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Research Paper

A Retrospective Analysis of Deep Surgical Site Infection Treatment after Instrumented Spinal Fusion with the Use of Supplementary Local Antibiotic Carriers

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Abstract

Background: There is no generally established treatment algorithm for the management of surgical site infection (SSI) and non-union after instrumented spinal surgery. In contrast to infected hip- and knee- arthroplasties, the use of a local gentamicin impregnated carrier in spinal surgery has not been widely reported in literature.

Patients and methods: We studied 48 deep SSI and non-union patients after instrumented spine surgery, treated between 1999 and 2016. The minimum follow-up was 1.5 years. All infections were treated with a treatment-regimen consisting of systemic antibiotics and repetitive surgical debridement, supplemented with local gentamicin releasing carriers.

We analysed the outcome of this treatment regimen with regard to healing of the infection, as well as patient- and surgery-characteristics of failed and successfully treated patients.

Results: 42 of the 48 (87.5%) patients showed successful resolution of the SSI without recurrence with a stable spine at the end of treatment.

36 patients' SSI were treated with debridement, local antibiotics, and retention or eventual restabilization of the instrumentation in case of loosening. 3 patients were treated without local antibiotics because of very mild infection signs during the revision operation. 3 patients were treated with debridement, local antibiotics and removal of instrumentation. One of these patients was restabilized in a second procedure.

Infection persisted or recurred in 6 patients. These patients had a worse physical status with a higher ASA-score. *Staphylococcus aureus* was the most frequent causative microorganism.

Interpretation: Debridement and retention of the instrumentation, in combination with systemic antibiotics and the addition of local antibiotics provided a successful treatment for SSI and non-union after instrumented spinal fusion.

Introduction

The incidence of surgical site infection (SSI) after spinal surgery ranges from 2 to 12%, depending on diagnosis, surgical approach, use of spinal instrumentation, and the complexity of the procedure [1-4].

SSI is a devastating complication that leads to prolonged treatment, with the need for subsequent reoperations and substantially increased overall health care costs. Moreover, SSI after instrumented spinal surgery is associated with higher rates of morbidity and mortality, and has a negative impact on functional clinical outcome [5-7].

There is no generally established treatment protocol for the management of deep SSI after

instrumented spinal surgery. As we know from SSI after general fracture management with osteosynthesis, instrumentation is preferably left *in situ* as preservation of stability is crucial to allow for bony union while the infection is managed. Likewise, in spinal fusion, as long as bony union has not occurred, stable instrumentation material should be left *in situ* in order to prevent loss of correction or development of pseudarthrosis due to mechanical instability [8, 9]. After bony consolidation, the instrumentation can be removed if necessary in a second stage for complete cure of the infection [10].

Gentamicin impregnated carriers

Polymethylmethacrylate (PMMA) or bone cement is able to release admixed powdery substances if these are soluble in water and heat stable during polymerization [11]. Buchholz admixed four heat stable antibiotic powders with bone cement and found that, except for tetracycline, the antibiotics indeed were released by a diffusion process for at least 2 weeks in a bactericidal concentration[11]. Subsequently, many handmade and commercially made combinations of antibiotics and bone cements were tested, of which gentamicin in combination with Palacos bone cement provided the best antibiotic release after implantation and best stability during polymerization.[12-14]

Gentamicin is very suitable for prevention or treatment of orthopedic infections since it exhibits a broad antibacterial spectrum including gram-positive and gram-negative germs, and a good bactericidal effect in low concentrations with a low rate of resistances development [15].

Gentamicin-impregnated bone cement was first introduced to prevent SSI after cemented implantation of joint arthroplasties[16]. Once on the market, it was also used to treat osteomyelitis by filling bone cavities after debridement. Because small beads of bone cement mixed with antibiotics were proven to be more effective, non-absorbable gentamicin impregnated PMMA beads (Septopal®) were commercially produced for local antibiotic treatment of infections, by admixing gentamicin to the liquid monomer and polymer powder, in combination with glycine as a filler to promote the gentamicin release [17].

In view of the successful treatment with these non-absorbable drug carriers, endeavours were made to develop absorbable materials that no longer needed removal. [18] Because collagen carriers are fully absorbed, gentamicin-collagen products can be used in one-step surgical procedures.

Pharmacokinetic release models have shown that the release of gentamicin from collagen fleeces is more rapid and less longstanding as compared to PMMA-beads [19]. Both carriers have shown a high local gentamicin concentration without toxic concentrations in the blood [19, 20].

Although commonly used in prosthetic joint infections (PJI) and osteomyelitis [21-23], the use of antibiotic loaded carriers in SSI after instrumented spinal fusion has not been widely reported [8, 20-24]. Because of good results in the use of gentamicin PMMA-beads or fleeces in the treatment of prosthetic joint infections [22, 23] we incorporated local gentamicin in the treatment of SSI after instrumented spinal fusion.

The aim of this study was to assess the treatment results after the use of a local gentamicin impregnated carriers, supplementary to operative debridement and administration of systemic antibiotics for SSI without union after instrumented spinal fusion, with an in-depth analysis of failed cases.

Material and methods

This is a retrospective case-series analysis of all non-union, deep SSI patients after instrumented thoracolumbar spinal fusion procedures that had been performed in the Department of Orthopedics of the Maastricht University Medical Centre, a secondary and tertiary academic referral center for spinal pathology and for orthopaedic infections, from January 1999 up to December 2015.

Diagnosis

The diagnosis of surgical site infection was based on criteria as described by the CDC (Centre for Disease Control and prevention) [25] and the Dutch national PREZIES network (*prevention of hospital infections through surveillance*) [26]. According to these criteria, a SSI was considered to be deep if it presented at the site of the operation with involvement of subfascial tissue [25].

Patients

We diagnosed 62 (6,9%) deep surgical site infections (30 female, 32 male) out of 898 instrumented spinal surgery procedures (14 anterior approach, 884 posterior approach). 14 patients (4 female, 10 male) with an SSI were excluded from analysis: One patient had been treated for spondylodiscitis as the index operation, two patients did not receive treatment for SSI because of terminal illness and one patient was excluded because of loss to follow up. 10 patients had a late SSI with bony union of the spondylodesis. These 10 union SSI were all successfully treated with removal of the instrumentation and with additional local antibiotic administration in 2 patients. We included 48 patients (47 after posterior instrumented spinal fusion and 1

after anterior instrumented spinal fusion).

Treatment protocol

Deep infections of instrumented spinal fusion without bony consolidation, and without signs of implant loosening were treated by surgical debridement, systemic antibiotics, irrigation and implant retention (DAIR), in combination with application of antibiotics loaded carriers (gentamicin PMMA-beads or fleeces).

In case of instrumentation loosening and an unstable spine, new instrumentation was inserted for re-stabilisation. (Figure 1)

The procedure consisted of debridement with removal of loose bone graft material, pulsed lavage with at least 3 litres of Ringer lactate and either retention, removal or re-stabilisation of the instrumentation depending on the stability of the instrumentation and spine. The patients were treated with systemic and local antibiotic therapy. As local antibiotic carrier we preferably used gentamicin PMMA beads with a diameter of 7 mm, containing 7.5 mg gentamicin sulphate, in chains of 30 or 60 beads (Septopal®, Merck GmbH, Darmstadt, Germany; Biomet GmbH, Berlin, Germany). We packed as many beads in the infected tissues as tensionless wound closure would allow in order to create a high local gentamicin concentration. Wounds were fully closed and the gentamycin beads were removed in a second procedure 2 weeks later.

Multiple tissue samples were taken for bacteriological cultures right before the administration of systemic antibiotics. The samples were cultured in the microbiology laboratory for at least 2 weeks in order to also detect slow growing micro-organisms. The minimal inhibitory concentration (MIC) value for gentamicin of the specific bacteria strain was then determined.

If infection signs had not resolved, the gentamicin beads were removed, a new debridement was performed, and new beads were left behind during a second procedure 2 weeks later.

In case of very mild intraoperative infection signs, one debridement was considered to be enough and only gentamicin collagen fleeces were used as local gentamicin impregnated antibiotic carrier. Gentamicin collagen fleeces (Septocoll®, containing 116 mg gentamicin sulphate and 350 mg gentamicin crobephate in 320 mg equine collagen fleece with a size of 10x8 cm; Merck GmbH, Darmstadt, Germany; Biomet GmbH, Berlin, Germany) were applied before closing the wound, to prolong the period with local antibiotics and obviate the need for removal of the beads in another operation.

Spinal instrumentation was removed if, infection persisted according to clinical and laboratory parameters despite one or more treatment periods of 2 weeks with gentamicin beads. In case of instability because of non-union as determined intraoperatively by visible motion across the fused segment(s) and the absence of bony continuity on inspection, the spine was restabilized directly with renewed instrumentation [27, 28]. The infection treatment was then continued with the local application of gentamicin PMMA beads and intravenous administration of antibiotics.

Figure 1. Treatment algorithm of deep surgical site infection after instrumented spinal fusion. * 45/48 infections were treated with debridement of the wound and a local gentamicin carrier (gentamicin fleeces in 3 SSI and gentamicin PMMA beads in 42 SSI) and 3/48 were treated without local gentamicin treatment because of very mild signs of a deep infection during operation. β 3/4 failures died sepsis-related during infection treatment. One failure presented with a recurrent infection with the same initial micro-organism (*Staphylococcus aureus*) that was successfully treated with removal of the instrumentation and local gentamicin PMMA beads. α 1 failure died during infection treatment because of sepsis. # 1 failure was a recurrence of infection of the anterior instrumentation that occurred more than 3 years after the secondary restabilization. This patient died during the second infection treatment because of a poor health condition (terminal metastatic renal cancer).

Systemic antibiotics

The surgical treatment was combined with high dosed systemic antibiotics, usually for a period of approximately 3 months, including a minimum of two weeks intravenous

administration during hospitalization and continued oral administration after discharge from the hospital. The choice and exact duration of the systemic antibiotic treatment was decided on an individual basis and based on antibiotic resistance pattern of the causative bacteria by consultation of a microbiologist specialized in orthopaedic infections.

Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell counts (WBC) were measured twice a week during hospitalisation and at all outpatient control visits for monitoring of infection healing. We considered these parameters as normal when CRP and WBC counts were within the normal range (CRP <10 mg/L; WBC<10,000 cells/mcL) at 2 subsequent outpatient control visits, and the ESR was decreased to less than 30 mm/h in patients without systemic disease and cessation of systemic antibiotic treatment.

Outcome

The treatment was considered successful when at follow up the infection was eradicated (normalized inflammatory blood markers and no clinical signs of infection) with a stable spine by instrumentation or by osseous fusion. Failure was diagnosed if the infection was not eradicated.

The subjective outcome (disabling back pain or leg pain with limitations in activities of daily living (ADL)) were noted as "yes" or "no" at the end of the follow-up at the outpatient clinic.

The follow-up period started at the date of the first operation for infection, and ended on the date of the last outpatient clinic visit, the last contact with the family doctor or the date of death. The minimum follow up was 1.5 year or shorter in case of death, either related or not to the SSI.

Statistical analysis

Patient characteristics (gender, age, BMI, smoking status, comorbidities, ASA-score, medication, trauma, radiation therapy, blood values, revision surgery, interval between primary surgery and infection treatment, antibiotic use and MIC genta) and operation variables (primary indication, combination surgery with a second incision, fused levels, anatomical levels, graft use, cage use, dural tear, micro-organism and soft tissue condition) were presented as either median with total range, or as mean with standard deviation (SD).

Additionally, the odds ratios (OR) with 95% confidence intervals (CI) were calculated for all patients' characteristics and risk factors for poor treatment outcome. The Mann Whitney U test was used to analyse differences of continuous variables between successfully treated patients and failures. SPSS (version 17.0) was used for all statistical calculations.

Results

48 patients with a deep SSI without bony union were treated, of which 42 (87.5%) were treated successfully. Recurrence of infection occurred after more than 2 years in 2 patients. Four patients died during infection treatment because of sepsis (Table 1 and Figure 2).

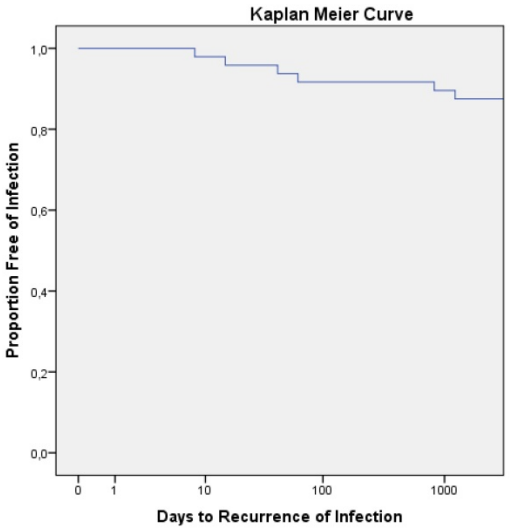

Figure 2. Kaplan-Meier survival curve that represents the proportion of all patients free of infection after treatment for deep SSI after instrumented spinal fusion.

37 of 48 patients were treated with debridement, retention of the stable instrumentation (DAIR), and local antibiotics: 33 of these 37 were treated successfully, while 4 failed.

8 of the 48 patients were treated with DAIR after restabilization of loose instrumentation of which 3 without local antibiotics, because there were minimal signs of infection intraoperatively.

Instrumentation was removed without spinal restabilization in 3 of the 48 patients, as the lumbar spine was considered stable after instrumentation removal. These 3 cases were all treated with gentamicin PMMA beads. One of these patients required anterior restabilization in a second stage after 2 periods of treatment with gentamicin PMMA beads. (Figure 1)

6 of the 48 patients were treated with only one debridement, and 24 were treated with 2 debridements, whereas 15 needed 3 debridements and only 3 patients needed 4 debridements of the wound.

The median time of systemic intravenous antibiotic treatment was 41 (3-95) days, followed by oral treatment for another 43 (0-196) days. The median total antibiotic therapy time was 84 (6-251) days. Oral

antibiotic treatment at the outpatient clinic was stopped when clinical and laboratory parameters were considered as normal. *Staphylococcus aureus* was found as the most frequent (24/48) causative microorganism (Table 2). There was no significant difference with respect to causative micro-organism between the failed and the successfully treated patients. No relation could be found between the MIC value for gentamicin of the causative bacteria and the success rate of the infection treatment. (Table 3)

5 of the 6 patients (83%) in whom the infection treatment failed had an ASA-score >2 compared to only 12 of 42 (29%) in the population with a successful treatment.

There were no other isolated patient characteristics or operation-related variables that differed significantly between the 6 patients in whom the infection treatment failed and the 42 successfully treated patients. (Table 2 and 3)

At the end of follow-up, 5 patients (10.4%) complained of residual disabling back pain with limitations in ADL, 2 patients (4.2%) complained of persisting disabling leg pain with limitations in ADL, and 3 patients (6.3%) had residual disabling back and leg pain with limitations in ADL.

In summary, 87.5% (42/48) of all patients with a SSI and non-union after an instrumented spinal procedure where treated successfully with a treatment regimen consisting of systemic antibiotics and repetitive surgical debridement supplemented with local gentamicin releasing carriers. 8% (4/48) died during infection treatment because of sepsis and in 4% (2/48) recurrence of infection occurred after more than 2 years.

Table 1. Details of the patients

Diagnosis	pathogen	Interval (days)	Debride-ments	FU	Outcome	Treatment	Subjective outcome
Fracture with threatened myelum	S. viridans	1	1	1062	Success	Debridement, restabilization, no local AB	Back pain & disabilities in ADLs
Scoliosis (degenerative)	E. Coli	8	2	962	Success	DIAR + fleeces	Back pain, no disabilities in ADLs
Degenerative spondylolysis	E. coli	9	3	1159	Success	DIAR + beads	Back pain, no disabilities in ADLs
Failed previous spine surgery	S. Aureus	9	3	1195	Success	DIAR + beads	No pain or disabilities in ADLs
HNP with threatened myelum	S. Aureus	9	3	882	Success	DIAR + beads	Disabilities in ADLs without pain
RIP with threatened myelum	E. Coli	10	2	875	Success	Debribement, restabilization + beads	Leg pain & disabilities in ADLs
RIP with threatened myelum	mixed flora	10	2	1277	Failure	Removal implants + beads, restabilization in second procedure	No pain or disabilities in ADLs
Failed previous spine surgery	mixed flora	11	1	371	Success	DIAR, no local AB	No pain or disabilities in ADLs
Fracture with threatened myelum	E. cloacae	12	2	1185	Success	DIAR + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	mixed flora	12	3	1402	Success	DIAR + beads	No pain or disabilities in ADLs
Fracture without threatened myelum	S. Aureus	12	2	733	Success	Debribement, restabilization + beads	Back pain, no disabilities in ADLs
Spinal stenosis	S. Aureus	13	3	406	Success	DIAR + beads	No pain or disabilities in ADLs
Fracture without threatened myelum	E. coli	13	2	884	Success	DIAR + beads	Disabilities in ADLs without pain
Fracture without threatened myelum	S. Aureus	13	2	1092	Failure	DIAR + beads	Back pain, no disabilities in ADLs
Degenerative spondylolisthesis	E. Coli	13	1	1106	Success	DIAR + fleeces	No pain or disabilities in ADLs
Degenerative spondylolisthesis	E. cloacae	14	2	519	Success	DIAR + beads	Back & leg pain & disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	14	4	1163	Success	DIAR + beads	Back & leg pain, no disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	15	3	251	Success	DIAR + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	15	3	1007	Success	DIAR + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. pyogenes	15	1	1334	Success	DIAR + beads	Back pain & disabilities in ADLs
Spinal stenosis	S. Aureus	15	2	1483	Success	DIAR + beads	Back pain & disabilities in ADLs
Lytic spondylolisthesis	mixed flora	16	2	1037	Success	DIAR + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	16	3	1039	Success	DIAR + beads	Back pain, no disabilities in ADLs
Pseudoartrosis	S. Aureus	16	1	1219	Success	Removal implants + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. mitis	17	3	762	Success	DIAR + beads	No pain or disabilities in ADLs
Scoliosis (degenerative)	CNS	17	2	854	Success	DIAR + beads	Leg pain & disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	17	3	745	Success	Removal implants + beads	Back & leg pain & disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	18	1	8	Failure	DIAR + beads	Dead
Degenerative spondylolisthesis	mixed flora	18	2	1466	Success	DIAR + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	CNS	19	3	976	Success	DIAR + beads	No pain or disabilities in ADLs
Fracture without threatened myelum	S. Aureus	20	1	15	Failure	DIAR + beads	Dead
Fracture with threatened myelum	E. coli	20	2	275	Success	DIAR + beads	Disabilities in ADLs without pain
Degenerative spondylolisthesis	mixed flora	20	4	741	Success	Debribement, restabilization + beads	Back & leg pain & disabilities in ADLs
Fracture without threatened myelum	S. Aureus	21	2	777	Success	DIAR + beads	No pain or disabilities in ADLs

Diagnosis	pathogen	Interval (days)	Debride-ments	FU	Outcome	Treatment	Subjective outcome
Spinal stenosis	S. Aureus	21	3	1065	Success	DIAR + beads	No pain or disabilities in ADLs
Fracture without threatened myelum	S. Aureus	21	2	5017	Success	Debribement, restabilization + beads	Back pain & disabilities in ADLs
Fracture with threatened myelum	E. Coli	22	1	1474	Success	DIAR + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	23	2	1187	Success	DIAR + beads	No pain or disabilities in ADLs
Spinal stenosis	S. Aureus	30	1	2770	Success	DIAR + beads	Back pain, no disabilities in ADLs
RIP with threatened myelum	S. Aureus	31	1	42	Failure	DIAR + beads	Dead
RIP with threatened myelum	CNS	33	2	583	Success	Debribement, restabilization + beads	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	48	2	62	Failure	Debribement, restabilization + beads	Dead
RIP with threatened myelum	S. Aureus	63	2	191	Success	DIAR + beads	Back pain, no disabilities in ADLs
Degenerative spondylolisthesis	G. elegans	66	1	458	Success	DIAR + beads	Leg pain, no disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	66	4	848	Success	DIAR + fleeces	Back pain & disabilities in ADLs
Fracture without threatened myelum	P. acnes	90	1	1112	Success	DIAR, no local AB	No pain or disabilities in ADLs
Degenerative spondylolisthesis	S. Aureus	141	2	378	Success	Debribement, restabilization + beads	No pain or disabilities in ADLs
Fracture without threatened myelum	S. pneumoniae	186	2	1080	Success	DIAR + beads	Back pain, no disabilities in ADLs
Failed previous spine surgery	negative	265	1	1035	Success	Removal implants + beads	Back pain & disabilities in ADLs
Fracture without threatened myelum	P. aeruginosa	308	1	1336	Success	Removal implants, no local AB	No pain or disabilities in ADLs
Failed previous spine surgery	negative	345	2	2920	Success	Removal implants + beads	Back & leg pain & disabilities in ADLs
Fracture without threatened myelum	S. intermedius	402	2	1058	Success	Removal implants, no local AB	Back pain & disabilities in ADLs
Failed previous spine surgery	P. acnes	525	1	2105	Success	Removal implants, no local AB	Back pain & disabilities in ADLs
Fracture without threatened myelum	P. acnes	531	1	1157	Success	Removal implants, no local AB	No pain or disabilities in ADLs
Degenerative disc disease/discopathy	P. acnes	691	1	1550	Success	Removal implants, no local AB	Back pain & disabilities in ADLs
Fracture with threatened myelum	P. acnes	934	1	811	Success	Removal implants, no local AB	No pain or disabilities in ADLs
Scoliosis, idiopathic	S. Aureus	2723	1	756	Success	Removal implants, no local AB	No pain or disabilities in ADLs
Fracture with threatened myelum	CNS	3292	1	1862	Success	Removal implants, no local AB	No pain or disabilities in ADLs

Table 2. Operation related variables

Operation-related variable	Overall	Successful (42) Infection treatment	Failed (6) Infection treatment	Odds-ratio	95%Cl	*p*-value
Operation-indication						
Fracture	12 (25.0%)	10 (23.8%)	2 (33.3%)	0.625	0.099-3.935	0.616
Degenerative spine-disorders	23 (47.9%)	21 (50.0%)	2 (33.3%)	2.000	0.329-12.123	0.451
Spinal stenosis	4 (8.3%)	4 (9.5%)	0	1.520	0.073-31.693	0.787
Spinal metastasis	5 (10.4%)	3 (7.1%)	2 (33.3%)	0.154	0.020-1.212	0.076
Failed previous spine surgery	2 (4.2%)	2 (4.8%)	0	0.803	0.035-18.677	0.891
Other	3 (6.3%)	3 (7.1%)	0	1.152	0.053-24.993	0.928
Combined surgery (second incision)	3 (6.3%)	3 (7.1%)	0	1.152	0.053-24.993	0.928
Levels fused						
Number	2.6 (1 – 9)	2.6 (1 – 9)	3.2 (1 – 6)	1.042	0.683 – 1.590	0.848
Anatomical levels						
Thoracic	7 (14.6%)	5 (11.9%)	2 (33.3%)	0.270	0.039-1.876	0.186
Thoracolumbar	8 (16.7%)	6 (14.3%)	2 (33.3%)	0.333	0.050-2.239	0.258
Lumbar	19 (39.6%)	18 (42.9%)	1 (1.7%)	3.750	0.402-34.957	0.246
Lumbosacral	13 (27.1%)	12 (28.6%)	1 (1.7%)	2.000	0.211-18.957	0.546
Thoracic, lumbar and sacral	1 (2.1%)	1 (2.4%)	0	0.470	0.017-12.813	0.654
Bone graft	41 (85.4%)	37 (88.1%)	4 (66.7%)	3.700	0.533-25.679	0.186
Other than Autograft	10 (20.8%)	7 (16.7%)	3 (50.0%)	0.200	0.033-1.203	0.079
Cage used	33 (68.8%)	31 (73.8%)	2 (33.3%)	5.636	0.903-35.189	0.064
Dural tear	7 (14.6%)	6 (14.3%)	1 (16.7%)	0.833	0.082-8.433	0.877
Micro-organism						
Staphylococcus Aureus	24 (50.0%)	19 (45.2%)	5 (83.3%)	0,165	0,018-1,539	0,114
Proprionibacterium acnes (spp.)	1 (2.1%)	1 (2.4%)	0	0.470	0.017-12.813	0.654
Coagulase negative staphylococcus	3 (6.3%)	3 (7.1%)	0	1.152	0.053-24.993	0.928
Enterobacter species	9 (18.8%)	9 (21.4%)	0	3.687	0.190-71.525	0.389
Streptococci species	5 (10.4%)	5 (11.9%)	0	1.907	0.094-38.778	0.675
Polymicrobial	6 (12.5%)	5 (11.9%)	1 (16.7%)	0.676	0.065-7.024	0.743
Soft tissue condition						
Intact	2 (4.2%)	1 (2.4%)	1 (16.7%)	0.122	0.007-2.268	0.158
Open (wet)	43 (89.6%)	38 (90.5%)	5 (83.3%)	1.900	0.176-20.560	0.597
Abscess/ fistula	3 (6.3%)	3 (7.1%)	0	1.152	0.053-24.993	0.928

Table 3. Patient related variables

Patient-related variables	Overall (58)	Successful (52) infection treatment	Failed (6) infection treatment	Odds-ratio	95%CI	*p*-value
Man	22 (45.8%)	19 (45.2%)	3 (50.0%)	0.826	0.149-4.576	0.827
Woman	26 (46.6%)	23 (46.2%)	3 (50.0%)	1.211	0.219-6.705	0.827
Age	58.3 (19-83)	56.3 (19 – 83)	65.1 (37 – 80)			0.177*
BMI	28.2 (17.7 – 41.3)	28.3 (17.7 – 41.3)	28.1 (22.4 – 34.7)			0.327*
Obesity (BMI > 30)	19 (39.6%)	18 (42.9%)	1 (16.7%)	3.750	0.402-34.957	0.246
Smoking	23 (47.1%)	21 (50.0%)	2 (33.3%)	2.000	0.330-12.123	0.451
Comorbidities						
Diabetes	6 (12.5%)	5 (11.9%)	1 (16.7%)	0.676	0.065-7.024	0.743
Pulmonary disease	14 (29.2%)	13 (31.0%)	1 (16.7%)	2.241	0.238-21.150	0.481
Rheumatic disease	8 (16.7%)	7 (16.7%)	1 (16.7%)	1.000	0.101-9.928	1.000
Cardiac disease	11 (22.9%)	9 (21.4%)	2 (33.3%)	0.546	0.086-3.471	0.521
Malignancy (active)	6 (12.5%)	4 (9.5%)	2 (33.3%)	0.211	0.029-1.533	0.124
ASA I	9 (18.8%)	9 (21.4%)	0	3.687	0.190-71.525	0.389
ASA II	21 (43.8%)	20 (47.6%)	1 (16.7%)	4.546	0.488-42.307	0.183
ASA III	17 (35.4%)	12 (28.6%)	5 (83.3%)	0.080	0.008-0.758	0.028
Medication						
Use Steroid	8 (16.7%)	6 (14.3%)	2 (33.3%)	0.333	0.050-2.239	0.258
Use of immunosuppressive	5 (10.4%)	3 (7.1%)	2 (33.3%)	0.154	0.020-1.212	0.076
Trauma patient	7 (14.6%)	5 (11.9%)	2 (33.3%)	0.270	0.039-1.876	0.186
Polytraumatic injury	2 (4.2%)	2 (4.8%)	0	0.803	0.035-18.677	0.891
UCI admission	3 (6.3%)	2 (4.8%)	1 (16.7%)	0.250	0.019-3.280	0.291
Radiation therapy after initial spine surgery	5 (10.4%)	3 (7.1%)	2 (33.3%)	0.154	0.020-1.212	0.076
Blood values preop.						
CRP	169.3 (6 – 584)	152.6 (6 – 584)	298.5 (209 – 414)			0,412*
ESR	57.7 (10 – 120)	55.7 (10 – 112)	75.2 (47 – 120)			0,617*
Leucocytes	16.1 (1 – 87)	16.5 (1 – 87)	12.8 (6.9 – 16.4)			0.904*
Temperature preop.	37.8 (36.4 – 40.0)	37.8 (36.4 – 40.0)	38.1 (36.4 – 39.5)			0.912*
Primary	35 (72.9%)	30 (76.2%)	5 (83.3%)	0.500	0.053-4.739	0.546
Revision	13 (27.1%)	12 (23.8%)	1 (16.7%)	2.000	0.211-18.957	0.546
Interval surgery to start infection symptoms	33 (1 – 186)	34 (1 – 186)	24 (10 – 49)			0.667*
Preop. use of AB	28 (58.3%)	24 (57.1%)	4 (66.7%)	0.667	0.110-4.050	0.660
Postop. duration AB iv	38.0 (6 – 95)	39.4 (8 – 95)	29.3 (6 – 59)			0.275*
Postop. duration AB oral	48.6 (0 – 196)	47.7 (14 – 133)	55.0 (0 – 196)			0.412*
Postop. duration AB total	78.7 (6 – 251)	79.3 (15 – 201)	75.2 (6 – 251)			0.242*
MIC-genta	27.5 (0.50 – 64)	30.6 (0.5 – 64)	1.5 (0.5 – 2.0)			0.509*
Total number of gentamicin-beads	123.3 (0 – 240)	121.4 (0 – 240)	142.5 (120 – 180)			0.412*

*= Mann Withney U test

Discussion

The present study analyzed treatment of SSI and non-union in patients who underwent instrumented fusion of the thoracolumbar spine, with the use of gentamicin impregnated carriers. 42 of the 48 (87.5%) patients showed successful resolution of infection with stable spinal fusion at the end of treatment, without recurrence of infection after a minimum of 1.5 years follow-up.

Although direct comparison with results from other studies in literature is difficult due to the heterogeneity of patient populations, the success rate of treatment in the present study appears to be quite high., Chen et al. reported an implant salvage success rate of 80.4% (41 in 51 patients) with repeated debridements (mean 1.7), systemic antibiotics, with adjunctive antibiotic-impregnated PMMA beads in 20 patients after a 2-year follow-up in patients with SSI after posterior spinal instrumentation.

In 8 of the 41 (19.5%) successfully treated cases, solid fusion was not achieved. Furthermore, only 2 out of 10 patients (20%) who underwent debridement with implant removal showed stable fusion. Unfortunately, the success rate of a subgroup of 20 patients who were treated with antibiotic loaded PMMA beads was not reported separately [29].

Glassman et al. treated 22 patients with SSI after instrumented spinal fusion with multiple debridements (mean 4.7), retention of the instrumentation, and antibiotic (tobramycin and vancomycin) impregnated PMMA beads. No patient showed recurrence of wound infection. Fusion was apparently solid in 14 patients, probable in four patients and nonunion occurred in one patient [30].

Compared to previous studies in which antibiotic carriers have not been used, the present study shows a favourable success rate. Kowalski et al. reported a success rate of 71% in 28 early onset spinal implant infections with retention of instrumentation,

and 84% in 32 late onset spinal implant infections with operative debridement and removal of instrumentation [31]. Collins et al. reported a cure rate of 40% in 15 acute infections following instrumented spinal fusion with long-term (systemic) antibiotics and debridement with retention of the instrumentation [6]. The lower eradication rates observed in these studies clearly illustrate the added value of local antibiotic carriers in infection treatment after instrumented spine surgery in our opinion.

Kim et al. treated 20 patients with SSI between 1 and 5 months after instrumented spinal surgery with implant removal and wide debridement to clear the infection, despite the risk of disc space collapse and loss of normal lordosis. The infection was eradicated in all 20 patients after a minimum follow up of 2 years, but instability and/or pseudarthrosis at the fused segments was observed in 14 patients, thus resulting in a poor clinical outcome [32].

Several other supplemental procedures have been reported in the treatment of SSI after instrumented spinal fusion aside from the use of antibiotic impregnated PMMA beads, such as continuous suction irrigation, vacuum-assisted wound closure, or local tissue flap coverage. These studies are difficult to compare, because of the different treatment procedures. However the success rate of the present study is in the higher range of the success rates reported for these alternative supplemental procedures. Rohmiller et al. treated 28 patients with post-operative spinal infection with one operative session consisting of incision, drainage and closed suction irrigation. 75% of infections were resolved without recurrence after an average follow-up of 22.3 months. [33]

Mehbod et al. achieved a clean closed wound after an average follow-up of 10 months (6-24 months) in all of 20 patients with SSI after spinal fusion, treated with an average of 1.8 (1-8) debridements prior to a vacuum-assisted wound closure procedure, and an ultimate VAC removal procedure in which the wound was closed over drains[34]. Labler et al. needed to exchange or remove the instrumentation in 12 of 13 infections after instrumented spinal surgery treated with vacuum assisted closure of the wound (15-40 months follow-up). One patient developed a recurrence infection at follow-up [35]. Sierra-Hoffman et al. reported a cure rate of 89% for early onset instrumented spinal infection in 19 patients by debridement with retention of the instrumentation, drainage and packed open with antibiotic solution soaked gauze and loose retention sutures. All patients returned to the operating room for follow-up debridement and closure over drains after 2-3 days, followed by systemic antibiotic administration. They noted a cure rate of 100% with no relapses for at least 3 years after therapy was reported in 7 late onset infections with removal of the instrumentation and 1 or 2 debridements [4].

In this study, a mean number of 2.3 (1-4) operations were needed including the removal of the PMMA beads, mostly a minor operation. Picada et al. reported that one-third of 26 patients required four or more debridements before obtaining a clean wound for closure [36]. Mehbod et al. reported a mean number of 3.25 (3-10) visits to the operating room to obtain a closed wound with vacuum-assisted wound closure in 20 patients [34].

In the present study 16.7% of the patients complained of residual disabling back pain at the end of the follow up, and 27.1% patients in total experienced limitations in activities of daily living because of residual back and/or leg pain. Similar to most studies in literature, our patients showed a less satisfactory outcome after instrumented spinal fusion with SSI compared with control groups without infection. [29, 37, 38]

We found *Staphylococcus aureus* (*S. aureus*) to be the most frequent (24/48) causative microorganism of SSI. This is comparable to literature [6, 29, 33, 39]. International literature reports suggest an increasing prevalence of MRSA [8, 32], but MRSA was not cultured in our patients. This may be the result of the strict MRSA policy in the Netherlands [40].

Those patients with a failure of infection treatment had a significantly higher ASA score preoperatively as compared to the patients with a successful treatment. This difference is similar to findings in the literature on the infection treatment of hip and knee prosthesis infections [22, 23]. No firm conclusion can be drawn due to of lack of statistical power.

The present study has several limitations. The study design is retrospective, and although the number of 48 patients was adequate as compared to other studies in literature, there were only 6/58 failures of treatment. The heterogeneity of patient and operation-related characteristics (time to infection treatment, indication of primary surgery, number of fused levels) in this study makes it hard to interpret outcome. A comparison to literature is even more difficult because of differences in treatment, definitions for outcome, patient characteristics, differences in surgical indications, and prevalence of micro-organisms. Another limitation was that the functional outcome was assessed by retrospective analysis of the files at the outpatient clinic.

All currently available clinical evidence regarding the treatment of postoperative infections after instrumented spinal surgery is based on

uncontrolled retrospective studies. It is hard to conduct randomized controlled trials, as it would the cooperation of many centres in this field would be required due to the low infection rates and heterogeneity of patient populations.

A valuable alternative for future research would be setting up national and international registries to compare data of diagnosis, operations, comorbidity, and treatment of the infection and outcome variables in large patient populations. Although of lower internal validity as compared to RCT's, evidence of high external validity could be obtained in this way as the included patients would genuinely reflect daily clinical practice.

Conclusion and Clinical Relevance

Debridement and retention of instrumentation in combination with systemic antibiotics and the addition of local antibiotics (gentamicin impregnated PMMA beads or fleeces) results in successful treatment for SSI and non-union after instrumented spinal fusion.

Competing Interests

The authors have declared that no competing interest exists.

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