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ARTICLE

Osteomyelitis and antibiotic treatment in patients with grade IV pressure injury and spinal cord lesion—a retrospective cohort study

Johanna Rigazzi[1], Carina Fähndrich[1,2], Rik Osinga[3,4], Sandro Baumgartner[1,5], Michael Baumberger[1], Jörg Krebs[1], Dirk Johannes Schaefer[4], Markus Vogt[5], Reto Wettstein[4] and Anke Scheel-Sailer[1,2]✉

STUDY DESIGN: Retrospective cohort study.
OBJECTIVES: To analyze characteristics and treatment of osteomyelitis (OM) in the treatment of grade IV pressure injury (PI) in patients with spinal cord injury/disorder (SCI/D) following the Basel Decubitus Concept.
SETTING: Acute care and rehabilitation clinic specialized in SCI/D.
METHODS: Patients with SCI/D were admitted for grade IV PI treatment between 1st January 2010 and 28th February 2015. Patients, SCI/D, and PI characteristics were collected from chart reviews. Descriptive statistics and differences between groups with and without OM were evaluated.
RESULTS: In total, 117 patients (87 male, 30 female) with 130 PI grade IV were included. In 95 patients (81%), OM was diagnosed histologically. In 87 cases, more than one bacterial species was involved. Out of 49 different bacterial species, Enterococcus faecalis and Staphylococus aureus were most frequently observed. Amoxicillin/clavulanic acid and ciprofloxacin were the most frequently used out of 24 different antibiotics. Length of antibiotic treatment varied between <8 days and >91 days with 31 patients receiving antibiotics for about 8 weeks. Complications occurred in all groups of antibiotic duration. Having a paraplegia, no OM and sacral PI was associated with increased complication rates, but the number of patients did not allow comprehensive risk factor analysis.
CONCLUSION: Because the variety of patients concerning SCI/D, PI, and OM characteristics did not show a conclusive relation between length of antibiotic treatment and complication rates, the development of a subgroup specific treatment concept for PI in patients with SCI/D would be favorable to further optimize antibiotic treatment.

Spinal Cord (2022) 60:540–547; https://doi.org/10.1038/s41393-022-00758-1

INTRODUCTION

The treatment of grade IV pressure injury (PI) with bone exposure according to the European Pressure Ulcer Advisory Panel (EPUAP) classification [1] with or without osteomyelitis (OM) in patients with spinal cord injury/disorder (SCI/D) remains challenging because of long healing and hospitalization times, complications, and recurrences associated with high healthcare costs [2, 3]. Several multidisciplinary and inter-professional concepts including plastic surgery, infectious disease, acute care, and complex rehabilitation services comprising wound care, respiratory therapy, nutritional support, psychological counselling, mobilization training, and the evaluation of auxiliary devices have been defined [4–12].

Many treatment concepts integrate surgical procedures that embrace the principle to reconstruct 'like with like', thus plastic surgical soft-tissue reconstruction with fasciocutaneous flaps. After flap surgery, the patient is immobilized on a specialized alternating pressure mattress, and regular pressure-release maneuvers are applied during 6 weeks [6, 13, 14]. Minor and major complication rates after flap surgery in patients with SCI/D and grade IV PI range from 17.3 [4] to 40% during the initial treatment phase [8, 15]. Risk factors such as age, time since SCI, smoking, diabetes, and renal function contribute to complication rates [5, 8, 12, 15].

According to these multidisciplinary concepts, the diagnosis and treatment of OM are essential [5, 7, 16]. The diagnosis of OM includes clinical aspects of local bone density and quality, histological findings, and microbiological results of bone biopsies. Radiological examinations, such as computer or magnetic resonance tomography, are conducted if indicated [3, 17], leading to OM detection rates of 97% [2, 18–20]. Starting point, length, and application of antibiotic treatment recommendations vary between no antibiotic treatment at all, starting before or after surgical reconstruction, antibiotic treatment for two, six, and up to 12 weeks [2, 5, 15–17, 21, 22]. Other concepts define the length of antibiotic treatment depending on microbiological and histological findings [2, 16] or standardize independently of the presence of OM [15]. Therefore, the aim of this study is to analyze the characteristics and treatment of OM using the Basel Decubitus Concept in a single specialized SCI/D center.

[1]Swiss Paraplegic Centre, Nottwil, Switzerland. [2]Department of Health Sciences and Medicine, University of Lucerne, Lucerne, Switzerland. [3]Center for Musculoskeletal Infections, University Hospital Basel, Basel, Switzerland. [4]Department of Plastic, Reconstructive, Aesthetic and Hand Surgery, University Hospital Basel, Basel, Switzerland. [5]Department of Internal Medicine, Infectious Diseases Service, Cantonal Hospital Zug, Baar, Switzerland. ✉email: anke.scheel-sailer@paraplegie.ch

Received: 10 October 2021 Revised: 20 January 2022 Accepted: 20 January 2022
Published online: 4 February 2022

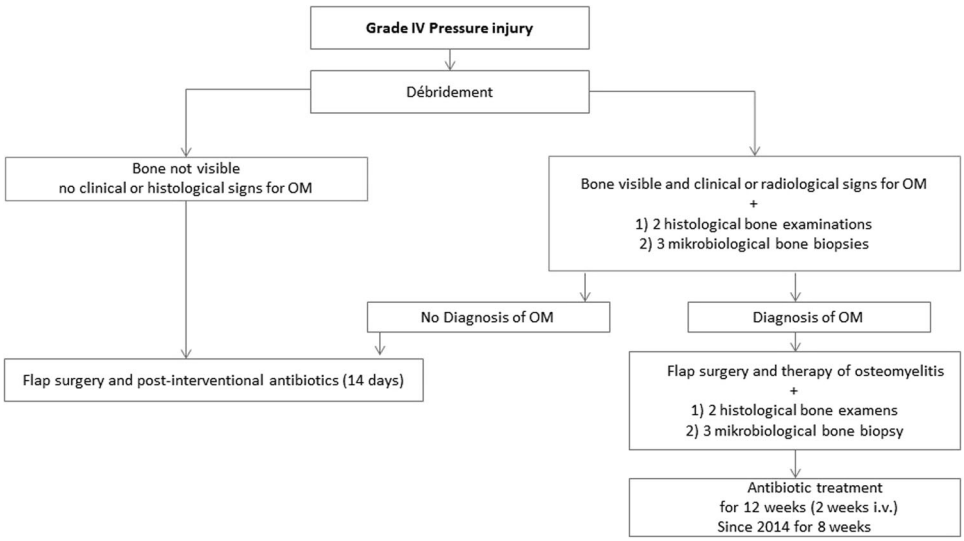

Fig. 1 The infectious disease concept as part of the Basel Decubitus Concept. OM = Osteomyelitis, i.v. = intravenose.

METHODS

Study design and setting

This study is a retrospective observational cohort study based on routinely collected health data at an acute care and rehabilitation clinic specialized in SCI/D. The conservative and surgical treatment of PI based on the Basel Decubitus Concept [6, 8, 13] was first implemented two decades ago and has been continuously adapted and improved [7, 9].

Basel decubitus concept

The concept is based on six principles: (1) pressure reduction by placing patients on specialized alternating pressure mattresses and regular pressure-release maneuvers; (2) early operative debridement and antibiotic treatment if necessary; (3) wound conditioning with moist dressing or negative pressure wound therapy (NPWT); (4) optimizing risk factors such as malnutrition; (5) plastic surgical soft-tissue reconstruction with fasciocutaneous flaps followed by 6 weeks of immobilization; and (6) patient education [6, 13]. The further development of the concept included inter-professional risk profile analyses and rehabilitation based on the biopsychosocial model according to the International Classification of Functioning [7, 23], specific nutrition screening and therapy [9], psychological support, and the process-based infectious disease concept presented in Fig. 1. Relevant milestones in the Basel Decubitus Concept are debridement, reconstructive surgery, start of mobilization, and discharge planning [7]. The length of immobilization time was usually 6 weeks, followed by a daily increased time of wheelchair mobilization as long as no complications occur.

Surgical procedure. After radical surgical debridement (second principle), six bony biopsies were taken if bone structures were exposed and/ or OM clinically suspected (three for bacteriological examination and three for histomorphological examination (Institute for Genetics and Pathology, University of Basel)). The wound was covered with moist dressings or NPWT (third principle). After wound conditioning, a second set of biopsies was taken right before soft-tissue reconstruction. The flaps were designed in such way that (i) tension during closure was minimized, (ii) the resulting scar was placed outside the primary pressure zone (bony prominence), and (iii) allowing re-raising and extending in case of recurrence. Therefore, no muscle flaps and no V–Y design was used. During flap mobilization, a maximum of perforating vessels were preserved. Flap insertion and wound closure was performed using a multi-layer adaptation technique. Drains were routinely inserted [6, 8].

Infectious disease concept. The biopsies were taken from the bone using a Luer forceps during the first debridement to diagnose acute or chronic OM histomorphologically [24] and identify the infectious agent (Fig. 1). Antibiotic treatment was started after the soft-tissues reconstructed based on the first bacterial results and adjusted if indicated by the second samples. In the absence of OM in the histomorphological workup of the bone antibiotic treatment for 2 weeks was recommended. If acute or chronic OM was detected, the treatment was extended to a maximum of 12 weeks. Selection of adequate antibiotics was based on susceptibility of the isolated bacteria and bone histology. Antibiotics were given intravenously for 2 weeks and, if necessary due to OM, orally or intravenously thereafter [22, 25]. Weekly blood checks including leucocytes and renal function were performed, and the dosages of antibiotics and other drugs were adjusted.

Cohort and observation period

All consecutively admitted patients with SCI/D and concomitant grade IV PI between January 1st 2010 and February 28th 2015 were included. Patients with multiple sclerosis, critical illness polyneuropathy, spastic spinal paralysis, brainstem encephalitis, tumor disease, patients in a palliative situation, and patients who denied the retrospective use of their data were excluded.

Data collection

Data were extracted from the hospital medical information systems MedFolio (Nexus ag, Switzerland, Version: 2.2.0.2317), ixserv4 (ix.mid Software Technologie GmbH, Version: R20.4), WiCareDoc (WigaSoft AG, Switzerland, Version: 7.1.3), and PHOENIX PACS (Phoenix-PACS GmbH, Germany, Version: 5.4). The following patient characteristics were recorded: lesion level and completeness of SCI according to the international standards of neurological classification (ISNCSCI); etiology for SCI/D (traumatic and non-traumatic) according to the ISCoS definition [26]; time since SCI/D; age and sex; comorbidities (diabetes and cardiac failure); body mass index; renal failure and nutrition parameters. Renal function was classified according to the estimated glomerular filtration rates (eGFR) into mild dysfunction GFR < 60, medium < 30, and severe < 10 ml/min using cystatine C [27]. The following PI characteristics were collected: location, grade of PI according to EPUAP, number of concomitant PIs, and previous surgeries at the current site of PI (recurrence). Only the first and second surgical procedures and related complications were analyzed. Bacterial species were analyzed using the Matrix Associated Laser-Desorption-Ionization Time of Flight technique, described, and then summarized as bacterial groups [25].

Postoperative flap-related complications were identified in the surgical documentation. Minor suture dehiscence or hematoma without the need for evacuation were considered minor complications. Hematoma, infection, seroma, wound dehiscence, and partial flap necrosis in need of surgery were classified as major complications.

Antibiotics were described as generic drug names and listed. The length of antibiotic treatment was recorded from the first day of application until the last day regardless of the administered antibiotic and grouped into the following categories: <8 days (≤1 week), 8–14 days (1–2 weeks), >14 days (>2 weeks) in case of no OM, ≤ 21 days (≤3 weeks), 22–35 days (4 weeks), 36–49 days (6 weeks), 50–63 days (8 weeks), 64–77 days (10 weeks), 78–91 days (12 weeks) and more than 91 days (>13 weeks) in case of OM. The application of antibiotics was categorized into immediate start after

Table 1. Characteristics of patients with spinal cord injury/ disorder ($N = 117$) and grade IV pressure injury ($N = 130$) after surgical treatment ($N = 125$).

	Total *n* (%)	PI IV° without OM *n* (%)	PI IV° with OM *n* (%)	*p* value[a]
Sex				0.20[1]
` Male	87 (74.4)	14 (63.6)	73 (76.8)	
Female	30 (25.6)	8 (36.4)	22 (23.2)	
Age at admission (year): median (IQR)	53 (22.3)	48 (20.6)	54 (23.5)	0.08[3]
Years since Injury: median (IQR)	21.6 (21.39)	22.3 (21.5)	21.6 (21.9)	0.77[4]
Etiology of SCI				0.23[1]
Traumatic SCI				
Traffic and transport activity	30 (25.6)	8 (36.4)	22 (23.2)	
Sports and leisure activity	11 (9.4)	2 (9.1)	9 (9.5)	
Fall	25 (21.4)	3 (13.6)	22 (23.2)	
Other accident cause	25 (21.4)	2 (9.1)	23 (24.2)	
Non-traumatic SCI				
MMC	9 (7.7)	1 (4.5)	8 (8.4)	
Spinal tumor	2 (1.7)	2 (9.1)	0	
Infection/Inflammation	4 (3.4)	0	4 (4.2)	
Other disease undefined	9 (7.7)	4 (18.2)	5 (5.3)	
Caused by surgical intervention	2 (1.7)	0	2 (2.1)	
Neurological level of SCI				0.08[2]
C1–C4 A,B,C	17 (14.5)	3 (13.6)	14 (14.7)	
C5–C8 A,B,C	26 (26.2)	9 (40.0)	17 (17.9)	
T1–S5 A,B,C	74 (63.2)	10 (45.5)	64 (67.4)	
ISNCSCI				0.29[2]
ISNCSCIA	92 (78.6)	16 (72.7)	76 (80.0)	
ISNCSCIB	15 (12.8)	5 (22.7)	10 (10.5)	
ISNCSCI C	10 (8.5)	1 (4.6)	9 (9.5)	
Comorbidities				
Diabetes mellitus	13 (11.1)	2 (1.7)	11 (9.4)	1.00[2]
Renal function				0.16[2]
GFR > 90	52 (48.1)	14 (63.6)	38 (44.2)	
GFR ≤ 90	29 (26.9)	7 (31.8)	22 (25.6)	
GFR ≤ 60	16 (14.8)	1 (4.5)	15 (17.4)	
GFR ≤ 30	10 (9.3)	0	10 (11.2)	
GFR ≤ 10	1 (0.9)	0	1(1.2)	
BMI				1.00[2]
18–25	46 (52.3)	9 (52.9)	37 (52.1)	
<18	4 (4.5)	1 (5.9)	3 (4.2)	
>25	38 (43.2)	7 (41.2)	31 (43.7)	
Number of PI grade I–IV per Patient				0.42[2]
1	85 (72.6)	17 (77.3)	68 (71.6)	
2	20 (17.1)	2 (9.1)	18 (18.9)	
3	10 (8.5)	2 (9.1)	8 (8.4)	
4	2 (1.7)	1 (4.5)	1 (1.1)	
Localization of the PI				0.65[2]
Ischium	75 (64.1)	16 (72.7)	59 (62.1)	
Coccyx/Sacrum	32 (27.4)	4 (18.2)	28 (29.5)	
Trochanter	10 (8.5)	2 (9.1)	8 (8.4)	
Recurrence of previous PI	55 (47.0)	7 (31.8)	48 (50.5)	0.11[1]
Previous OM	40 (34.2)	2 (9.1)	38 (40.0)	**0.01[2]**
Complications				
Overall complication after surgery	73 (62.4)	18 (81.8)	55 (57.9)	**0.05[2]**
Minor complication after surgery	48 (41.0)	10 (45.5)	38 (40.0)	
Major complication after surgery	25 (21.4)	8 (36.6)	17 (17.9)	

P values ≤ 0.05 are indicated in bold.
°Grade.
BMI Body Mass Index, *GFR* Glomerular Filtration Rate, *IQR* Interquartile Range, *ISNCSCI* International Standard for Neurological Classification in Spinal Cord Injury, *MMC* Meningomyelocele, *OM* Osteomyelitis, *PI* Pressure Injury, *SCI* Spinal Cord Injury.
[a]Chi-square[1], Fisher's exact[2], *t*-test[3] or Wilcoxon rank-sum[4] test.

soft-tissue reconstruction (within 24 h h), 1–7 days delay, start after 8 days, and start before the soft-tissue reconstruction. If there was an interruption in the antibiotic therapy of more than 7 days, or if the treatment was started later than 28 days after soft-tissue reconstruction, the period of antibiotic therapy was not considered PI-related.

Statistical analysis

Quantitative data were presented as median with upper and lower quartiles. Categorical data were presented as frequency and percentage. To examine differences of categorical data between the OM and the control group, the Chi-square or Fisher's exact test were used. Two-group

comparison of quantitative data were performed using the unpaired *t*-test or the Wilcoxon rank-sum test according to the data distribution. Binary logistic regression analysis was used to investigate the effects of sex, age, time since SCI, severity (tetraplegia/paraplegia), presence of OM, PI recurrence, comorbidities (renal function and diabetes mellitus), PI location (sacral/ischial//trochanteric), and duration of antibiotic treatment for the occurrence of complications (minor and major versus no, only minor versus no and only major versus no or minor complication).

The statistical analyses were performed using StataSE-16 (64-bit) statistical software for windows. A p value of ≤0.05 was considered to indicate statistical significance.

RESULTS

Patient and disease characteristics

One-hundred and seventeen patients met the inclusion criteria. Of these, 43 (36.8%) patients had a cervical SCI/D and 74 (63.3%) patients a thoracic SCI/D (Table 1). 92 (78.6%) patients showed a complete SCI/D lesion (ISNCSCI A). The median age at the time of admission of all patients (30 (25.6%) female, 87 (74.4%) male) was 53 years (22 quartiles). The median years since injury was 22 years (21 quartiles). The localization of the grade IV PIs was at the ischial tuberosity in 75 (64.1%), at the sacrum or coccyx in 32 (27.4%), and at the greater trochanter in 10 (8.5%) patients. Fifty-five (47%) patients out of 117 patients were seen because of recurrent PI. 85 (72.6%) patients only had 1 PI, 20 (17.1%) patients had 2 PI, 10 (8.5%) patients had 3 PIs and 2 (1.7%) patients had 4 PIs. In 95 patients (81%), OM was diagnosed histologically. Forty-four (44.2%) patients had already had an OM in the previous PI. There were no significant ($p \geq 0.08$) differences regarding patient and PI characteristics between patients with and those without OM (Table 1). A previous OM was significantly associated with the development of an OM ($p = 0.01$). However, significantly ($p \leq 0.05$) more patients without OM suffered from post-operative complications (Table 1). Significant ($p \leq 0.05$) differences in blood and nutrition parameters between both groups (with/without OM) were observed in c reactive protein and potassium (Table 2).

Osteomyelitis

A total of 321 bony biopsies were taken from 125 PIs in 117 patients. In nine PIs, the plastic surgeon had decided not to take bony biopsies intra-operatively because the bone was completely covered, and there were no clinical signs of OM. In 12 of the 321 biopsies, no bacterial growth or OM was detected. In the 309 positive biopsies, 54 different bacterial species and Candida albicans were identified (Supplementary Material Table 1). Enterococcus faecalis and Staphylococcus aureus species were identified in 44 (14%) and 43 biopsies (14%), respectively (Fig. 2). A methicillin-resistant Staphylococcus was identified once. A total of 70.8% ($n = 188$) were gram-positive bacteria, and 29.1% ($n = 84$) were gram-negative bacteria. In most biopsies, two ($n = 31$/29%) or three species ($n = 25$/24%) were identified (Supplementary Material Table 1).

Plastic surgical reconstructive techniques

A total of 125 reconstructive plastic surgical procedures were performed. Six patients received two surgical procedures, and one patient received three surgical procedures. The most commonly used flap was a fasciocutaneous posterior thigh flap for ischial PI in 77 patients, followed by a fasciocutaneous gluteal rotation flap for sacral PI in 35 patients, and a fasciocutaneous flap based on the M. tensor fascia lata perforator for trochanteric PI in five patients (Supplementary Material Table 2). The other PIs healed according to the conservative wound treatment concept.

Antibiotic treatment

In total, 24 different antibiotics were applied. The most frequently used antibiotics were amoxicillin/clavulanic acid, followed by ciprofloxacin, piperacillin-tazobactam, and clindamycin (Table 3).

Table 2. Description and comparison of the blood and nutrition parameters in patients with SCI and grade IV PI without ($N = 22$) and with ($N = 95$) osteomyelitis.

	Reference values	All patients			Patients with PU IV° without OM			Patients with PU IV° with OM			MD	Pathologic
Nutrition parameter	**Normal population**	***N***	**MD (IQR)**	**Pathologic n/%**	***N***	**MD (IQR)**	**Pathologic n/%**	***N***	**MD (IQR)**	**Pathologic n/%**	***p* value[1]**	***p* value[2]**
Albumin	35–50 g/l	114	35 (7)	51/43.6	22	37 (6.5)	7/31.8	92	35 (8)	44/46.3	0.25	0.37
Protein	64–83 g/l	114	64 (9.5)	54/46.2	22	64 (9)	10/45.5	92	64 (10)	44/46.3	0.54	0.99
Hemoglobin	140–170 g/l	114	128 (30)	83/70.9	22	129 (27.3)	15/68.2	92	127 (30)	68/71.6	0.79	0.60
CRP	<5 mg/l	112	42.5 (59.3)	98/83.8	21	17 (58)	16 / 72.7	91	43 (59.5)	82/86.3	**0.05**	0.19
Creatinine	59–104 µmol/l	117	47 (10)	93/79.5	22	44.5 (15.5)	20/90.9	95	49 (22)	73/76.8	0.10	0.28
Sodium	135–145 mmol/l	117	137 (4)	25/21.4	22	138 (2.8)	4/18.2	95	137 (4)	21/22.1	0.28	0.23
Potassium	3.5–5.1 mmol/l	117	4.2 (0.5)	5/4.3	22	4.5 (0.3)	1/4.5	95	4.2 (0.5)	4/4.2	**0.001**	0.38
GFR	>90 ml/min	108	89 (49.5)	56/47.9	22	97.5 (33)	7/31.8	86	83 (70.75)	49/51.6	0.06	0.64

P values ≤ 0.05 are indicated in bold.
°Grade.
N number, *MD* median, *IQR* Interquartile Range, *ISNCSCI* International Standard for Neurological Classification in Spinal Cord Injury, *MMC* Meningomyelocele, *OM* Osteomyelitis, *PI* Pressure Injury, *SCI* Spinal Cord Injury, *CRP* c reactive protein, *GFR* Glomerular filtration rate.
[1]Mann–Whitney U test (continuous variables), [2]Chi-square or Fisher's exact, (categorial variables).

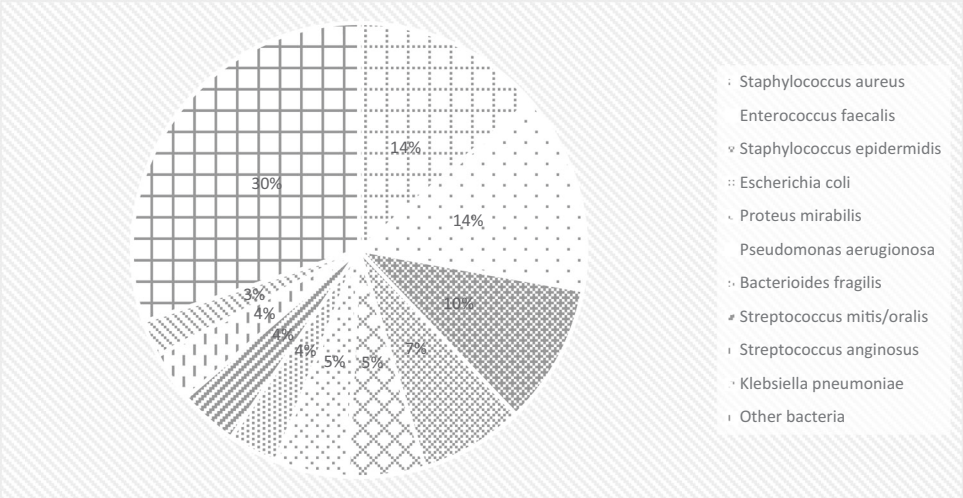

Fig. 2 Bacteria found in biopsies from pressure injury IV taken during debridement. % indicate the percentage of detected bacteria in all biopsies.

Table 3. Antibiotic therapy according to surgical procedures in patients with SCI/D and grade IV PI.

Antibimicrobial agent	Number of use
Amoxicillin/clavulanic acid	67
Ciprofloxacin	53
Piperacillin/Tazobactam	41
Clindamycin	46
Vancomycin	20
Daptomycin	26
Amoxicillin	10
Imipenem/Cilastatin	21
Ceftriaxon	10
Rifampicin	6
Norfloxacin	1
Fluconazol	7
Sulfamethoxazol/Trimethoprim	24
Cefuroxim	4
Metronidazol	6
Linezolid	10
Meropenem	6
Colistimethat natrium	3
Ceftazidim	4
Gentamicin	2
Tobramycin	1
Flucloxacillin	5
Cefazolin	1
Ertapenem	3

Twenty-two patients received one, 15 patients received two, 29 patients received three, 24 patients received four, and 1 patient received eight different antibiotics over the entire treatment course. Approximately one quarter of the patients ($N = 31/26.5\%$) received antibiotics for 8 weeks (50–63 days) (Fig. 3).

Complication rates

Minor complications occurred in 10 (45%) and major in 8 (36%) out of 22 patients without OM (Fig. 3). In patients with OM minor complication occurred in 38 patients (40%) and major in 17 (18%) out of 95 patients. Major complications were found in all groups of antibiotic treatment time (Fig. 3). In the group of around 8 weeks antibiotic treatment we found 15 patients without complications, 14 patients with minor and only 2 with major complications. Having a paraplegia (Odds Ratio (OR) 2.74), no OM (OR 4.38), and a sacral PI (OR 3.07) increased the risk for minor or major complications significantly (Table 4).

DISCUSSION

By applying the Basel Decubitus Concept for diagnosis and therapy of OM in patients with SCI/D and grade IV PI, we found an OM rate of 81%. History of previous OM and elevated signs of infection were associated with presence of OM. 54 different bacterial species and Candida albicans were identified and 24 different antibiotics were given to treat the infection according their susceptibility. Length of antibiotic treatment varied in this sample and complication rates after surgery were not related to this.

According to the Basel Decubitus Concept diagnosing the OM is essential. We used data on the histopathological examination for each debridement and before reconstruction of the PI, following previous recommendations [24]. Because radiological examinations are not regularly performed to diagnose OM, association between radiological examinations and histopathological findings, could not be explored. The OM rates in our cohort of consecutive patients reached roughly 80% and were higher compared with other studies [4, 15]. The bone examination techniques included microbiological and histopathological examinations, but no differentiation between different depths and intensities of OM nor between superficial and deep bacteria. Therefore, the 54 different bacteria were a mixture of superficial and OM bacteria. In other studies, the detected bacteria included only 17 different bacteria in seven defined subgroups [4, 15]. A standardized technique for extracting bone samples might be an important step toward choosing the best antibiotic substance and the required length of therapy. To reduce over- or undertreatment in acute or chronic infections in this variety of bacteria, integrated infectiology support is necessary. This guarantees the implementation of the newest guidelines and principles of the Stewardship Program [25, 28]. The histopathological examination can differentiate between acute and chronic OM to further develop specific and personalized treatment [3] and should be included in future decubitus concept. Recent discussions have highlighted specific diagnostics of infected bone structures, such as depth and severity of infection, to specify the length of antibiotic treatment [2, 29].

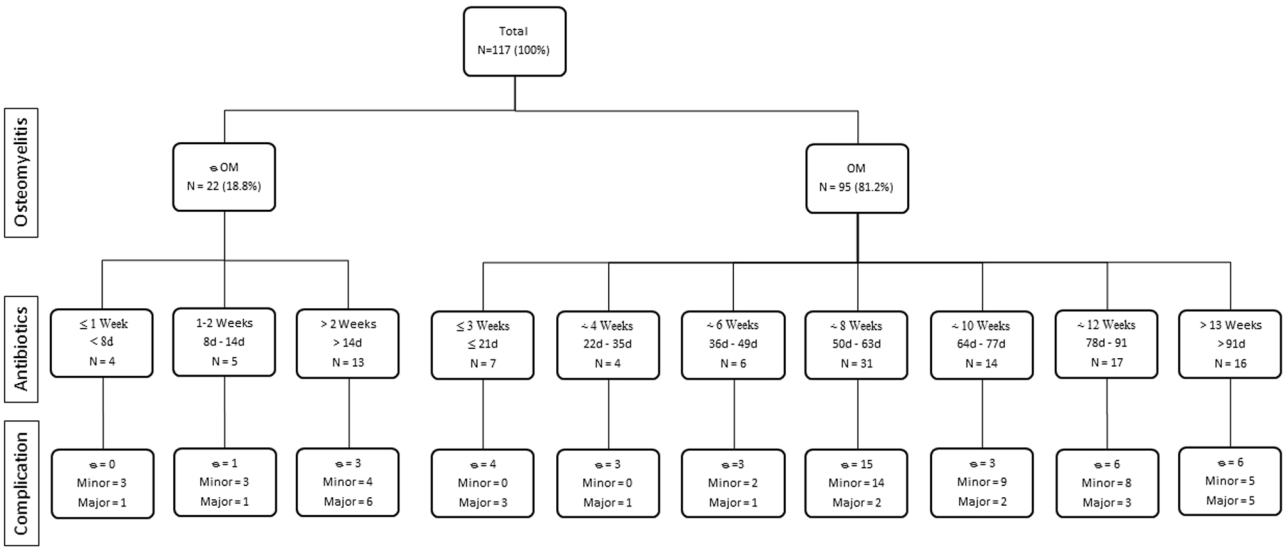

Fig. 3 Groups of antibiotic treatment around reconstructive surgery in the modified Basel Decubitus Concept in patients with spinal cord injury and pressure injury. d: days; OM: Osteomyelitis.

Table 4. Major, minor, and both complications after flap surgery in individuals with spinal cord injury and pressure injury.

Predictors (reference category)	Minor or major complication			Major complication			Minor complication		
	p	Exp(B)	95% CI Exp(B)	*P*	Exp(B)	95% CI Exp(B)	*P*	Exp(B)	95% CI Exp(B)
Gender (men)	0.92	0.95	0.36–2.48	0.56	0.70	0.21–2.33	0.91	1.06	0.38–3.02
Age at admission	0.39	0.99	0.95–1.02	0.17	1.03	0.99–1.07	0.16	0.97	0.94–1.01
Years since SCI	0.11	1.03	0.99–1.06	0.50	0.99	0.95–1.02	0.06	1.03	1.00–1.07
Injury severity (paraplegia)	**0.03**	2.74	1.14–6.60	**0.00**	12.27	2.55–58.92	0.31	1.64	0.64–4.26
Osteomyelitis (no)	**0.02**	4.38	1.25–15.40	**0.00**	9.55	2.41–37.82	0.22	2.44	0.58–10.28
Recurrence (no)	0.61	1.23	0.54-2.81	0.91	0.94	0.31–2.86	0.61	1.26	0.51–3.14
Renal function (<90 GFR)	0.88	1.07	0.44–2.57	0.68	1.28	0.39–4.17	0.89	1.07	0.42–2.73
Diabetes mellitus (no)	0.79	1.20	0.31–4.64	0.50	1.82	0.32–10.37	0.99	0.99	0.20–4.75
Localization (sacral)	**0.04**	3.07	1.07–8.78	**0.00**	8.18	2.41–27.79	0.30	1.91	0.56–6.48

$N = 98$. *P* values ≤ 0.05 are indicated in bold.
Exp(B) odds ratio predicted by model, *CI* confidence interval, *SCI* spinal cord injury.

Such diagnostics might be a scientific and clinically feasible way to determine the patient tailored length of antibiotic therapy, to address individual patient needs and reduce recurrence of OM and complication rates.

In analyzing the antibiotic treatment, we realized that the adherence to the Basel Decubitus Concept including two weeks antibiotics if no OM and eight to 12 weeks antibiotic in case of OM could have been feasible. However, due to the retrospective character of the study, the individual reasons for non-adherence to this concept could not be elaborated in detail. To optimize concept adherence and understand reasons for non-adherence prospective data collection including documentation of individual reasons of non-adherence to the concept might be a necessary next step. To overcome challenges in the clinical management, continuous education of specialist and the use of computerized decision support systems could stimulate implementation of complex treatment concepts [30, 31].

The quality of infectious disease concept can be evaluated by observing healing after PI surgery and the occurrence of major complications in relation to the choice and length of antibiotic therapy. Major complications however may be not only caused by the choice and suboptimal length of antibiotic therapy, but also by patients' PI characteristics, comorbidities, and surgical and inter-professional procedures [6–8]. Therefore, the characteristics of the observed cohort and the other interventions must be considered in observing the effects of the different elements in the Basel Decubitus concept. In our cohort, complications were higher in patients not having OM, having a paraplegia and a sacral PI compared with other cohorts in which older age, low serum albumin, over- or underweight [32] male sex, complete SCI (AIS A), ischial area [15], and African ethnicity [4] were associated with an increased risk of complications. Considering all relevant influencing factors, our sample appeared to small for complex statistical analyses and data from a larger cohort should be collected.

In summary, to further develop the concept of multidisciplinary and inter-professional treatment of PI in patients with SCI/D, detailed description of patient, PI, and OM characteristics should be defined. Without a relevant classification of these influencing factors, the effects of different elements cannot be compared and specified. Analyses of PI recurrence rates after discharge are the next step for further evaluating this comprehensive treatment concept. To optimize the length of antibiotic therapy more specific concepts according to superficial or deep OM and related to different bacteria groups might be the next step. Because of its complexity, the treatment of PI in patients with SCI/D requires a specialized setting and clearly integrated clinical processes. A prospective cohort study or a register that include patients, PI and OM characteristics, treatment elements and milestones as well as

complications would be the best step to evaluate the concept as a whole and each single intervention element.

LIMITATIONS

First, our study used a retrospective observational cohort design, and the data were extracted from regular clinical documentation. Therefore, the quality of the data on some risk factors was reduced because some standardized documentation was missing (e.g., smoking, self-efficacy, and depressive mood). The number of patients did not allow risk analyses of special subgroups. Nevertheless, our cohort is one of the largest, and most of the relevant risk factors were analyzed. Due to the observation period covering only the inpatient stay the topic of recurrence after discharge cannot be answered. This should be addressed in further research. The main advantage of our study is, that the treatment concept was performed in one specialized center, and the quality of the clinical treatment was consistent.

CONCLUSION

Using the modified Basel Decubitus Concept, OM was diagnosed in 80% of all patients with SCI/D and grade IV PI around the pelvis. The variety of patients concerning SCI/D, PI, and OM characteristics did not allow a conclusive relation between length of antibiotic treatment and major or minor complication. The development of a subgroup specific treatment concept for PI in people with SCI/D might be the next step for increasing quality and reducing complication and recurrence rates considering the risk constellations of patients with SCI/D and PI. Differentiated OM diagnoses and classifications might be relevant in developing patient-tailored antibiotic treatment as part of a new, more comprehensive concept.

DATA AVAILABILITY

All data are stored with the corresponding author and can be asked directly (anke.scheel-sailer@paraplegie.ch).

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ACKNOWLEDGEMENTS

We acknowledge the Decu Care Team (Karin Gläsche, Jessica Decker, Rita Müller, Zamzow) as the supported data collection and discussions in relation to clinical implementation of the results.

AUTHOR CONTRIBUTIONS

JR developed the study, collected the data, wrote the paper and finalized the paper. RO, SB, MB, DJS, MV, RW were involved in creating the study, gave relevant feedback for the paper and approved the final version of the paper. JK and CF approved the study method, performed the statistical analyses, and gave valuable feedback regarding the paper. ASS developed the study, wrote the paper, and finalized the paper.

COMPETING INTERESTS

The authors declare no competing interests with respect to this research, authorship, and publication of this paper. The work was a part of JE's doctoral thesis (Dr med. Promotion).

ETHICS APPROVAL

This study was conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP as well as all national legal and regulatory requirements, and excluded patients who denied their consent of further use of their data. All data were kept confidential and processed anonymously. The study received ethical permission from the Ethics Committee Northwest and Central Switzerland (EKNZ 2014-107). The RECORD checklist was applied in this observational study [33].

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41393-022-00758-1.

Correspondence and requests for materials should be addressed to Anke Scheel-Sailer.