the patient were evaluated.

Results

During the period between January 2019 and December 2021 seven patients (4 males, 3 females) were treated with DAPRI for FRI at our institution. Of these patients, 5 had acute pelvic and acetabular fracture (3 acetabular fractures, 1 vertical shear and 1

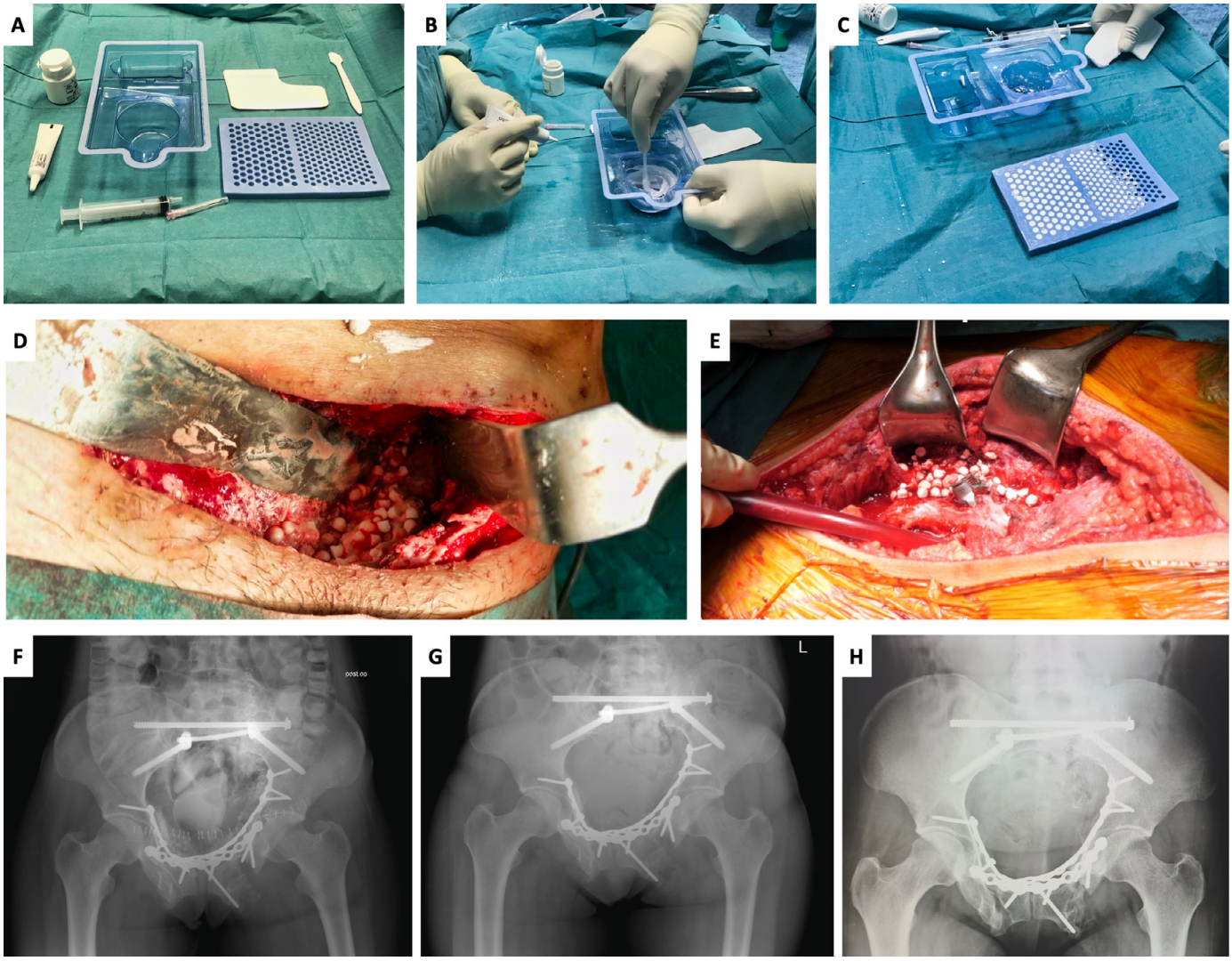

Fig. 1. Intraoperative images of calcium sulfate application and postoperative radiographs in Patient 4. A: calcium sulfate preparation kit on a new back table, ready for beads preparation. B: mixing process after antibiotic addition. C: calcium sulfate beads preparation using 4.8- and 6-mm diameter molds. D-E: positioning of calcium sulfate beads near acetabular and spino-pelvic fixation devices after debridement. F: calcium sulfate beads as seen post-operatively in plain radiography near acetabular and spino-pelvic implants. G: pelvic radiography taken at 1-month follow-up shows almost complete reabsorption of calcium sulfate beads. H: pelvic radiography taken at 12-month follow-up shows complete reabsorption of calcium sulfate and good bone formation.

with open combined fractures) in addition to 2 malunited pelvic cases treated with corrective osteotomies. The mean age of the patients was 38.7 years (range: 16–53 y/o, SD: ±12.3 years). The average time from initial surgery to the first debridement procedure was 12.3 days (range: 8–19 days, SD:± 4.5 days). The total number of surgeries performed in each patient to treat the infection ranged from 2 to 5 (see Table 1). After the DAPRI procedure no further surgical debridement was required in all patients. Complete wound healing was achieved in all patients. Average hospital stay was 35.2 days (range, 21–75 days), including the initial surgical treatment of osteosynthesis. We were able to identify the pathogenic organism in 5 out of 7 cases.

The average follow-up was 9 months (range, 6–16 months). In all patients, radiological evidence of complete bone healing was found during follow-up evaluation, with no need for implant removal. Average time of bony union was 4.3 months (range, 3–6 months). All patients regained full weight-bearing and walking without aids with satisfactory functional recovery.

Out of the possible complications described in literature relating to the use of Stimulan, we reported two cases of excessive wound drainage with a superficial fluid collection that needed surgical drainage; after cultural examination of the fluid no pathogen was detected. No cases of transient hypercalcemia and heterotopic ossification were observed. No clinical, laboratory or radiological evidence of infection was detected during follow-up in all cases.

Discussion

The present study described the use of a DAPRI technique in early onset deep pelvic infections with the aim of improving the outcomes of the standard debridement procedures. According to the preliminary results reported in the present study, the success rate of the DAPRI technique in both eradicating infection and allowing bone union in early FRI of the pelvis and acetabulum was 100%.

We believe these results may be associated with multiple factors, including:

- appropriate timing in early onset infections
- performance of serial debridement surgeries with thorough removal of macroscopically infected tissue

- abundant vascularization of the pelvic region
- high local concentration of antibiotics
- use of chlorhexidine gluconate

All patients in our study had early onset infection, treated within four weeks from internal fixation, and local conditions allowed for the possibility of doing an extensive debridement. In the early stage of FRI, biofilm formation appears to be in an immature stage without obvious osteomyelitis, therefore debridement may eradicate most of the bacteria and/or biofilm [21].

The choice of performing multiple debridement surgeries was a major difference between our technique and the traditional DAPRI proposed for PJIs. While a meticulous open debridement in a single surgical intervention has been shown to lead to good healing rates in acute infections, as the biofilm is still immature [14,22,23], previous articles have described the possibility of performing serial debridements with good clinical results both when dealing with FRIs and PJIs [24,25]. Buijs et al., in particular, have described the need for multiple debridements in 52% of FRI patients treated with a DAIR procedure [25]. A single-stage eradication, when possible, should always be the primary aim for FRI, especially when considering the possible drawbacks involved with multiple operations such as multiple anesthesia, damage to local tissues, increased risk of wound healing complications and worse functional outcomes. However, when dealing with pelvic and acetabular trauma in particular, the surgeon should be aware that serial debridement procedures might be required and therefore, the need for a multi-step surgical treatment has to be carefully considered. There are many features specific for pelvic trauma that led us to choose serial debridement as our preferred treatment option in this case series. The DAPRI technique described by Ghirardelli et al. [15] for infected total hip arthroplasty is applied only after isolation of the micro-organism following a fluoroscopy guided hip aspiration (culture positive PJI). This aspiration procedure is not applicable in the setting of pelvic ring or acetabular fractures, due to the surrounding anatomical structures and the absence of a delimited joint cavity. In addition, infections in the pelvis have a higher risk of causing systemic sepsis than joint infections; consequently, it is often necessary to carry out a first debridement as soon as possible, without waiting for the results of culture tests.

In summary, we believe that the need for multiple debridement surgeries in pelvic ring and acetabulum FRI is mainly related to:

- the absence of a well-defined cavity containing the infection
- the presence of anatomical structures that must be preserved, even if in close contact with the infected area (e.g., urinary bladder, nerves, etc.…)
- the inability to ensure complete removal of the biofilm in a single surgery: the eradication of the infection must be confirmed by subsequent cultures on surgical specimens

Of course, subjecting patients to multiple surgeries also carries risks related to repeated general anesthesia and the aforementioned possible increase in complications. However, taking into account risks and benefits, we consider it appropriate to perform serial debridement surgeries in order to eradicate the infection and promote patient recovery. We believe that a single-stage surgical eradication of infection, and placement of local antibiotic carrier, can still be considered for these patients, but only in the event of satisfactory radical debridement and local conditions. Further clinical research will be necessary in order to confirm the real efficacy of serial debridement, compared with single-stage procedures, in patients with acute FRI after pelvic surgery.

As previously mentioned, there are multiple factors we believed contributed to the positive clinical outcomes in this case series. The extensive vascular supply of the pelvic region allows for rapid bone consolidation and abundant local supply of systemic antibiotics [13]. Chlorhexidine gluconate is one of the most widely used antiseptics for decontaminating skin, mucous membranes and medical devices; it has a direct bactericidal effect due to precipitation and/or coagulation of bacterial cytoplasmic contents caused by protein cross-linking [26]. Based on our findings and experience, the use of a 4% chlorhexidine gluconate-added brush allowed us to mechanically and chemically remove the preformed biofilm in these early FRI.

The use of local antibiotic therapy through a bioabsorbable carrier may play an important role in the management of early infection. Historically, polymethylmethacrylate (PMMA) beads have been used in PJI. However, PMMA is not resorbable, so its use requires a second intervention to remove it. It also has the intrinsic risk of becoming a substrate for bacterial colonization and favoring the development of antibiotic resistance [27]. The addition of calcium sulfate beads constitutes a remarkable innovation as it allows to create an environment unfavorable to bacterial proliferation and biofilm synthesis for a period of time up to 40 days [28,29]; moreover, these beads are completely re-absorbable, leaving no media for the proliferation of pathogens. Another advantage of calcium sulfate beads is their flexibility in terms of being mixed with antibiogram-driven antibiotics; furthermore, heat labile antibiotics can be added because there are no exothermic reactions during calcium sulfate beads preparation on the back table [30]. Nevertheless, the use of calcium sulfate beads is not completely free from complications. McPherson et al. [31]. reported the presence of a copious discharge from the wound requiring surgical intervention in 3.2% of patients following the use of calcium sulfate beads to treat PJI. The formation of heterotopic ossifications is also another complication reported in 1.2% of patients following calcium sulfate beads use. We reported two cases of excessive superficial fluid discharge that required drainage. However, no pathogens were detected in the fluid and these patients achieved bony union and infection eradication similarly to the others.

The current study has many limitations. The small sample size, the retrospective nature of the study, the relative short-term follow-up and combination of acute fractures with malunited cases are the main ones. On considering that pelvic fractures make up approximately 3% of all fractures, and that prevalence of surgical site infection following fixation of pelvic ring injury is 2.1% [3], this disastrous complication fortunately represents a rare occurrence. This limits collection of an adequate sample in a single center. Therefore, there will be a need for multicentric studies to confirm the efficacy of the DAPRI technique in patients with early pelvic FRI.

Conclusion

DAPRI is a promising technique, which can be used safely in the treatment of early pelvic fracture-related infections. The preliminary results in the present study were encouraging, which indicated that this technique may play a role in the management of early infection after osteosynthesis in trauma patients.

Declaration of Competing Interest

Authors had nothing to disclose about conflict of interest.

References

[1] McCormack R, Strauss EJ, Alwattar BJ, Tejwani NC. Diagnosis and management of pelvic fractures. Bull NYU Hosp Jt Dis 2010;68:281–91.
[2] Papakostidis C, Kanakaris NK, Kontakis G, Giannoudis PV. Pelvic ring disruptions: treatment modalities and analysis of outcomes. Int Orthop 2009;33:329–38. doi:10.1007/s00264-008-0555-6.
[3] Kanakaris NK, Ciriello V, Stavrou PZ, West RM, Giannoudis PV. Deep infection following reconstruction of pelvic fractures: prevalence, characteristics, and predisposing risk factors. Eur J Trauma Emerg Surg 2021. doi:10.1007/s00068-021-01618-y.

[4] Tschoeke S.K., Ertel W., Franklin C.B. Immunoparalysis after multiple trauma 2007:1346–57. doi:10.1016/j.injury.2007.08.041.
[5] Sagi HC, Dziadosz D, Mir H, Virani N, Olson C. Obesity, leukocytosis, embolization, and injury severity increase the risk for deep postoperative wound infection after pelvic and acetabular surgery. J Orthop Trauma 2013;27:6–10. doi:10.1097/BOT.0b013e31825cf382.
[6] Suzuki T, Morgan SJ, Smith WR, Stahel PF, Gillani SA, Hak DJ. Postoperative surgical site infection following acetabular fracture fixation. Injury 2010;41:396–9. doi:10.1016/j.injury.2009.11.005.
[7] Bezstarosti H, Van Lieshout EMM, Voskamp LW, Kortram K, Obremskey W, McNally MA, et al. Insights into treatment and outcome of fracture-related infection: a systematic literature review. Arch Orthop Trauma Surg 2019;139:61–72. doi:10.1007/s00402-018-3048-0.
[8] Qiu XS, Cheng B, Chen YX, Qi XY, Sha WP, Chen GZ. Coating the plate with antibiotic cement to treat early infection after fracture fixation with retention of the implants: a technical note. BMC Musculoskelet Disord 2018;19:1–6. doi:10.1186/s12891-018-2285-2.
[9] Berkes M, Obremskey WT, Scannell B, Ellington JK, Hymes RA, Bosse M. Maintenance of Hardware After Early Postoperative Infection Following Fracture Internal Fixation. J Bone Jt Surg-Am Vol 2010;92:823–8. doi:10.2106/JBJS.I.00470.
[10] Rightmire E, Zurakowski D, Vrahas M. Acute infections after fracture repair: management with hardware in place. Clin Orthop 2008;466:466–72. doi:10.1007/s11999-007-0053-y.
[11] Trampuz A, Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. Injury 2006;37:59–66. doi:10.1016/j.injury.2006.04.010.
[12] Steinmetz S, Wernly D, Moerenhout K, Trampuz A, Borens O. Infection after Fracture Fixation. EFORT Open Rev 2019;4:145–52. doi:10.1302/2058-5241.4.180093.
[13] Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, et al. Fracture-related infection: a consensus on definition from an international expert group. Injury 2018;49:505–10. doi:10.1016/j.injury.2017.08.040.
[14] Calanna F, Chen F, Risitano S, Vorhies JS, Franceschini M, Giori NJ, et al. Debridement, antibiotic pearls, and retention of the implant (DAPRI): a modified technique for implant retention in total knee arthroplasty PJI treatment. J Orthop Surg 2019;27:1–6. doi:10.1177/2309499019874413.
[15] Ghirardelli S, Fidanza A, Prati P, Iannotti F, Indelli PF. Debridement, antibiotic pearls, and retention of the implant in the treatment of infected total hip arthroplasty. HIP Int 2020;30:34–41. doi:10.1177/1120700020929314.
[16] Aboltins CA, Dowsey MM, Buising KL, Peel TN, Daffy JR, Choong PFM, et al. Gram-negative prosthetic joint infection treated with debridement, prosthesis retention and antibiotic regimens including a fluoroquinolone. Clin Microbiol Infect 2011;17:862–7. doi:10.1111/j.1469-0691.2010.03361.x.
[17] Metsemakers W-J, Fragomen AT, Moriarty TF, Morgenstern M, Egol KA, Zalavras C, et al. Evidence-Based Recommendations for Local Antimicrobial Strategies and Dead Space Management in Fracture-Related Infection. J Orthop Trauma 2020;34:18–29. doi:10.1097/BOT.0000000000001615.
[18] Metsemakers W-J, Morgenstern M, Senneville E, Borens O, Govaert GAM, et al., On behalf of the Fracture-Related Infection (FRI) group General treatment principles for fracture-related infection: recommendations from an international expert group. Arch Orthop Trauma Surg 2020;140:1013–27. doi:10.1007/s00402-019-03287-4.
[19] Tetreault MW, Wetters NG, Aggarwal V, Mont M, Parvizi J, Della Valle CJ. The Chitranjan Ranawat Award: should prophylactic antibiotics be withheld before revision surgery to obtain appropriate cultures? Clin Orthop 2014;472:52–6. doi:10.1007/s11999-013-3016-5.
[20] Bedenčič K, Kavčič M, Faganeli N, Mihalič R, Mavčič B, Dolenc J, et al. Does preoperative antimicrobial prophylaxis influence the diagnostic potential of periprosthetic tissues in hip or knee infections? Clin Orthop 2016;474:258–64. doi:10.1007/s11999-015-4486-4.
[21] Nishitani K, Sutipornpalangkul W, de Mesy, Bentley KL, Varrone JJ, Bello-Irizarry SN, Ito H, et al. Quantifying the natural history of biofilm formation in vivo during the establishment of chronic implant-associated *Staphylococcus aureus* osteomyelitis in mice to identify critical pathogen and host factors: QUANTIFYING IMPLANT BIOFILM IN MICE. J Orthop Res 2015;33:1311–19. doi:10.1002/jor.22907.
[22] Sendi P, Lötscher PO, Kessler B, Graber P, Zimmerli W, Clauss M. Debridement and implant retention in the management of hip periprosthetic joint infection: outcomes following guided and rapid treatment at a single centre. Bone Jt J 2017;99-B:330–6. doi:10.1302/0301-620X.99B3.BJJ-2016-0609.R1.
[23] Grammatopoulos G, Kendrick B, McNally M, Athanasou NA, Atkins B, McLardy-Smith P, et al. Outcome following debridement, antibiotics, and implant retention in hip periprosthetic joint infection—an 18-year experience. J Arthroplasty 2017;32:2248–55. doi:10.1016/j.arth.2017.02.066.
[24] Chung AS, Niesen MC, Graber TJ, Schwartz AJ, Beauchamp CP, Clarke HD, et al. Two-stage debridement with prosthesis retention for acute periprosthetic joint infections. J Arthroplasty 2019;34:1207–13. doi:10.1016/j.arth.2019.02.013.
[25] Buijs MaS, van den Kieboom J, Sliepen J, Wever KLH, van Breugel JM, Hietbrink F, et al. Outcome and risk factors for recurrence of early onset fracture-related infections treated with debridement, antibiotics and implant retention: results of a large retrospective multicentre cohort study. Injury 2022;53:3930–7. doi:10.1016/j.injury.2022.10.017.
[26] Schmidt K, Estes C, McLaren A, Spangehl MJ. Chlorhexidine antiseptic irrigation eradicates staphylococcus epidermidis from biofilm: an in vitro study. Clin Orthop 2018;476:648–53. doi:10.1007/s11999.0000000000000052.
[27] Chen AF, Parvizi J. Antibiotic-loaded bone cement and periprosthetic joint infection. J Long Term Eff Med Implants 2014;24:89–97. doi:10.1615/jlongtermeffmedimplants.2013010238.
[28] Aiken SS, Cooper JJ, Florance H, Robinson MT, Michell S. Local release of antibiotics for surgical site infection management using high-purity calcium sulfate: an in vitro elution study. Surg Infect 2015;16:54–61. doi:10.1089/sur.2013.162.
[29] Cooper J, Florance H, McKinnon J, Laycock P, Aiken S. Elution profiles of tobramycin and vancomycin from high-purity calcium sulphate beads incubated in a range of simulated body fluids. J Biomater Appl 2016;31:357–65. doi:10.1177/0885328216663392.
[30] Knecht CS, Moley JP, McGrath MS, Granger JF, Stoodley P, Dusane DH. Antibiotic loaded calcium sulfate bead and pulse lavage eradicates biofilms on metal implant materials in vitro. J Orthop Res 2018;36:2349–54. doi:10.1002/jor.23903.
[31] McPherson MD FACS E, Dipane BA M, Sherif MD S. Dissolvable antibiotic beads in treatment of periprosthetic joint infection and revision arthroplasty - the use of synthetic pure calcium sulfate (stimulan®) impregnated with vancomycin & tobramycin. Reconstr Rev 2013;3. doi:10.15438/rr.v3i1.27.