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Original Study • DOI: 10.2478/ahem-2023-0022 • AHEM • Vol. 77 Issue 1/2023 • 176–181

AHEM

Advances in Hygiene and Experimental Medicine
Postępy Higieny i Medycyny Doświadczalnej

Defensive antibacterial coating (DAC) hydrogel with gentamycin and vancomycin for the therapy of achilles tendon infection after surgical repair without massive soft-tissue defect. Results in 8 cases

Original Study

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Received 21 August, 2023, Accepted 10 November, 2023

Abstract

Introduction. We report the results of revision surgery in postoperative infection after Achilles tendon (AT) suturing consisting of debridement of AT together with a local application of hyaluronic acid and polylactic acid hydrogel with an addition of gentamicin and vancomycin in suture canals and into an operative wound.
Materials and Methods. A retrospective study included eight patients operated due to a postoperative and unsuccessfully treated infection after AT suture. Before revision with defensive antibacterial coating (DAC) hydrogel, all patients underwent an unsuccessful antibiotic therapy, removal of sutures via the sinus tract. In none of the cases was there a skin defect due to a previous surgery and infection. In all cases, the AT healed at revision surgery, residual stiches were removed, and suture canals and adjacent soft tissue and anchor canals in the bone were debrided and filled with 5 ml DAC hydrogel with an addition of gentamicin and vancomycin.
Results. During the follow-up ranging from 6 to 43 months, all patients obtained a complete resolution of inflammation. No side effects related to DAC hydrogel were observed.
Conclusion. The use of 5 ml antibacterial DAC® hydrogel containing 160 mg gentamycin and 50 mg of vancomycin applied during revision surgery on the surface of AT and in suture canals in AT as an adjunct to surgical debridement for infection complicating repair of AT without a massive soft-tissue defect proved to be safe and effective. Level of Evidence: IV (case series).

Keywords

infection • surgical repair of Achilles tendon • DAC hydrogel • local antibiotics

1. Introduction

Infection after surgical repair of Achilles tendon (ISRAT) is a severe complication with a reported frequency of about 0.2% to 3.6%, which can lead to a defect of the skin covering the tendon or even a defect of the tendon itself and thus compromise the function of the extremity [1]. This is due to a limited blood supply to the covering skin, which becomes compromised during surgical preparation. A clinical manifestation of ISRAT can vary from a superficial wound infection without skin and tendon dehiscence, through a deep infection with a skin defect but maintain continuity of the sutured tendon to a dehiscence of the sutured tendon and a skin defect. ISRAT is a complication that is difficult to treat, and many treatment options are described in the literature. The initial treatment of ISRAT should include a thorough debridement of all infected tissues, a removal of retained sutures, foreign materials, and cultures for identification of the pathogen. A suppressive antibiotic therapy according to the culture result should be continued until inflammatory markers and clinical symptoms normalize. In the presence of a significant soft tissue defect over the tendon, soft tissue coverage over the tendon should usually be done first, and the reconstruction of the tendon should be delayed until the infection is cleared. Skin defects can be reconstructed by free- or locoregional flap transfers: a short fibular, flexor digitorum, lateral supramalleolar cutaneo-aponeurotic, lateral arm and latissimus dorsi muscle flap [2]. In the case of necrosis of the Achilles tendon (AT), so called reinforcement flaps have been described (from the tensor fascia lata, palmaris longus, extensor carpi radialis, m. plantaris) to reconstruct or reinforce the AT. Reconstructions, however, are associated with potential problems in the donor site and the risk of flap necrosis, with the risk of the recurrence of infection in the place of reconstruction of the skin or tendon defect [2]. Additional variations of the treatment include staged procedures with the utilization of cement spacers, tissue expanders, and negative-pressure wound therapy (NPWT) [3]. In the cases of ISRAT without a soft tissue defect, multiple debridement of limited aggressiveness is usually performed. Due to the location of the AT, directly under the skin, solid local antibiotic carriers like acrylic cement with antibiotics, bioglass, or ceramics are not preferred because they can cause difficulties in wound closure

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after revision. Also, a collagen sponge with an antibiotic deposed close to the revised tendon will separate the tendon from the skin and after a few days create a dead space filled with a mass of collagen increasing the risk of wound dehiscence.

Positive effects of the use of hyaluronic acid hydrogel, defensive antibacterial coating (DAC), with antibiotics as prophylaxis of infection in patients with fracture healing, joint arthroplasty, and even in anterior cruciate ligament reconstruction was an inspiration for the application of DAC in the therapy of ISRAT without a skin defect [4, 5, 6, 7]. We assumed that antibiotic-loaded DAC hydrogel with two antibiotics active against most pathogens infecting the wounds will increase the effectiveness of the revision of the infected AT. DAC hydrogel consists of two biocompatible components: hyaluronic acid (HA) and polylactic acid (PLA), which should not deteriorate healing of the wound and tendon. HA has several clinical applications in otorhinolaryngology, dermatology, aesthetic surgery, dentistry, urology, orthopaedics, and ophthalmology. HA has proved to be effective in local applications in recurrent or chronic middle ear inflammations, chronic adenoiditis, chronic urinary tract infections, in dentistry—improving wound healing after scaling and root planning [8, 9, 10, 11]. HA has also been reported to exert a bacteriostatic, dose-dependent effect on different planktonic forms of bacteria [12, 13]. PLA is a synthetic polyester widely used for orthopaedic implants [14]. PLA as a compound of DAC hydrogel is slowing down the susceptibility of DAC to hydrolysis. The *in vitro* test of cell compatibility of DAC® HA-g-PLA hydrogel showed that the hydrogel does not decrease cell viability of human dermal fibroblasts [15]. DAC® hydrogel is a Conformité Européene (CE)-marked medical device, intended to be used as a disposable, quickly bioresorbable antibacterial coating for implants. The DAC® hydrogel kit is composed of a prefilled syringe, containing 300 mg sterile DAC® powder, which is filled at surgery with a solution of 5 mL sterile water for injection, and eventually mixed with the desired antibiotics [16]. DAC® is characterized by a high biocompatibility and a short resorption time of about 72 hours. Gentamycin, vancomycin, daptomycin, meropenem, rifamycin, and ciprofloxacin can be added to DAC®. The application of DAC® with antibiotics in the therapy of septic complications after hip and knee primary and revision arthroplasty, and osteosynthesis of closed fractures was described, but the use of DAC® in therapy of ISRAT has not been published yet.

The aim of the paper is to present the technique and early results of revision surgery due to ISRAT in cases without skin defect with the use of a local application of DAC® hydrogel with gentamycin and vancomycin.

2. Materials and methods

The study involved eight consecutive cases with an infection after AT suturing with nonabsorbable sutures (Fibertape, Arthrex); seven cases were operated by open and one by percutaneous technique. In one case, a suture with a titanium anchor was used for the attachment of the tendon to the calcaneus. There were three women and five men at the ages of 19–62. The infection presented early after surgery with inflammation signs and sinus tract over the tendon. An antibiotic therapy, hyperbaric oxygen therapy, and the removal of sutures from the sinus tract were not successful. Four patients had comorbidities, which were risk factors for postoperative wound healing problems and infection: psoriasis, systemic lupus erythematosus, steroid injection in the region of the AT before the rupture, and reconstruction of the AT combined with a transfer of the central part of triceps surae muscle.

Operation technique: a revision surgery was performed with the patient in a prone position using initially a tourniquet. The incision was made in scar tissue resulting from the previous surgery over the AT (Fig. 1). When the tendon healed, it was incised longitudinally in an "open book" manner avoiding preparation of the sutured tendon from surrounding tissues. The sutures, suture anchors, and biofilm were removed from the suture canals in the tendon and bone by curettage and lavage (Fig. 2). After debridement, the tourniquet was deflated and thorough hemostasis was established. DAC® was prepared according

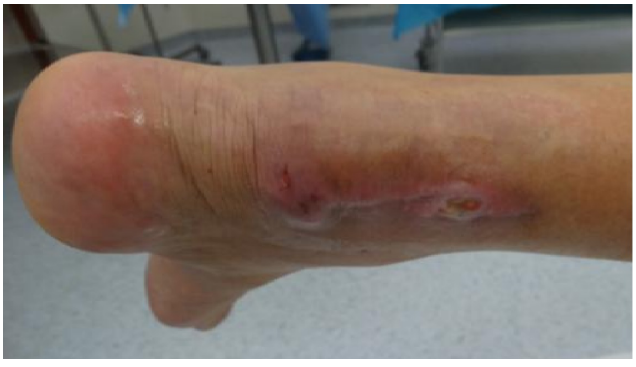


Figure 1. Preoperative appearance of an infection after a surgical repair of the Achilles tendon

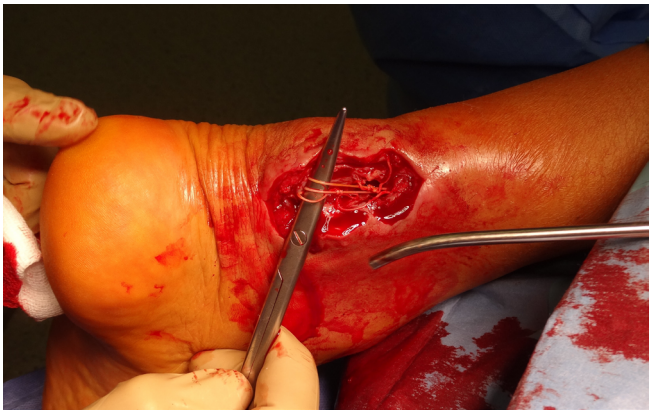
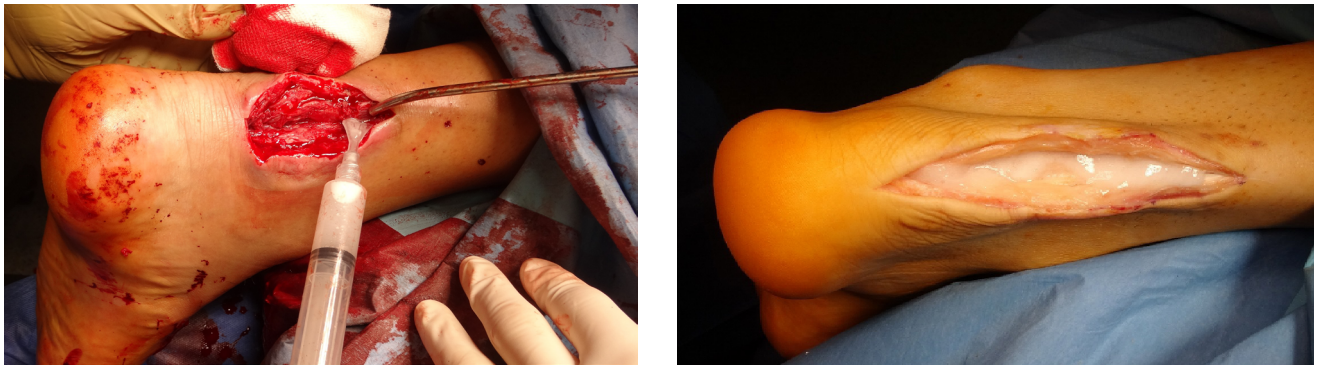


Figure 2. Intraoperative appearance of an operated and infected Achilles tendon: removal of residual sutures, maintained tendon continuity

Table 1. Demographic data and characteristics of patients treated with defensive antibacterial coating (DAC) with gentamycin and vancomycin for Achilles tendon infection after surgical repair
*Table legend: M: male; F: female; AT-Achilles tendon; ATB-cs: antibiotics; TMP-SMX – Trimethoprim -sulfamethoxazole; Post OP ATB-cs: postoperative antibiotics; NRIH: number of revisions until infection healed; HBO – hyperbaric oxygen therapy; VAC – vacuum-assisted closure dressing; CoINF: cure of infection; FU - follow-up (in months)**;** FAAM – foot and ankle ability measures*

Patient; gender; age; risk factors	Course of treatment	Pathogen	Post OP ATB-cs	NRIH	FU	CoINF	FAAM (max 84 points); Pre- versus postoperative function (%)
1. F; 26 years	AT traumatic rupture; open suture; rupture of suture, 2nd suture. Infection; infection of DAC into AT sheet; revision with DAC	*E. coli*	Ciprofloxacin +TMP-SMX 4 weeks	1	14	Yes	FAAM score 87/84; 80%;
2. M; 57 years, Psoriasis	AT traumatic rupture; open suture, infection; revision with DAC;	*S. aureus MSSA*	Ciprofloxacin + TMP-SMX 4 weeks	1	10	Yes	FAAM score 80/80; 95%;
3. F; 29 years, SLE	AT traumatic rupture; percutaneous suture, infection; revision with DAC	*S. aureus MSSA*	Cefuroxime + Ciprofloxacin 2 weeks	1	9	Yes	FAAM score 81/84; 98%;
4. F; 19 years	AT traumatic rupture; open suture, infection; revision with DAC	*Pseudomonas aeruginosa*	Ciprofloxacin + clindamycin 2 weeks	1	8	Yes	FAAM score 77/84; 70%;
5. M; 57 years	Nontraumatic AT rupture; 1 week after steroid injection; open suture; infection; HBO; revision with DAC	*S. aureus MSSA*	Cefuroxime 10 days	1	7	Yes	FAAM score 83/84; 100%;
6. M; 41 years	AT traumatic rupture; reconstruction with FiberWire suture + transfer of central part of triceps surae; infection; revision with DAC, VAC	*Klebsiella oxytoca; Serratia marcescens*	Ciprofloxacin 2 weeks	1	6	Yes	FAAM score 80/84; 80%;
7. M; 62 years	AT traumatic rupture; open suture, revision due to suture insufficiency; infection; revision with DAC	*Enterococcus faecalis, Finegoldia magna*	Cloxacillin + metronidazole 7 days	1	30	Yes	FAAM score 81/84; 95%;
8. M; 31 years	AT traumatic rupture; open suture with anchor; infection, revision with DAC	*S. aureus MSSA*	Clindamycin, cefuroxime + RMPC 4 weeks	1	43	Yes	FAAM score 84/84; 95%;



A B

Figure 3A and 3B: Application of DAC hydrogel after debridement of the Achilles tendon

to the manufacturers' recommendations: 4 ml of gentamycin (160 mg) and 1 ml of vancomycin solution (50 mg vancomycin dissolved in sterile *aqua pro injectione*) was added to 300 mg of powder supplied in a prefilled syringe. Six to ten minutes after the preparation of hydrogel by mixing compounds in a syringe, the mixture was injected in the canals after removal of the sutures and anchor, applied on the tendon surface, and even injected into surrounding subcutaneous tissue (Fig. 3A and 3B). Postoperatively, the extremity was immobilized in a walking boot (Walker orthosis) until the wound was healed and the patient started physiotherapy. Table 1 summarizes the data of operated patients.

Both the results of initial treatment of the injured tendon and of the revision surgery with DAC were assessed on the basis of a physical examination, that is, healing of the wound without signs of inflammation signs and an ability to return to daily activities, job, and sports (Fig. 4 and 5). In five out of eight patients, an ultrasound examination of the operated AT was performed after six weeks to assess the course of healing of the tendon. The function of the operated limb was assessed subjectively with the Foot and Ankle Ability Measure (FAAM) score, available online [17]. Originally published in 2005, FAAM was developed to assess physical functions of individuals with musculoskeletal

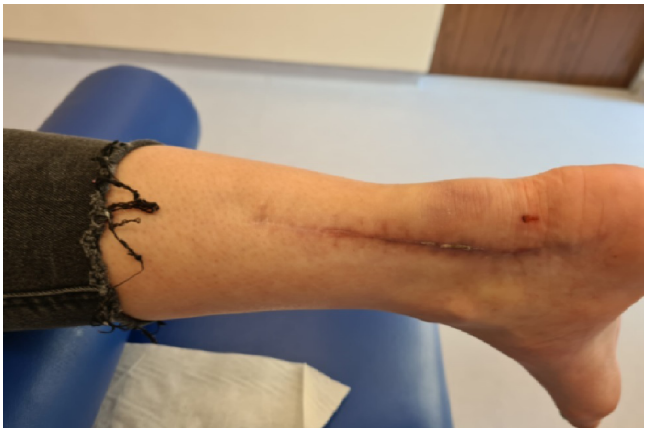


Figure 4. Healed wound after debridement and application of DAC hydrogel

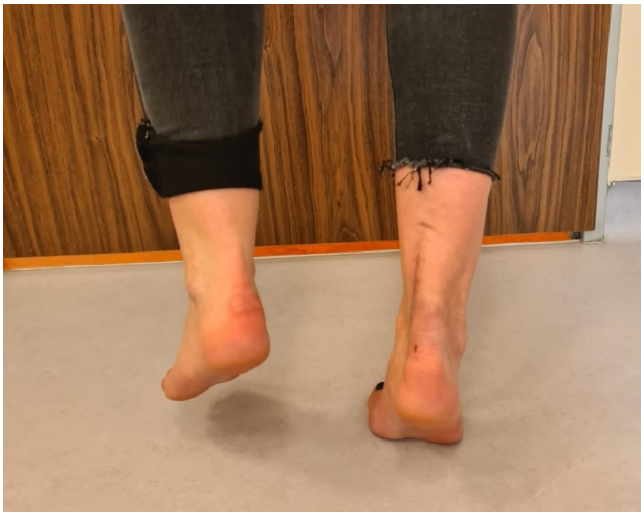


Figure 5. Clinical assessment two months after revision for an infected Achilles tendon: one-leg raising (isokinetic plantar flexion)

disorders of the leg, foot, and ankle [18]. The FAAM is a patient-completed instrument that consists of an "Activities of Daily Living" (ADL) subscale (21 scored items) and a "Sports" subscale (7 scored items), in which response options range from 0 to 4. Scores for each subscale range from 0% (least function) to 100% (most function). A maximum score of 84/84 can be achieved if there is no decrease of function of the injured limb. Additionally, a comparison of pre- and postoperative function level of the operated extremity is subjectively assessed by patients from 0 to 100% [17]. The FAAM scores were obtained by a standardized phone survey.

The study was performed following the Declaration of Helsinki principles, and informed consent was obtained from each patient prior to the inclusion in the study. The study was approved by responsible authorities of the Carolina Medical Center in Warsaw. The ethics committee approval was not applicable.

3. Results

The follow-up time ranged from 6 to 43 months (Table 1). All but one patient underwent an uneventful wound healing and a complete resolution of inflammation. One patient required NPWT of the wound. In none of the cases was any complication related to DAC® noted, such as a leakage of the DAC® hydrogel from the wound. In one case, there was an attempt to avoid surgery, and DAC was injected under ultrasound control into the tendon sheet, but the infection relapsed after eight weeks, and eventually an open revision with DAC® was performed. An ultrasound examination of the operated AT was performed in five out of eight patients after six weeks and showed undisturbed healing of the AT.

A dynamic and static function of the operated leg was acceptable for all patients. The assessment of the function of the operated limb with FAAM score showed the score ranging from 77/84 to 84/84 (mean 81/84) (Table 1). A comparison of pre- and postoperative function levels of operated extremity was subjectively assessed by patients from 70% to 98% (mean 89.13%). According to the FAAM score, the mostly impaired activity was squatting (5 pts), coming up on toes (3 pts), going downstairs (2 pts), recreational activities (2 pts), walking on uneven ground (1 pt), and difficulties in light to moderate work (1 pt). Patients reported mostly slight (10 answers) or moderate (3 answers) difficulties, and nobody reported extreme difficulties or inability to do any activity. There was no deterioration in ankle range of motion or the strength of the triceps muscle on the operated site (ability to stand on one leg) in comparison to the pre-revision status.

4. Discussion

Infections of tendons, by contrast to bone and joints infections, are different regarding pathophysiology and therapeutic possibilities. This is due to differences in anatomical structure, tissue compound, blood supply, and mechanical functions of each structure in the musculoskeletal system. There are numerous reports with different treatment protocols depending on the extent of infection, with multiple debridement procedures as necessary [2].

According to a consensus published in 2019, the recommended treatment algorithm for Infection After Achilles Tendon Repair/Reconstruction should include a thorough debridement of all infected tissues, removal of retained sutures or foreign material, collection of the cultures at the time of debridement, and antibiotic therapy according to the result of the culture continued until inflammatory markers and clinical symptoms normalize. If a significant soft tissue defect in the overlying area remains, the choice of tendon reconstruction and/or transfer with soft tissue coverage should be left up to the discretion of the treating surgeon based on his/her preference and expertise. A revision reconstruction should be delayed

until the infection is cleared [3]. In the cases of ISRAT without a soft-tissue defect, repeated debridement surgeries of limited aggressiveness are usually performed.

Our study concerns ISRAT previously treated without success with suppressive antibiotic therapy and removal of stiches from the sinus tract, but without a local application of an antimicrobial carrier—harmless for the tendon and surrounding soft tissues. We focused on two aspects of ISRAT: first, the strategy of the surgical procedure for the infected AT and, second, the application of DAC® hydrogel with gentamycin and vancomycin as local antibiotic delivery. An application of DAC® was performed with an intention to increase the likelihood of infection cure and not to disturb wound healing in this specific region. In our study, we focused on the assessment of effectiveness and safety of the local application of DAC® hydrogel with gentamicin and vancomycin in patients with preoperative cultures from the sinus tracts revealing pathogens (*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella oxytoca, Serratia marcescens, Enterococcus faecalis and Finegoldia magna*) sensitive *in vitro* to gentamycin. An addition of vancomycin was intended to increase a potential antibacterial spectrum of DAC® and was recommended by the manufacturer. Our study showed good tolerance and no side effects of DAC® on healing of the wound and the AT itself, a positive effect on an infection control, and no need of repeated debridement due to relapse of infection.

ISRAT has a negative effect on postoperative rehabilitation and physical activity. In the study by Payala, 9 patients from a group of 409 sustained ISRAT; they had multiple factors influencing negatively functional outcomes. Two of the patients in the ISRAT group had a fair clinical outcome, five had a poor outcome; a mean isokinetic plantar flexion strength deficit in that group was 35%, and the authors conclude that the results after a deep infection are often devastating [1]. In the study by Bowers, twenty patients were treated for ISRAT. All wounds had healed, but three patients (15%) required repeated debridement. All patients were able to walk without the use of a walking aid. Five out of twenty patients required a continued use of a boot or brace during ambulation. Patients participating in the FAAM ADL survey had a mean FAAM score of 87 (range from 71.4 to 100). At a last follow-up, most patients reported their overall function as "normal" or "nearly normal" [2]. Results in our group of eight patients showed no need for a repeated revision or debridement after combined debridement with the use of DAC® hydrogel with antibiotics, but also no effect of application DAC® alone without revision with a removal of stiches. A functional assessment in our group using the FAAM questionnaire with a maximum of 84 points, showed a mean score of 81 points (range from 77 to 84). A subjective assessment of pre- and postoperative function level of the operated extremity revealed a mean of 89.13% (range 70% to 98%), both of which are comparable or better results than those by Payala and Bowers. In our study, two out of eight patients were able to return to high-level sport activities: patient nr 3 started climbing three months after revision with DAC and patient nr 8 started running two months after revision, started full trainings four months after revision, and 26 months after revision became a Paralympic medal winner.

The possibility of releasing antibiotics (ciprofloxacin, gentamicin, and vancomycin) from HA-based gels, without toxicity to eukaryotic cells, was shown in laboratory studies and animal models [19, 20, 21]. Also, antibiotics-loaded collagen has been investigated in treating bacterial osteomyelitis, but the results showed inadequate evidence quality, making it challenging to guide any clinical decision. Recently, a combination of topical antibiotic delivery with a heparinized nano-hydroxyapatite/collagen bone substitute loaded with vancomycin showed release of high concentrations of vancomycin for 19 days above the MIC of MRSA [22]. We assumed that the optimal product for application in ISRAT will be CE-marked DAC® hydrogel with gentamicin and vancomycin.

5. Limitations of the study

This is a retrospective review from a single institution with multiple surgeons performing the procedures. Because ISRAT is a rare complication, there is a small number of patients, and no control group was used. Despite these limitations, we believe this study is important to help diminish the risk of repeated revisions in patients who must undergo a treatment for the infected AT.

6. Conclusion

Our study shows that the use of 5-ml antibacterial DAC® hydrogel containing 160 mg gentamycin and 50 mg of vancomycin as an adjunct to surgical debridement for infection complicating a repair of the AT without a massive soft-tissue defect proved to be safe and effective.

Authors' Contribution

I. Babiak—Research concept and design, supervising the project, acquisition of data, data analysis and interpretation, writing—original draft preparation, writing—review and editing, literature review, final proofreading and approval of the version for publication; J. Banasiewicz—Data analysis and interpretation, writing—review and editing, literature review, final proofreading and approval of the version for publication; Ł. Luboiński—Acquisition of data, final proofreading, and approval of the version for publication; K. Sieczych—Acquisition of data, final proofreading, and approval of the version for publication

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Conflict of interest

The authors have no potential conflicts of interest to declare.

Ethics approval

Due to the nature of the research, the consent of the ethics committee was not required.

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