

# Risk prediction for major postoperative complications in people with chronic spinal cord injury/disorder and stage III and IV pressure injury

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## Summary

**BACKGROUND:** Approximately 20% of flap surgeries in people with spinal cord injury/disorder and stage III and IV pressure injury result in a major complication requiring re-surgery. Although several factors are associated with postoperative complications according to the literature, there is no risk prediction model for major postoperative complications in the treatment of stage III and IV pressure injuries in people with spinal cord injury/disorder.

**STUDY AIM:** The study aims to predict the risk of major postoperative complications in people with spinal cord injury/disorder and stage III and IV pressure injury at hospital admission.

**SETTING:** The study was conducted in a Swiss acute and rehabilitation hospital for people with spinal cord injury/disorder that specialises in the treatment of people with spinal cord injury/disorder using the Basel Decubitus Approach.

**METHODS:** We performed a retrospective cohort study based on routinely collected clinical data in a Swiss hospital. Risk predictors for major postoperative complications during hospitalisation in pressure injuries over the sacrum/coccyx, ischium or trochanter between 01/2016 and 12/2022 were identified using a mixed effects logistic Bayesian LASSO analysis.

**RESULTS:** We included 252 treatment procedures in 167 individuals. Major complications occurred in 48 (19%) treatment procedures. Estimated glomerular filtration rate (eGFR) according to the cystatin formula (odds ratio [OR] 0.91, confidence interval [CI] 0.62–1.02), vitamin D (25-hydroxy vitamin D; OR 1.05, CI 0.98–1.23), vitamin B<sub>12</sub> (OR 0.91, CI 0.74–1.05), sodium (OR 0.75, CI 0.16–1.05) and C-reactive protein (CRP; OR 0.98, CI 0.79–1.07) were found to be predictive of major complications at hospital admission.

**CONCLUSION:** For the Basel Decubitus Approach, high levels of eGFR, vitamin B<sub>12</sub> and sodium negatively affected major postoperative complications and should, therefore, be assessed during hospital stay. Further investigation is needed to determine the positive effect of high vitamin D and low CRP levels on major postoperative complications.

## Introduction

Among people with spinal cord injury or spinal cord disorder living in the community, the prevalence rates of pressure injury range from 26% to 54% within a one-year reporting period [1]. The lifetime incidence of at least one pressure injury in individuals with spinal cord injury/disorder is as high as 85%, and it is expected that 30% of these people will experience recurrent pressure injuries [1–4]. Pressure injuries often negatively affect an individual's health, functioning and social participation [5, 6]. Stage III and IV pressure injuries, as categorised by the European Pressure Ulcer Advisory Panel, usually require surgical management [7]. The risk of postoperative complications such as hematoma formation, infection, wound dehiscence, partial flap necrosis and recurrence is high [8–10]. In the Clavien-Dindo classification, these postoperative complications are categorised as minor if they can be treated conservatively and major if they require reoperation [11]. Approximately 20% of flap surgeries in people with spinal cord injury/disorder and stage III and IV pressure injury result in a major complication [8, 12, 13]. Major complications not only prolong immobilisation and hospitalisation, thereby reducing quality of life, but also increase healthcare costs [8, 13–15]. Preoperative and postoperative care are crucial to the success of flap surgery [15]. Therefore, treatment approaches for stage III and IV pressure injuries, such as the Basel Decubitus Approach, have been developed, which consist of a multi-layered, coordinated involvement of different disciplines and professions [14–19]. Treatment approaches aim to address

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factors associated with postoperative complications [13]. Typical treatment elements include pressure relief, immobilisation, risk screening and optimisation of comorbidities, infection control, wound conditioning, debridement and flap surgery [13].

To reduce the incidence of major complications, decrease healthcare costs, and shorten hospital stays, it is necessary to identify risk predictors of major complications and modify clinical practice accordingly [20]. Based on the literature, there are several factors associated with postoperative complications in the treatment of stage III and IV pressure injuries in people with spinal cord injury/disorder, including older age, overweight and underweight, tensor fasciae latae flap, presence or absence of osteomyelitis, low serum albumin and pathological blood concentrations of cystatin C, calcium and vitamin B<sub>12</sub> [9, 10, 13, 21–23]. However, it is unknown how the combination of these factors influences major complications [9, 10, 13, 21, 22]. In surgery, risk prediction models are used to predict the risk of an adverse outcome, such as major complications [24]. A risk prediction model is a statistical model that combines information from several different factors to estimate the probability of an individual experiencing a health outcome [24]. They are used to facilitate clinical decision making, such as preventive interventions for people at high risk [24, 25]. However, no risk prediction model exists for major postoperative complications in the treatment of stage III and IV pressure injuries in people with spinal cord injury/disorder. Thus, major complications sometimes occur unforeseeably. Therefore, this study aims to develop a risk prediction model for major complications in individuals with spinal cord injury/disorder and stage III or IV pressure

injury at hospital admission using mixed effects logistic Bayesian Least Absolute Shrinkage and Selection Operator (LASSO) regression.

## Methods

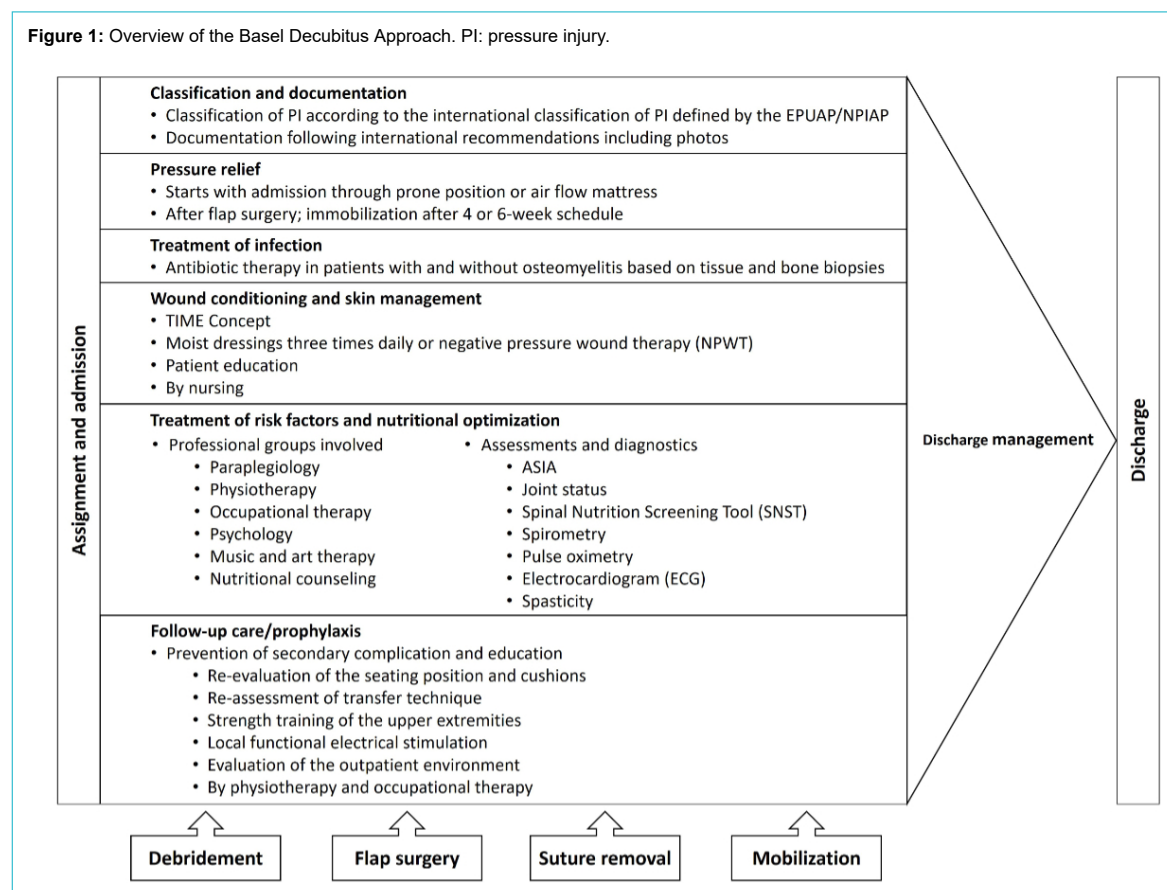
### Study design and study setting

This retrospective cohort examined routinely collected clinical data in a Swiss acute and rehabilitation hospital for people with spinal cord injury/disorder using the Basel Decubitus Approach to manage stage III and IV pressure injuries [17, 19, 26]. This approach consists of pressure injury classification, pressure relief and immobilisation, debridement, flap surgery, wound conditioning before and after flap surgery, infection control, risk screening and optimisation of comorbidities (e.g. nutritional therapy) as well as prevention of secondary complications and education [26–28]. This approach also contains the four milestones of debridement, flap surgery, suture removal and mobilisation in a wheelchair (figure 1) [26, 27].

### Eligibility criteria

We collected data from all consecutive adults with spinal cord injury/disorder hospitalised between 1 January 2016 and 31 December 2022 for stage III or IV pressure injuries over the sacrum/coccyx, ischium or trochanter. We considered individuals who underwent their first flap surgery and data from subsequent treatment procedures in these individuals during this period. We predefined exclusion criteria: individuals who refused retrospective use of their data, those undergoing initial rehabilitation, those under 18

**Figure 1:** Overview of the Basel Decubitus Approach. PI: pressure injury.



years of age, those with other neurological or malignant conditions, those treated conservatively, and those who died during treatment of another condition unrelated to a postoperative complication or pressure injury. Patients transferred to another hospital for severe additional comorbidities (e.g. vascular surgery) for which treatment is unavailable at our hospital were also excluded. These individuals had to be treated in another highly specialised academic hospital to achieve adequate safety.

### Data collection

As it is unknown how the combination of different possible risk factors influences major complications during the treatment of stage III and IV pressure injuries in people with spinal cord injury/disorder, we collected data on patients' characteristics, pressure injury characteristics, comorbidities, surgical characteristics, and laboratory results. Patient characteristics included sex, age, years post-injury, lesion level, ASIA classification (A, B, C or D) and aetiology cause (transport activity, sports and leisure activity, fall, violence, other accident cause, inflammation/infection, bleeding, congenital, vascular disorders, other disease, caused by surgical intervention or unknown cause). The ASIA/ISCoS International Standard for Neurological Classification of SCI (ISNCSCI) was used to document neurological impairment, lesion level and completeness [29]. Pressure injury characteristics included pressure injury stage (III or IV), pressure injury location (trochanter, ischium or coccyx/sacrum), number of pressure injuries in these locations (1, 2, 3 or more), additional deep pressure injury in another location (e.g. foot) and recurrence of pressure injury (none, same location or different location). Comorbidities included the presence (yes or no) of osteomyelitis (based on tissue and bone biopsy in stage IV pressure injury), diabetes (6.5% HbA1c), psychiatric diagnosis, vascular comorbidity (peripheral arterial occlusive disease or chronic venous insufficiency), hypertension ( $>140$  mm Hg), osteoarthritis, scoliosis, amputation, smoking, obstructive sleep apnoea and spasticity (based on AS-WORTH scale). Surgical characteristics included type of flap surgery (fasciocutaneous gluteal rotation flap, fasciocutaneous posterior thigh flap, lateral advancement flap, local Limberg flap, other or unknown), number of previous flap surgeries, length of immobilisation and length of hospital stay. In addition, laboratory results were collected, including sodium (135–245 mmol/l), potassium (3.5–5.1 mmol/l), calcium (2.2–2.6 mmol/l), ferritin (15–150 µg/l), creatinine (59–104 µmol/l), cystatin C (0.61–0.95 mg/l), estimated glomerular filtration rate (eGFR) according to the cystatin formula ( $\geq 90$  mg/l), total protein (64–83 g/l), albumin (32–50 g/l), C-reactive protein (CRP;  $<5$  mg/l), total cholesterol ( $<5.2$  mmol/l), HDL cholesterol (0.9–2.0 mmol/l), triglycerides (0.1–2.3 mmol/l), glucose (3.6–5.8 mmol/l), vitamin D (25-hydroxy vitamin D;  $\geq 75$  nmol/l), vitamin B<sub>12</sub> (200–1000 ng/l), folic acid (5–20 µg/l), haemoglobin (140–170 g/l), thyroid stimulating hormone (TSH; 0.4–4.0 mU/l) and international normalised ratio (INR; 0.9–1.3). Laboratory results were collected once at hospital admission. Data were retrieved from electronic databases used in clinical routine: KIS (Nexus, Switzerland), WicareDoc (Wigasoft, Switzerland), d.3one (D.velop, Switzerland) and ixserve.4 (ixmid Software

Technologie GmbH, Germany). Due to the retrospective nature of this study, some factors such as pressure injury size, BMI or HbA1c could not be analysed due to missing or incomplete documentation.

### Risk prediction model

We developed a risk prediction model to predict the occurrence of major postoperative complications between flap surgery and hospital discharge in people with spinal cord injury/disorder and stage III or IV pressure injury. The model is intended for use at hospital admission to assist physicians in making informed therapeutic decisions. The model was developed without external validation, using dependent data.

### Statistical analysis

We conducted a mixed-effects logistic Bayesian LASSO regression according to Park and Casella [30]. The Bayesian LASSO method is robust for small sample sizes and can be combined with multiple imputation, mixed effects and logistic regression. Moreover, the LASSO model uses a shrinkage penalty that shrinks the coefficients of some features towards zero, thus leading to a parsimonious model. Therefore, LASSO is the method to use in case of multicollinearity. Unlike ordinary logistic regressions, the shrinkage penalty of the LASSO model results in a sparser model with fewer features having non-zero coefficients, which improves the interpretability and simplicity of the model and reduces overfitting compared to ordinary logistic regression. Furthermore, the odds ratios (OR) determined with the LASSO model have the same interpretation as those derived from ordinary logistic regression. Both represent the change in odds resulting from a one-unit change in the explanatory variable, assuming that the other variables are held constant. An OR of  $<1$  indicates a negative effect and  $>1$  a positive effect.

The dataset contained missing values, which were addressed through multiple imputation according to Zhou and Reiter [31]. Repeated surgeries on the same patient were captured using random intercepts with normal priors with zero mean and inverse gamma (0.01, 0.01) prior for the variance. For the regression coefficients, we used the Laplace prior with zero mean and the scale parameter depending on the variance and the squared penalisation hyperparameter. Park and Casella suggested using the gamma prior with scale 1/1.78 as the prior for the squared penalisation hyperparameter. Moreover, for the intercept and variance, we used non-informative priors: normal (0, 1,000,000) and Jeffreys prior. For parameter estimation, we used Markov chain Monte Carlo (MCMC) with a burn-in period of 1000, thinning of 10, to obtain a sample of size 3000. All traces were visually checked for convergence and autocorrelation (Appendix). Afterwards, we selected variables with non-zero coefficients based on the posterior probabilities [32]. We calculated the odds ratios and 95% credible intervals (95% CI) of these variables.

Descriptive analysis was conducted to present the study population. Count ( $n$ ) was used to present categorical variables, while median and interquartile range (IQR), according to the Shapiro-Wilk test, were used for continuous data.

The data were analysed using the statistical program Stata/MP (version 17, 64-bit) for Windows.

### Ethical approval

This study was approved by the Swiss Ethics Committee for Northwest/Central Switzerland (trial registration number: 2014-107).

## Results

### Study population

During the observational period, 397 flap surgeries were performed in 174 individuals for stage III or IV pressure injuries over the sacrum/coccyx, ischium or trochanter (figure 1). Of these, 29 individuals refused the use of their data and were excluded. Additionally, 14 individuals with minor complications were excluded. Four individuals died during the immobilisation phase, four to six weeks post-operatively, due to pneumonia or cardiac failure, and one individual died nine months after flap surgery due to pre-existing renal failure and pneumonia. Therefore, these five individuals were excluded from this study. Finally, we included 252 treatment procedures of 167 individuals (figure 2).

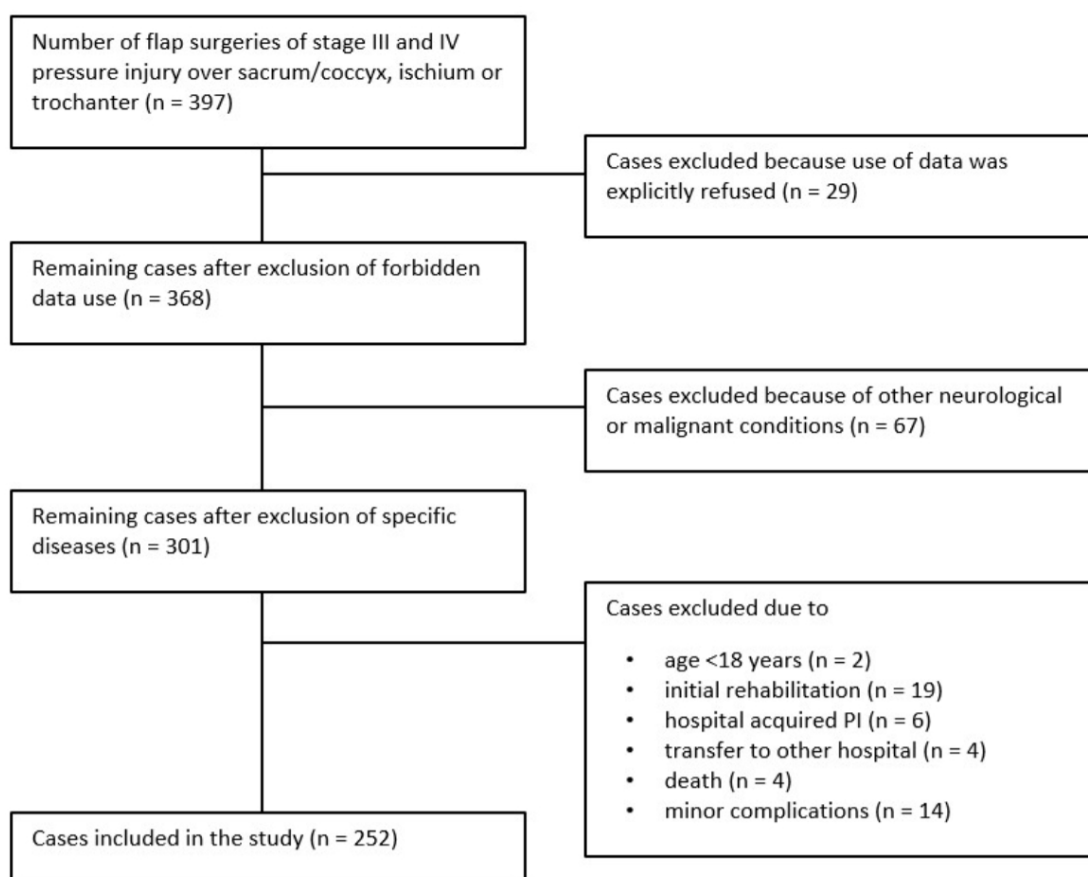
### Person, pressure injury and complication characteristics

Of the 252 treatment procedures analysed, 48 (19%) resulted in major complications. The study population consisted of 189 (75%) men and 153 (61%) individuals with a traumatic spinal cord injury. Of the total, 168 (67%) had paraplegia, 192 (76%) had ISNCSCI A and 157 (62%) had a stage IV pressure injury. Additionally, 170 (67%) had only one pressure injury, while 44 (17%) had a further pressure injury at another location. Furthermore, 155 (62%) had no previous pressure injury, 145 (58%) had no osteomyelitis and 214 (85%) were non-smokers. Out of all individuals, 138 (55%) had a pressure injury over the ischium, 69 (27%) over the coccyx/sacrum and 45 (18%) over the trochanter. On average, the individuals were 60 years old, immobilised for 40 days, and hospitalised for 104 days. The mean time since injury was 23 years (table 1).

### Variable selection

The mixed-effects logistic Bayesian LASSO regression identified eGFR, vitamin D, vitamin B<sub>12</sub>, sodium and CRP as relevant predictors. While eGFR (OR 0.91, CI 0.62–1.02), vitamin B<sub>12</sub> (OR 0.91, CI 0.74–1.05), sodium (OR 0.75, CI 0.16–1.05) and CRP (OR 0.98, CI 0.79–1.07) had a negative effect on major postoperative complication, vitamin D (OR 1.05, CI 0.98–1.23) had a positive effect.

**Figure 2:** Flow chart of case selection.



However, although these variables have been selected as relevant predictors by Bayesian LASSO regression, their effects were not statistically significant as the credible interval included one (table 2). Therefore, their effects require further validation.

**Table 1:**  
Patients' characteristics by complication.

| Patient characteristic                                 |                        |                            | Total   |      | No complication |      | Major complication |      |
|--------------------------------------------------------|------------------------|----------------------------|---------|------|-----------------|------|--------------------|------|
|                                                        |                        |                            | n = 252 |      | n = 204         |      | n = 48             |      |
|                                                        |                        |                            | n       | (%)  | n               | (%)  | n                  | (%)  |
| Sex                                                    | Male                   |                            | 189     | (75) | 155             | (76) | 34                 | (71) |
|                                                        | Female                 |                            | 63      | (25) | 49              | (24) | 14                 | (29) |
| Aetiology of spinal cord injury or spinal cord disease | Traumatic SCI          | Transport activity         | 71      | (28) | 56              | (27) | 15                 | (31) |
|                                                        |                        | Sports or leisure activity | 37      | (15) | 28              | (14) | 9                  | (19) |
|                                                        |                        | Fall                       | 29      | (12) | 25              | (12) | 4                  | (8)  |
|                                                        |                        | Violence                   | 4       | (2)  | 4               | (2)  | 0                  | (0)  |
|                                                        |                        | Surgical intervention      | 10      | (4)  | 7               | (3)  | 3                  | (6)  |
|                                                        |                        | Other accident cause       | 12      | (5)  | 10              | (5)  | 2                  | (4)  |
|                                                        | Non-traumatic SCI      | Inflammation/Infection     | 6       | (2)  | 4               | (2)  | 2                  | (4)  |
|                                                        |                        | Bleeding                   | 2       | (1)  | 2               | (1)  | 0                  | (0)  |
|                                                        |                        | Congenital                 | 11      | (4)  | 11              | (5)  | 0                  | (0)  |
|                                                        |                        | Other disease (undefined)  | 37      | (15) | 29              | (14) | 8                  | (17) |
| Unknown cause                                          |                        | 33                         | (13)    | 28   | (14)            | 5    | (10)               |      |
| Neurological level of SCI                              | C1–C4                  |                            | 23      | (9)  | 18              | (9)  | 5                  | (10) |
|                                                        | C5–C8                  |                            | 61      | (24) | 48              | (24) | 13                 | (27) |
|                                                        | T1–S5                  |                            | 168     | (67) | 138             | (68) | 30                 | (63) |
| ISNCSCI                                                | ISNCSCI A              |                            | 192     | (76) | 153             | (75) | 39                 | (81) |
|                                                        | ISNCSCI B              |                            | 35      | (14) | 31              | (15) | 4                  | (8)  |
|                                                        | ISNCSCI C              |                            | 17      | (7)  | 14              | (7)  | 3                  | (6)  |
|                                                        | ISNCSCI D at any level |                            | 8       | (3)  | 6               | (3)  | 2                  | (4)  |
| Pressure injury stage                                  | III                    |                            | 95      | (38) | 86              | (42) | 9                  | (19) |
|                                                        | IV                     |                            | 157     | (62) | 118             | (58) | 39                 | (81) |
| Localisation of the pressure injury                    | Coccyx/Sacrum          |                            | 69      | (27) | 49              | (24) | 20                 | (42) |
|                                                        | Ischium                |                            | 138     | (55) | 118             | (58) | 20                 | (42) |
|                                                        | Trochanter             |                            | 45      | (18) | 37              | (18) | 8                  | (17) |
| Number of pressure injuries in this location           | 1                      |                            | 170     | (67) | 133             | (65) | 37                 | (77) |
|                                                        | 2                      |                            | 63      | (25) | 54              | (26) | 9                  | (19) |
|                                                        | ≥3                     |                            | 19      | (8)  | 17              | (8)  | 2                  | (4)  |
| A further pressure injury in another location          | No                     |                            | 208     | (83) | 171             | (84) | 37                 | (77) |
|                                                        | Yes                    |                            | 44      | (17) | 33              | (16) | 11                 | (23) |
| Recurrence of previous pressure injury                 | No                     |                            | 155     | (62) | 129             | (63) | 26                 | (54) |
|                                                        | Yes                    |                            | 97      | (38) | 75              | (37) | 22                 | (46) |
|                                                        |                        | Same location              | 50      | (20) | 37              | (18) | 13                 | (27) |
|                                                        |                        | Different location         | 47      | (19) | 38              | (19) | 9                  | (19) |
| Osteomyelitis                                          | No                     |                            | 145     | (58) | 111             | (54) | 34                 | (71) |
|                                                        | Yes                    |                            | 107     | (42) | 93              | (46) | 14                 | (29) |
| Smoking                                                | No                     |                            | 214     | (85) | 175             | (86) | 39                 | (81) |
|                                                        | Yes                    |                            | 38      | (15) | 29              | (14) | 9                  | (19) |
| Age at admission (year): median (IQR)                  |                        |                            | 60      | (18) | 60              | (18) | 63                 | (18) |
| Years post-injury: median (IQR)                        |                        |                            | 23      | (24) | 24              | (25) | 22                 | (23) |
| Immobilisation (days): median (IQR)                    |                        |                            | 49      | (17) | 44              | (15) | 68                 | (34) |
| Hospital stay (days): median (IQR)                     |                        |                            | 104     | (53) | 98              | (50) | 132                | (63) |

ISNCSCI; International Standard for Neurological Classification of Spinal Cord Injury; IQR: Interquartile range.

**Table 2:**  
Selected variables with odds ratios and credible intervals.

| Variable                               | Odds ratio | CI (95%) |      |
|----------------------------------------|------------|----------|------|
| eGFR* (per 10 ml/min)                  | 0.91       | 0.62     | 1.02 |
| Vitamin D** (per 10 nmol/l)            | 1.05       | 0.98     | 1.23 |
| Vitamin B <sub>12</sub> (per 100 ng/l) | 0.91       | 0.74     | 1.05 |
| Sodium (per 10 mmol/l)                 | 0.75       | 0.16     | 1.05 |
| CRP (per 10 mg/l)                      | 0.98       | 0.79     | 1.07 |

CI: Credible interval; CRP: C-reactive protein; eGFR: Estimated glomerular filtration rate.

\* eGFR according to the cystatin formula

\*\* 25-hydroxy vitamin D

## Discussion

Multidisciplinary treatment approaches have been developed to address factors associated with complications to reduce complications during the treatment of deep pressure injuries in people with spinal cord injury / disorder [26]. This study focused on a risk prediction that combines information from different factors to further develop the Basel Decubitus Approach [26]. The LASSO regression model identified eGFR, vitamin D, vitamin B<sub>12</sub>, sodium and CRP as predicting major postoperative complications at hospital admission. Although these factors were identified as risk predictors of major complications, their effects were not statistically significant.

Renal dysfunction, vitamin D and CRP are known to be associated with the presence of pressure injuries [5, 7, 33, 34], and might play a role in predicting major postoperative complications in people with spinal cord injury/disorder and deep pressure injuries. In our study, Bayesian LASSO regression identified the renal marker eGFR as a predictive variable of major postoperative complications. The eGFR is considered the best overall index of renal dysfunction [35, 36]. In this cohort, only 26% (65) of the individuals had a normal eGFR ( $\geq 90$  ml/min), while the rest of the individuals showed mild to severe impairment. We found the eGFR to have a slight negative effect on major complications. For every 10 ml/min increase in the eGFR, the odds of having a major complication decreased by 9% (95% CI 0.62–1.02). According to the literature, renal dysfunction affects wound healing and increases the risk of developing postoperative wound infections [37, 38]. This notion is consistent with Fährndrich et al., who showed that cystatin C was associated with major complications after flap surgery in individuals with spinal cord injury/disorder and deep pressure injury [13]. The result of our study indicates that renal dysfunction and especially the eGFR should be assessed and monitored during the treatment of stage III and IV pressure injuries in people with spinal cord injury/disorder [13]. If possible, it should also be treated or integrated into the risk prediction before flap surgery is performed.

Based on our study, vitamin D is a risk predictor for major postoperative complications. Individuals with spinal cord injury/disorder are already at high risk for vitamin D deficiency ( $<75$  nmol/l) [39]. If they also have a pressure injury, they are even more likely to have low vitamin D levels [40]. The odds of having a major complication increased by 5% (95% CI 0.98–1.23) for every 10 nmol/l increase in vitamin D. In contrast, the literature shows that low vitamin D levels are associated with pressure injuries and negatively impact wound healing [34, 41, 42]. Therefore, vitamin D supplementation during pressure injury treatment is recommended to achieve better wound healing [34, 43]. In our clinic, we have been supplementing vitamin D in those with a deficiency since 2016. Our results indicate that vitamin D plays a role in predicting major postoperative complications, which might be due to the treatment of vitamin D deficiency under the Basel Decubitus Approach. Nutritional status is routinely assessed at hospital admission and treated accordingly [17, 26]. In our cohort, 73% (146) of the individuals had a vitamin D deficiency. Individuals with high vitamin D levels at admission are not treated with vitamin D. Therefore, vita-

min D supplementation might have been a protective factor for major complications because optimal levels were achieved during hospitalisation. It usually takes about 12 weeks to reach optimal vitamin D levels in deficient individuals [44]. However, we did not collect data on vitamin D levels during hospitalisation. Therefore, we do not know if normal vitamin D levels were achieved during treatment. We recommend observing vitamin D levels during hospitalisation regarding major complications.

Regarding vitamin B<sub>12</sub>, we found that 19% (37) of the individuals in our cohort had a deficiency ( $<200$  ng/l). In our cohort, for every 100 ng/l increase in vitamin B<sub>12</sub>, the odds of having a major complication decreased by 9% (95% CI 0.74–1.07). As in the study by Fährndrich et al., our findings suggest that vitamin B<sub>12</sub> deficiency is involved in predicting major complications [13]. No studies have been conducted on the association between vitamin B<sub>12</sub> deficiency and surgical outcomes in individuals with spinal cord injury/disorder. Meyer et al. observed the impact of vitamin B<sub>12</sub> deficiency in geriatric patients undergoing orthopaedic surgery [45]. They found that vitamin B<sub>12</sub> deficiency did not impact complications [45]. The relationship between vitamin B<sub>12</sub> deficiency and successful surgical outcomes in people with spinal cord injury/disorder needs to be elucidated in future studies.

According to our results, sodium is involved in predicting major complications. In our study, we found that the odds of having a major complication decreased by 25% (95% CI 0.16–1.05) for every 10 mmol/l increase in sodium. Furthermore, around 25% (63) of the individuals had low sodium levels. Teo et al. performed a systematic review and meta-analysis of 32 observational studies to estimate the association of hyponatremia ( $<135$  mmol/l) with major postoperative complications [46]. They found that preoperative hyponatremia was associated with a 2.5-fold increased risk of having a major complication after surgical procedures [46]. Teo et al. also observed that hyponatremia was a specific risk predictor of major postoperative complications in individuals without spinal cord injury / disorder [46]. Moreover, it is known that individuals with spinal cord injury/disorder have an increased risk of hyponatremia compared to individuals without spinal cord injury / disorder and that the risk increases with higher lesion levels [47, 48]. Based on these findings, we recommend that hyponatremia should be considered as a risk predictor for major complications [46]. Thus, sodium levels should be assessed and treated before flap surgery [34, 46].

Finally, in our cohort, for every 10 mg/l increase in CRP, the odds of having a major complication decreased by 2% (95% CI 0.79–1.07). The effect of only 2% at an increase of 10 mg/l might not be large enough to play a role in clinical decision-making. Nevertheless, CRP was selected as a relevant risk predictor by Bayesian LASSO regression and is therefore discussed. Elevated CRP levels ( $>5$  mg/l) are frequently observed in people with pressure injuries [33, 34, 49, 50]. In our cohort, 92% (231) of the individuals had elevated CRP levels. No studies have observed preoperative CRP levels to predict major complications after flap surgery in people with spinal cord injury/disorder. However, studies unrelated to spinal cord injury/disorder and pressure injury have shown that preoperative elevated CRP levels were predictors of increased major and mi-

nor postoperative complications [51, 52]. In contrast, we found a slight negative effect of high CRP levels on major complications. In the Basel Decubitus Approach, the CRP level is also routinely assessed at hospital admission [17, 26]. CRP is a non-specific inflammatory marker, indicating any acute inflammation, tissue damage or infection [33, 50]. Therefore, it is difficult to interpret our result as there are many reasons for elevated CRP levels at hospital admission. One possible explanation might be the association between high CRP levels and osteomyelitis. Rigazzi et al. found that CRP levels were statistically significantly higher in individuals with osteomyelitis than in individuals without osteomyelitis [22]. In addition, Fährndrich et al. found that people with osteomyelitis had fewer major complications than those without osteomyelitis with the Basel Decubitus Approach [13]. Individuals with osteomyelitis receive individualised antibiotic treatment based on tissue samples, as opposed to standardised treatment for those without osteomyelitis [13, 26]. Fährndrich et al. concluded that an individualised antibiotic treatment might have been the reason for fewer complications in individuals with osteomyelitis [13]. The same might apply to elevated CRP levels, as a high CRP level may indicate underlying osteomyelitis [22]. The individualised use of antibiotics might be more effective in treating the infection and, therefore, reduce major complications [13], which might explain the positive association between major complications and low CRP levels. However, based on our study, the effect of lower CRP levels on major postoperative complications cannot yet be explained because CRP levels are influenced by several factors. Therefore, further investigation is required to determine the role of CRP in major postoperative complications in individuals with spinal cord injury/disorder.

Ultimately, as eGFR, vitamin D, vitamin B<sub>12</sub>, sodium and CRP are routinely assessed at hospital admission for the Basel Decubitus Approach, the prediction model can be used by the physician's at hospital admission to predict the patient's risk of major postoperative complications during the treatment of stage III and IV pressure injuries in people with spinal cord injury/disorder.

This study was conducted in the context of the Basel Decubitus Approach. Therefore, a limitation of this study is that the results may not be applicable in settings without a similar treatment approach. Logistic Bayesian LASSO regression is a powerful technique, especially for variable selection and dealing with multicollinearity. However, we extracted data retrospectively from regular clinical documentation. Therefore, the quality of the data for some variables was limited due to the lack of standardised documentation, which required multiple imputations. Prospective cohort studies with a larger sample size and a pilot study using the risk prediction model at baseline are recommended for future research. Furthermore, we recommend prospective observation of other factors, such as the size of the pressure injury. Another limitation is that the results cannot be generalised to people with other severe additional comorbidities that require treatment in other hospitals, as we excluded them in this study.

## Conclusions

For the Basel Decubitus Approach, the eGFR, vitamin D, vitamin B<sub>12</sub>, sodium and CRP at hospital admission were risk predictors for major postoperative complications. In this study, high eGFR, vitamin B<sub>12</sub>, sodium and CRP levels negatively affected major postoperative complications. Therefore, assessing the identified risk predictors during hospital stay should be considered during the Basel Decubitus Approach. In contrast, based on this study, high vitamin D levels positively affected major postoperative complications. Vitamin D supplementation in vitamin D-deficient individuals might be the reason for this finding. Furthermore, a lower CRP level was identified as a relevant risk predictor for major postoperative complications by Bayesian LASSO regression. One explanation for this finding might be underlying osteomyelitis, which is treated with individualised antibiotics, as opposed to standardised antibiotics for those without osteomyelitis. However, the effect of CRP on major postoperative complications cannot yet be explained because CRP levels at hospital admission are influenced by many factors. Therefore, the role of CRP in major complications needs to be further investigated.

## Data availability statement

All data are stored in Stata/MP (version 17, 64-bit) with the corresponding author. The deidentified study data are now available with the codebook and statistical analysis plan and can be requested directly (carina.fahndrich[at]paraplegie.ch).

All codes are stored with the corresponding author and can be requested directly (carina.fahndrich[at]paraplegie.ch).

## Author contributions

CF developed the study, collected the data, performed the analyses, wrote the first draft and finalised the manuscript. AG conceptualised the study, supported the statistical analyses and provided valuable feedback on the manuscript. MB, MH, DJS and RW were involved in conceptualising the study and provided relevant feedback on the manuscript. ASS conceptualised the study and provided relevant feedback on the manuscript. All authors approved the final version of the manuscript.

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## Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. AG received consulting fees from AbbVie Switzerland that were unrelated to this article. No other potential conflicts of interest related to the content of this manuscript were disclosed.

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## Appendix

### Traces and Autocorrelation

