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One-Stage Revision with Cage Replacement as Treatment for Refractory Infections after Tibial Tuberosity Advancement in 7 Dogs

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Abstract

The aim of this article was to report surgical and medical management, and to evaluate complications and outcome of dogs treated for refractory infection after tibial tuberosity advancement (TTA) with a one-stage revision surgery consisting of implant removal and replacement of a TTA cage. It was a retrospective case series. Seven cases were included in this study. Loss of advancement of the tibial tuberosity or tibial crest fractures did not occur in any case. One-stage revision surgery was successful in 5/7 cases (71%) with good long-term outcomes. Persistent infection resulted in removal of the replaced new cage in 2/7 cases (29%), of which one was associated with septic arthritis caused by multi-resistant bacteria. One-stage revision with immediate replacement of a new TTA cage successfully prevented loss of advancement of the tibial tuberosity and tibial crest fractures in this short case series. Further studies investigating possible improvements in the treatment protocol for refractory infection after TTA are warranted.

Keywords
- tibial tuberosity advancement cage
- one-stage revision
- surgical site infection
- dogs
- implant removal

Introduction

Tibial tuberosity advancement (TTA) is a commonly performed surgical technique to treat dogs with cranial cruciate ligament deficiency.[1–4] The tibial tuberosity is maintained in an advanced position by a cage placed in the osteotomy gap and stabilized using a separate plate or a combined plate/cage construct.[4,5] The most frequent complication seen with this procedure is surgical site infection (SSI), reported in 5.4 to 7.4% of cases.[1–3,6] Based on criteria developed by the US Centers for Disease Control and Prevention (CDC), SSI can be classified as either superficial SSI, deep SSI or organ/space SSI.[7,8] Whereas medical treatment is usually successful in case of a superficial SSI, deep and organ/space SSI associated with orthopaedic implants frequently necessitate implant removal.[2,9–12] After TTA specifically, implants were removed in 33% of cases with a deep SSI and in 8% of cases this included the TTA cage.[1–3,6] Tibial tuberosity advancement cage removal results in reduced buttress support of the tibial crest, leading to a fracture of the tibial crest necessitating further surgery in 15% of cases.[12] Additionally, we have observed loss of advancement of the tibial tuberosity due to remodelling of the bone and collapse of the osteotomy gap (unpublished data). In order to prevent loss of advancement and tibial crest fractures, a one-stage revision surgery consisting of implant removal and replacement of the TTA cage (hereafter referred to as 'one-stage revision') can be considered. The purpose of this study was to report surgical and medical management, and to evaluate complications and outcome of dogs treated for refractory infection after TTA with one-stage revision.

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Materials and Methods

Medical records of cases that underwent one-stage revision between September 2016 and March 2021 were retrieved from two referral centres. For inclusion, a deep or organ/space SSI involving the cage had to be present. By definition, a deep SSI involves deeper tissues such as fascia and muscle, and includes at least one of the following criteria: purulent drainage from the deep incision; spontaneous deep incisional dehiscence; abscess or other evidence of infection identified in deep tissues via examination, reoperation, histopathology, or radiographic examination.[7,8] When the SSI involves structures deeper than the fascial/muscle layers that are opened during surgery, such as bone or a joint space, it is classified as an organ/space SSI.[7] In the current CDC guidelines, implant-related infections are classified as SSI only when they occur within 90 days of surgery.[7,12] As many of these infections in veterinary surgery are diagnosed after this time frame, this criterium was not applied.[12] Information was collected regarding signalment, findings of physical and radiographic examinations, initial and revision surgical procedures, results of bacterial cultures, use of antibiotic medications and clinical and radiological follow-up. Intra- and postoperative complications were graded as minor when no further therapy was needed or as major when further medical or surgical treatment related to the revision was indicated.[13] Follow-up was considered short-term (< 3 months since revision), mid-term (3–12 months since revision) or long-term (> 12 months since revision). Outcome was graded as successful when clinical and/or radiographic signs of infection did not recur at long-term follow-up after cage replacement.[7] Outcome was graded as unsuccessful when signs of infection recurred or persisted or the reimplanted cage was removed.

Results

Patient Characteristics

Eight cases were identified in which a TTA cage was replaced. One case was excluded because it did not fulfil the SSI criteria mentioned above. The remaining seven cases were included (►**Table 1**). There were four neutered females, one intact female and two neutered males, aged between 14 and 90 months (median = 68 months), with a bodyweight ranging from 24 to 52 kg (median = 33 kg). There were no recorded comorbidities. As primary surgery, six cases had undergone a medial mini-arthrotomy and standard TTA procedure at one of the two referral centres participating in this study (implants from Eickemeyer, Tuttlingen, Germany [$n = 3$], or Kyon AG, Zurich, Switzerland [$n = 3$]). Case number 7 had undergone a TTA Rapid procedure and arthroscopy at a referring clinic (implants from Rita Leibinger GmbH & Co. KG., Mühlheim an der Donau, Germany). All applied implants were made of titanium. Infections were first suspected between 7 and 122 days after surgery (median = 35 days). All dogs were lame on the operated limb, graded as 5/6 in three cases (barely weight-bearing) and not graded in the other cases. Abnormalities indicating involvement of the TTA cage were present in all cases and consisted of osteolysis adjacent to the cage ($n = 4$, ►**Fig. 1**) and/or a sinus tract ($n = 4$) or fluctuant swelling ($n = 2$) over the cage. One case developed an open wound over the implants. Septic arthritis was diagnosed in 3/6 cases in which synovial fluid analysis was performed. In five cases, bony healing was below expectation, based on the authors' experience, with no bone bridging the proximal half of the osteotomy gap at the time of revision surgery. All cases had a positive bacterial culture obtained pre- and/or intra-operative. Bacteriology results and instituted antibacterial treatment are summarized in ►**Table 1**. In case number 1 the attending surgeon performed revision surgery directly after finding a multi-drug-resistant bacterial strain. In the other cases, antibiotic therapy resulted in complete (case number 2, 3, 4, and 6) or partial (case number 5 and 7) remission of clinical signs. After termination of antibiotic therapy, signs of infection recurred or worsened in all cases and lameness worsened in 6/7 cases. Lameness did not reoccur in case number 5, but ongoing infection was evident from a sinus tract originating from the cage. In this case, the plate and the fork were previously removed and radiographs showed osteolysis cranial to the cage.

Revision Surgery

The interval between the original surgery and revision was 45 to 244 days (median = 118 days). After informing the owners about different treatment options, with or without placement of a new cage, owner consent was obtained. Anaesthetic and analgesic protocols differed based on surgeon preference. A medial parapatellar arthrotomy was performed before implant removal in five cases. In case number 2 and 3, a medial meniscal injury was found and treated. In case number 4, 6, and 7 septic arthritis was present and the stifle was flushed with sterile saline and in one case macerated material was removed from the joint and a gentamicin-impregnated collagen sponge (Garacol 32.5 mg, EUSA Pharma [Europe] Ltd., Oxford, UK) was placed intra-articularly. Preoperative arthrocentesis was performed in one of the two cases in which an arthrotomy was not performed, revealing normal synovia and a negative bacterial culture.

After routine closure of the joint, implant removal was performed through an incision directly over the implants. All implants were removed, with the exception of a broken screw in case number 7 and a broken prong in case number 4. Macroscopically abnormal tissue was debrided, followed by curettage of bone that had been in contact with the cage and any loose screws. Hereby, abnormal soft tissues and spongiosa were removed while cortical bone was retained. After extensive flushing, a new titanium cage of the same size and manufacturer was placed in the original opening. In the majority of cases the new cage had a press-fit, occasionally requiring careful impaction with a mallet. This resulted in a stable cage, except in case number 5, in which a single screw was placed for stabilization. Auxiliary local treatment was variably used, with demineralized bone matrix with biphasic calcium phosphate ($n = 1$; Fusion Xpress, Kyon AG, Zurich, Switzerland), a gentamicin-impregnated collagen sponge

Table 1 Overview of patient characteristics, bacteriology results, treatment and outcome

Case	Signalment	Bacteriology results (material used for bacterial culture)		Antibiotic therapy before revision	Septic arthritis	Antibiotic therapy during and after revision	Auxiliary local treatment	Follow-up duration (mo)	Successful outcome
		Pre-operative	Intra-operative						
1	Labrador Retriever Sex: FN Age: 5 y 1 mo BW: 30 kg	Staphylococcus aureus R: cephalosporins, amoxycillin/clavulanic acid S: fluoroquinolones (FNA fluctuant swelling)	Not performed	None after bacteriology	No; synovial fluid analysis not performed	Perioperative: IV marbofloxacin Postoperative: PO marbofloxacin 5 weeks	None	33	Yes
2	Galgo Espagnol Sex: FN Age: 5 y 8 mo BW: 33 kg	Staphylococcus intermedius S: cephalosporins, amoxycillin/clavulanic acid (swab from sinus tract)	Staphylococcus intermedius S: cephalosporins, amoxycillin/clavulanic acid (swab of implant surface)	PO amoxycillin/clavulanic acid for 6 weeks	No	Perioperative: IV amoxycillin/clavulanic acid Postoperative: PO amoxycillin/clavulanic acid for 4 weeks	Garacol[a] in cage Fusion Xpress[b]	31	Yes
3	Entlebucher Mountain dog Sex: MN Age: 6 y 10 mo BW: 24 kg	Not performed	Staphylococcus intermedius S: cephalosporins, amoxycillin/clavulanic acid (implant)	PO amoxycillin/clavulanic acid for 6 weeks	No	Perioperative: IV amoxycillin/clavulanic acid Postoperative: PO amoxycillin/clavulanic acid for 6 weeks	None	5	No
4	Akita Inu Sex: FN Age: 6 y 1 mo BW: 35 kg	Staphylococcus aureus S: cephalosporins, amoxycillin/clavulanic acid (FNA fluctuant swelling)	Negative (implant)	PO amoxycillin/clavulanic acid for 4 weeks, cefalexin for 3 weeks	Yes	Perioperative: IV cefazoline Postoperative: PO cefalexin for 20 days	Cancellous bone autograft	42	Yes
5	American Staffordshire Terrier Sex: FN Age: 6 y 6 mo BW: 26 kg	Negative (arthrocentesis)	Staphylococcus pseudointermedius S: cephalosporins, amoxycillin/clavulanic acid (implant)	PO amoxycillin/clavulanic acid[a] for 15 days	No	Perioperative: IV cefazoline Postoperative: PO cefalexin for 15 days	Screw fixation	18	Yes
6	Bandog Sex: MN Age: 2 y 3 mo BW: 52 kg	Staphylococcus aureus S: cephalosporins, amoxycillin/clavulanic acid, doxycycline (swab from sinus tract and arthrocentesis, same result)	Staphylococcus aureus S: cephalosporins, amoxycillin/clavulanic acid, doxycycline (implant)	PO doxycycline for 8 weeks	Yes	Perioperative: none Postoperative: SC enrofloxacin for 10 days	Cancellous bone autograft	60	Yes
7	Anatolian Shepherd, Sex: F Age: 1 y 2 mo BW: 52 kg	Pseudomomonas aeruginosa R: cephalosporins, amoxycillin/clavulanic acid I: fluoroquinolones S: gentamicin (swab from sinus tract)	Not performed	SC gentamycin for 7 days,	Yes	Perioperative: IV cefazoline Postoperative: intra-articular gentamicin twice with one week interval, starting 2 weeks after revision	Garacol[a] IA and in cage	18	No

Abbreviations: BW, body weight; FN, female neutered; FNA, fine-needle aspiration; I, antibiotics for which bacterial strain shows intermediate susceptibility; IA, intra-articularly; IV, intravenously; MN, male neutered; PO, per os; R, antibiotics that bacterial strain is resistant to; S, antibiotics that bacterial strain is susceptible to; SC, subcutaneously.

[a]Gentamicin-impregnated collagen sponge, Garacol 32.5 mg, EUSA Pharma (Europe) Ltd., Oxford, UK

[b]Demineralized bone matrix with biphasic calcium phosphate, Fusion Xpress, Kyon AG, Zurich, Switzerland

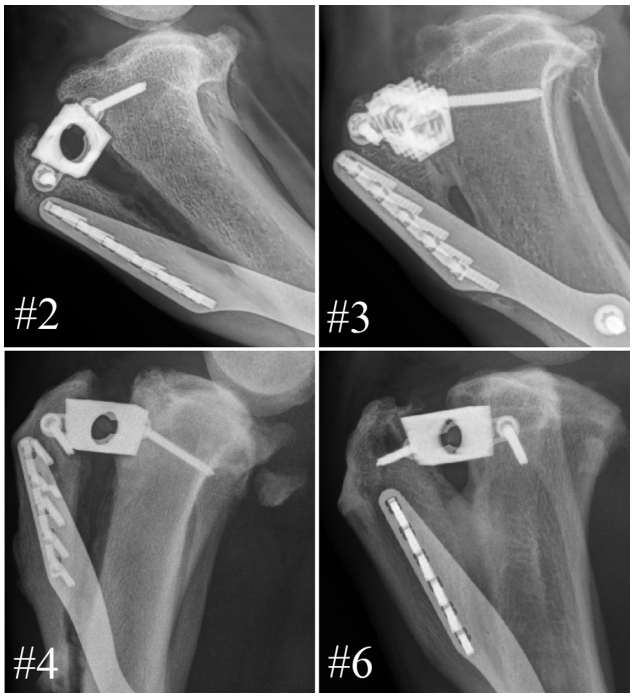

Fig. 1 Radiographs of cases 2, 3, 4, and 6 taken directly before revision, showing osteolysis surrounding the cage (case 2) or craniodistal (cases 3 and 4) or cranioproximal (case 6) to the cage. Revision took place 4, 8, 3, and 4 months after the original procedure respectively.

($n=2$; Garacol 32.5mg, EUSA Pharma Ltd., Oxford, UK) or autologous cancellous bone ($n=2$) placed in and surrounding the cage. Postoperative radiographs were available in six cases and showed no signs of complications such as displacement of the tibial crest, fissures or fractures in five cases. In case number 7 positioning was inadequate for proper assessment. Peri- and postoperative antibiotic medications were administered based on the antibiogram, as detailed in ►**Table 1**. Non-steroidal anti-inflammatory drugs (NSAIDs) ± tramadol or gabapentin were prescribed for 10 to 21 days postoperatively. Owners were instructed to restrict activity to leash walks for 6 weeks and in one case a soft padded bandage was placed for 2 weeks.

Follow-Up

Short-term follow-up included clinical examinations at 2 to 3 weeks ($n=7$) and at 5 to 8 weeks ($n=6$) after revision. Arthrocentesis was performed in case number 1 (6 weeks after revision) and case number 7 (2 weeks after revision). Radiographs were obtained 6 to 8 weeks after revision for case number 1, 2, and 3. One minor postoperative complication occurred, with self-limiting pressure sores developing in the case in which a soft padded bandage was applied. There were two major postoperative complications, consisting of removal of the new cage in case number 3 and 7, detailed below. Abnormalities indicating infection were not noted in the remaining five cases.

In case number 3, lameness recurred 3 weeks after discontinuation of antibiotic medications. Radiography revealed thickening of the patellar tendon and persistent lucency surrounding the cage. In the opening of the cage, bone was visible. The cage was explanted 2.5 months after revision. There were no clear signs of infection but the cage was subjectively easy to remove due to the absence of osseointegration. Bacterial culture of the cage was negative. In the interval between revision and removal of the new cage, a bony bridge formed between the tibial metaphysis and proximal tibial crest, lateral to the cage. This bone was not present at the time of revision, 8 months after the original TTA procedure (►**Fig. 2**). Two months after final implant removal, the owner reported lameness to be minimal.

In case number 7, lameness decreased after revision but was still considered excessive. Two weeks after revision, arthrocentesis revealed clouded synovia and growth of the

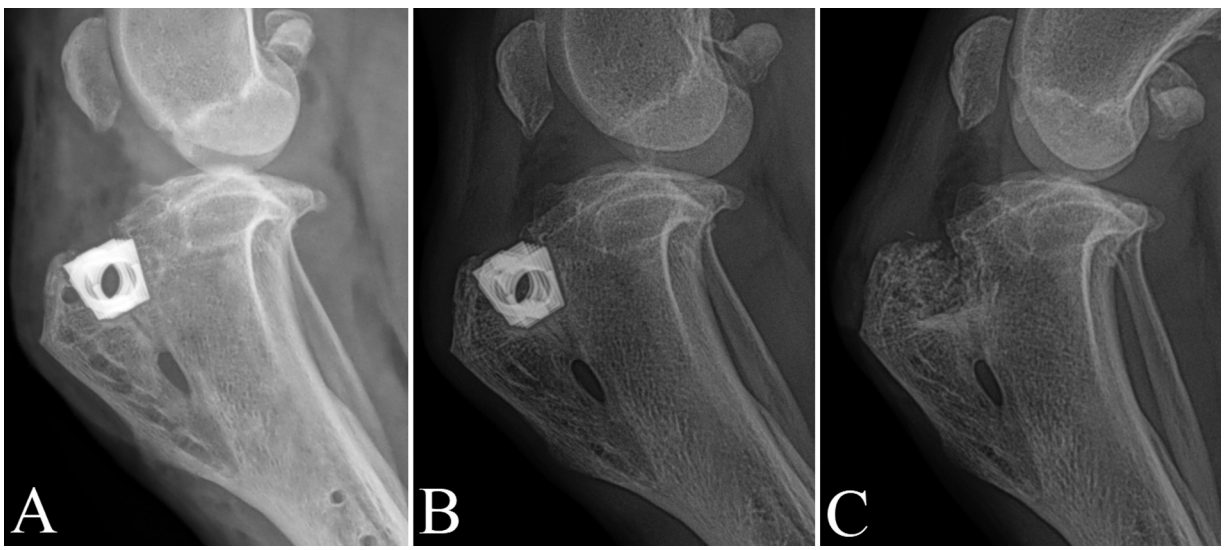

Fig. 2 Radiographs of case 3, directly after revision (**A**) and directly before (**B**) and after (**C**) definitive removal of the cage. Note that bone is visible in the opening of the cage in B, but not in A. After removal of the cage, a bony bridge between the tibial metaphysis and proximal tibial crest is visible.

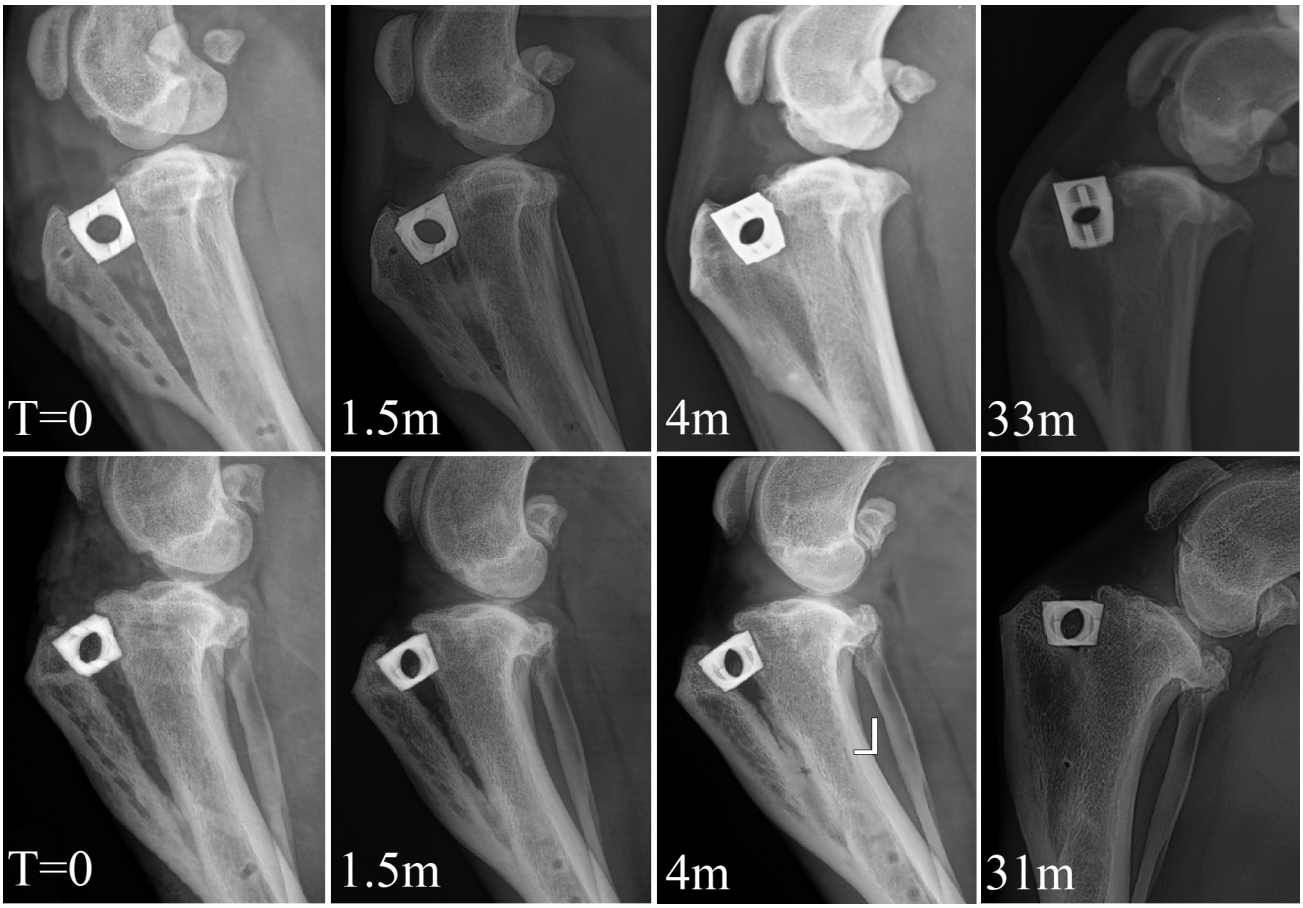

Fig. 3 Radiographs of cases 1 (*top*) and 2 (*bottom*). Radiographs directly after revision show the new cage in situ, without screw fixation. As revision took place respectively 4 and 8 months after the original procedure in these cases, bone formation in the osteotomy is clearly below expectations. Radiographs taken at 1.5, 4, and 33 or 31 months after revision show progressive bone formation in the osteotomy, albeit slower in the second case.

same bacterial strain cultured preoperatively, susceptible to gentamicin only. Due to concerns about renal toxicity, gentamicin was not administered systemically. Flushing the stifle and intra-articular administration of gentamicin twice in 2 weeks was unsuccessful and the new cage was removed 5 weeks after revision. The remainder of the broken screw, left in place during revision, was not removed. Radiographs were not acquired shortly after cage removal and thus we could not evaluate progression of osteotomy gap healing. Articular weekly flushing and intra-articular gentamicin administration were still unsuccessful. Removal of the remaining part of the screw and three consecutive days of intravenous gentamicin and ceftazidime plus intra- and periarticular gentamicin-impregnated gelatin sponges ultimately resolved the infection. A fracture or collapse of the tibial crest did not occur, and 8 months after final implant removal osteotomy gap healing was complete. Weight-bearing lameness persisted despite analgesics.

At mid-term follow-up in case number 1 and 2, clinical examination and radiographs showed progressive bone formation in the osteotomy gap and no signs of infection 4 months after revision (►**Fig. 3**). In case number 2, the lucent line surrounding the cage, that was still visible 4 months after revision, had disappeared by month 7.

Long term follow-up for the five cases with a retained cage was available for 18 to 60 months after revision (median = 33 months). Clinical examination (case number 1, 2, and 4) or telephone interviews (case number 5 and 6) did not indicate infection or other implant-related complications. Radiographs of case number 1 and 2, taken 33 and 31 months after revision, revealed no signs of persistent infection (►**Fig. 3**). Case number 1 and 4 were receiving NSAIDs due to mild lameness related to the stifle, which was attributed to osteoarthritis based on clinical examination findings, combined with, in case number 1, radiographs and synovial fluid analysis. Case number 2, 5, and 6 had a normal activity level and were free of lameness, besides mild stiffness when rising in case number 6.

Outcome was graded as successful in 5/7 and unsuccessful in 2/7.

Discussion

This is the second study to describe the outcome after TTA cage removal and the first study describing the outcome of one-stage revision to treat refractory infections after TTA.[12] Loss of advancement or tibial crest fractures were not observed in any of our cases. One-stage revision surgery was successful in 5/7 cases (71%), with good long-term

outcomes. In 2/7 cases (29%) the new cage was ultimately removed. In one of these, the new cage was in place long enough to allow bone formation to support the proximal tibial crest. In the study by Serratore and Barnhart, cage removal resulted in tibial crest fractures in 15% of cases.[12] Considering the severe consequences of tibial crest fractures or loss of advancement of the tibial tuberosity, providing prophylactic internal stabilization when a cage is removed seems appropriate, especially when healing of the osteotomy gap is limited as is seen in some of our cases. As revision cages were removed in 2/7 cases in this study, improvements in treatment protocol should be pursued.

Temporary pin fixation could provide an alternative stabilization technique. In two cases in the study by Serratore and Barnhart, a pin was placed proximal to the insertion point of the straight patellar ligament at the time of cage removal. The pins were ultimately removed, but tibial crest fractures did not occur in these cases. Degree of osteotomy gap healing was not reported.[12] Differences in the mean interval between the original procedure and onset of clinical signs of SSI exists between the study by Serratore and Barnhart (403 days) and our study (44 days).[12] Because in our study SSI occurred early after TTA surgery, there was less time for the osteotomy gap to heal. Therefore, it could be that the degree of osteotomy gap healing is lower, and thus the need for buttress support of the tibial crest is higher. Further studies are required to analyse whether pins can provide sufficient buttress support in cases with limited osteotomy gap healing.

In human medicine, one-stage revision is frequently performed to treat periprosthetic joint infections.[14,15] Successful one-stage revision of infected total hip replacements has also been described in four dogs.[16–19] Three key principles for successful one-stage revision of periprosthetic joint infections are identification of a causative organism susceptible to available antibiotic medications, radical debridement of affected tissues and administration of local and systemic antibiotics.[20]

Local antibiotic treatment in our study, used in 2/7 cases, consisted of gentamicin-impregnated gelatin sponges or repeated intra-articular gentamicin injections. Resulting local concentrations with gentamicin-impregnated gelatin sponges are initially high but fall to concentrations below the minimum inhibitory concentration (MIC) within 24 hours when placed in the inflamed canine stifle.[21] The same is expected with intra-articular gentamicin injections. In healthy horses, gentamicin administration by intra-articular injection or a gentamicin-impregnated collagen sponge leads to synovial concentrations above MIC for more than 24 hours.[22] However, synovitis is hypothesized to accelerate redistribution of gentamicin out of the joint and continuous joint infusion is advocated in clinical cases.[21,23] For prolonged effective concentrations, other carrier materials could be considered, such as polymerized polymethylmethacrylate or resorbable materials. These result in gentamicin concentrations above MIC for 7 to 12 and more than 30 days, respectively, in in vitro studies.[24] These findings are supported by human in vivo studies measuring gentamicin in drainage fluid and urine.[25,26] Once the antibiotic medication has dissolved, polymerized polymethylmethacrylate has a surface ideal for bacterial attachment and is best removed, whereas resorbable beads can be left in place.[16,24,27] Resorbable materials can also replace the metal TTA cage, possibly preventing persistent infection as the implant is resorbed completely. In addition, these materials can be loaded with antibiotic medications.[28] Resorbable cages were retained without consequences in four dogs with SSI, but whether the cages were involved in the SSI in these cases is unclear.[12,29,30] Alternatively, implants coated with an antimicrobial layer can be used. Titanium TTA cages with a silver coating (HyProtect, BioGate AG, Nürnberg, Germany) are available. In vitro studies evaluating silver-coated implants show prolonged ($>$ 28 days) suppression of bacterial growth and prevention of biofilm formation, good biocompatibility and no negative effect on osseointegration.[31,32] Human studies have confirmed lower rates of SSI with silver-coated implants and in 64 dogs treated with silver-coated tibial plateau levelling osteotomy plates only one infection occurred.[33–36]

Postoperative antibiotic medications were administered for 10 days to 6 weeks. Although a duration of at least 4 to 8 weeks, as recommended for osteomyelitis, seems prudent, the three cases with postoperative antibiotic medications for only 10 to 20 days were all successful.[37] The required duration of post-revision antibiotic medications remains to be determined.

Failure to identify the causative pathogen, or the presence of a pathogen resistant to available oral or local antibiotic medications, such as present in case number 7, would be a contra-indication for one-stage revision in human medicine.[20] Septic arthritis prevents radical debridement of all affected tissues as this would require en bloc removal of the entire joint capsule, which is not feasible in the context of TTA revision.[34] As two cases diagnosed with septic arthritis in our study had a successful outcome, it seems this is not a strict contra-indication for one-stage revision. However, factors that increase the risk for persistent infection could be reason to apply alternative stabilization techniques, such as temporary pins, which require further investigation.[38]

As a retrospective study including cases treated over the course of several years and at two different clinics, variation exists in the exact diagnostics and instituted treatments. Due to low numbers, drawing firm conclusions based on the differences between cases and their outcome is impossible. Available follow-up was variable and outcome was based on owner assessment in two cases. Radiographical and bacteriological examination at follow-up was lacking in three and four cases, respectively, including one of the two cases receiving NSAIDs. We believe, however, that the available long-term follow-up makes clinically relevant persistent infection, loss of advancement or tibial tuberosity fractures unlikely.

Although the reported rate of cage removal after TTA is low, management of these cases is relevant considering the large number of TTA procedures performed worldwide.[1–3,12] One-stage revision successfully prevented loss of

advancement of the tibial tuberosity and tibial crest fractures, although subsequent removal of the revision cage was performed in 2/7 cases (29%). Improvements in treatment protocol are possible and additional studies are warranted to evaluate their effectiveness.

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None.

Conflicts of Interest
None declared.

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