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ORIGINAL ARTICLE

Association of age with the timing of acute spine surgery–effects on neurological outcome after traumatic spinal cord injury

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Abstract

Purpose To investigate the association of age with delay in spine surgery and the effects on neurological outcome after traumatic spinal cord injury (SCI).

Methods Ambispective cohort study (2011–2017) in $n = 213$ patients consecutively enrolled in a Level I trauma center with SCI care in a metropolitan region in Germany. Age-related differences in the injury to surgery interval and conditions associated with its delay (> 12 h after SCI) were explored using age categories or continuous variables and natural cubic splines. Effects of delayed surgery or age with outcome were analyzed using multiple logistic regression.

Results The median age of the study population was 58.8 years (42.0–74.6 IQR). Older age (≥ 75y) was associated with a prolonged injury to surgery interval of 22.8 h (7.2–121.3) compared to 6.6 h (4.4–47.9) in younger patients (≤ 44y). Main reasons for delayed surgery in older individuals were secondary referrals and multimorbidity. Shorter time span to surgery (≤ 12 h) was associated with higher rates of ASIA impairment scale (AIS) conversion (OR 4.22, 95%CI 1.85–9.65), as mirrored by adjusted spline curves (< 20 h 20–25%, 20–60 h 10–20%, > 60 h < 10% probability of AIS conversion). In incomplete SCI, the probability of AIS conversion was lower in older patients [e.g., OR 0.09 (0.02–0.44) for'45-59y' vs.' ≤ 44y'], as confirmed by spline curves (< 40y 20–80%, ≥ 40y 5–20% probability).

Conclusion Older patient age complexifies surgical SCI care and research. Tackling secondary referral to Level I trauma centers and delayed spine surgery imposes as tangible opportunity to improve the outcome of older SCI patients.

Keywords Injury to surgery interval · Secondary referral · Age · Demographic change · Neurological outcome

Introduction

The aging society in industrialized high-income countries is introducing profound changes in the epidemiology of central nervous system (CNS) injuries. In traumatic brain injury (TBI), the demographic change of the recent decades is characterized by shifting patterns of etiology and premorbidity [1, 2]. A similar global trend with increasing rates of elderly patients is observed in traumatic spinal cord injury (SCI) [3] and has implications for emergency medicine, acute surgical care, and translational research [4].

Spine surgery performed as early as possible after the injury is recognized as outcome relevant after SCI [5]. However, multimorbidity and other age-related conditions may restrict the feasibility to perform spine surgery early after the injury. On the other hand, a link between age and poor neurofunctional outcome after SCI has been described [6–9], albeit neuroanatomical correlates of an age-related decline in axonal regeneration, evident in experimental models [10], could not be revealed in human pilot data [11]. This implies the question to what extent age is independently associated with neurological recovery after SCI and if age-related restrictions in acute surgical management may additionally confound neurological outcome.

This study explores the association of age with the injury to surgery interval and the conditions associated with the

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violation of the study center's guideline to start the first spine surgery within 12 h (≤ 12 h) after SCI. In addition, the study investigates effects of the injury to surgery interval and age on neurological outcome.

Methods

Study oversight

The study was conducted within the Comparative Outcome and Treatment Evaluation in Spinal Cord Injury (COaT-SCI) project, which consecutively enrolls SCI patients aged 14 years or older admitted to the BG Hospital Unfallkrankenhaus Berlin, a Level 1 trauma center with 24 h/7d spine surgery service and a specialized treatment center for SCI (60 beds) located in the metropolitan region of Berlin, Germany.

The ambispective study included acute traumatic SCI patients enrolled from 2011 to 2017. Data were collected prospectively from May 2015 to December 2017 using case report forms. Retrospective data for the period from January 2011 to April 2015 were collected by chart review and were stored in a versioned database. For explorative comparison of patient characteristics and outcomes between both enrollment periods, see Supplementary Table 1.

Patients who did not undergo spine surgery or whose initial surgery was performed at another center were excluded. Decisions to postpone surgery because of initially minor neurological deficits or spontaneous neurological improvement in association with spinal stenosis and/or central cord syndrome were additional exclusion criteria as they represented exemptions from the study center's guideline to start the spine surgery ≤ 12 h after SCI. Patients who died during primary hospitalization were excluded only from the analysis of neurological outcome (Fig. 1).

Variable definitions

For the explorative analysis of age effects, the International Spinal Cord Injury Core Data Set age categories for large sample sizes [12] were modified in a way that the younger age categories were combined to' ≤ 44 years' (≤ 44y) and compared to the'45–59 years' (45-59y),'60–74 years' (60–74y), and' ≥ 75 years' (≥ 75y) categories in order to achieve age groups of a similar size. Other demographic baseline characteristics included gender, body mass index (BMI), and the Charlson comorbidity index (CCI) based on pre-existing health conditions obtained from the medical records and by questioning the patients or their relatives. The CCI was calculated as described elsewhere [13]. TBI was graded according to the Glasgow Coma Scale as mild

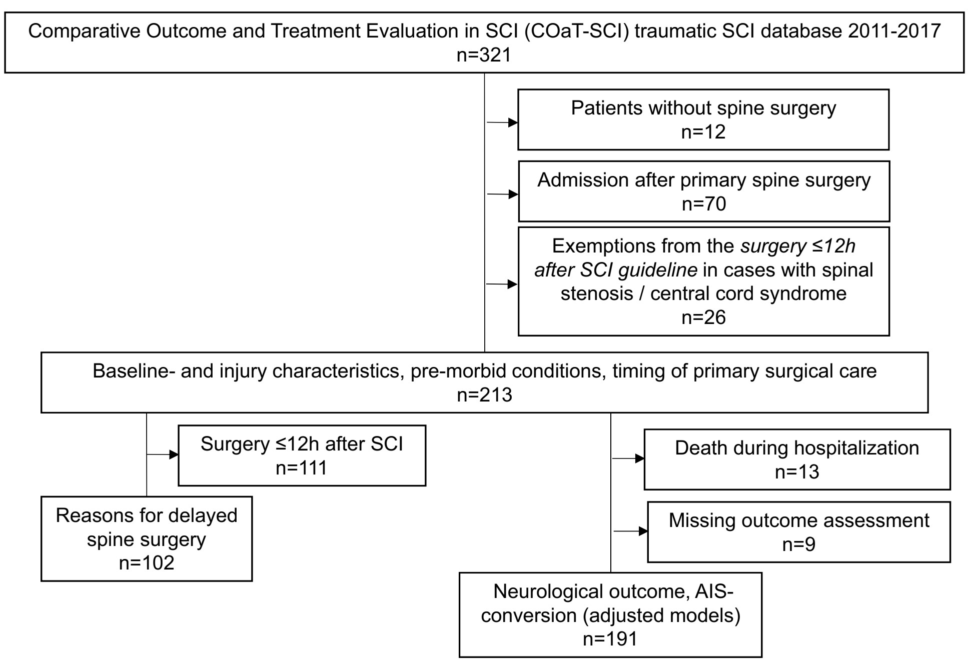


Fig. 1 Data analysis chart. Horizontal arrows indicate excluded patients. Cases without spine surgery or admitted after the first spine surgery were excluded. In addition, cases with minor neurological deficits or spontaneous neurological improvement in the context of spinal stenosis and/or central cord syndrome were excluded because they were exemptions to the study center's internal guideline to start the surgery ≤ 12 h after SCI. The reasons for delayed spine surgery were recorded only if the ≤ 12 h timeframe was exceeded. Patients who died during primary hospitalization, or with missing neurological examination at discharge were excluded from the outcome analyses. Abbreviations: AIS = ASIA Impairment Scale, SCI = spinal cord injury

(I°), moderate (II°), or severe (III°). Other accompanying injuries include sternal-rib fractures, injury to the chest or abdominal cavities, fractures of the pelvis or the upper or lower extremities, or large vessel injuries. The etiology of SCI was categorized into falls, traffic accidents, and other types of injury comprising sports accidents, acts of violence, suicide attempts, and falling objects. The time of SCI was extracted from emergency medical records. Admission to the study center and the start of surgery (incision time) were documented in the electronic hospital information system. The exact time intervals from SCI to first spine surgery, from SCI to admission, and from admission to first spine surgery were calculated. The daytime of surgery was recorded and categorized into 7am–5 pm and 5 pm–7am. Spine surgery was categorized as delayed when the ≤ 12 h threshold representing the study center's internal guideline for the start of the first spine surgery (cut time) was exceeded. As no common recommendations about the exact timing of early spine surgery are available [14] and the variability in clinical practice is huge [15], the trial center has determined the 12-h time window for spine surgery routines after acute traumatic SCI based on available literature and on feasibility considerations regarding transport routes and required diagnostics. In cases with the start of surgery > 12 h, the circumstances or health conditions contributing to the decision made by the team of emergency physicians, anesthesiologists, and spine surgeons to postpone the surgery were recorded.

For neurological classification at admission and discharge, the ASIA impairment scale (AIS) and the neurological level of injury (NLI) were assessed according to ISNCSCI [16] by physicians experienced in the treatment of SCI. For neurological outcome analysis, AIS changes over time were dichotomized into 'non-conversion' vs. 'conversion' and improvements in the NLI by at least two segments were considered as relevant. The follow-up ends at discharge from primary surgical or rehabilitation care. The median (IQR) time of follow-up in the study sample is 90 days (55–124).

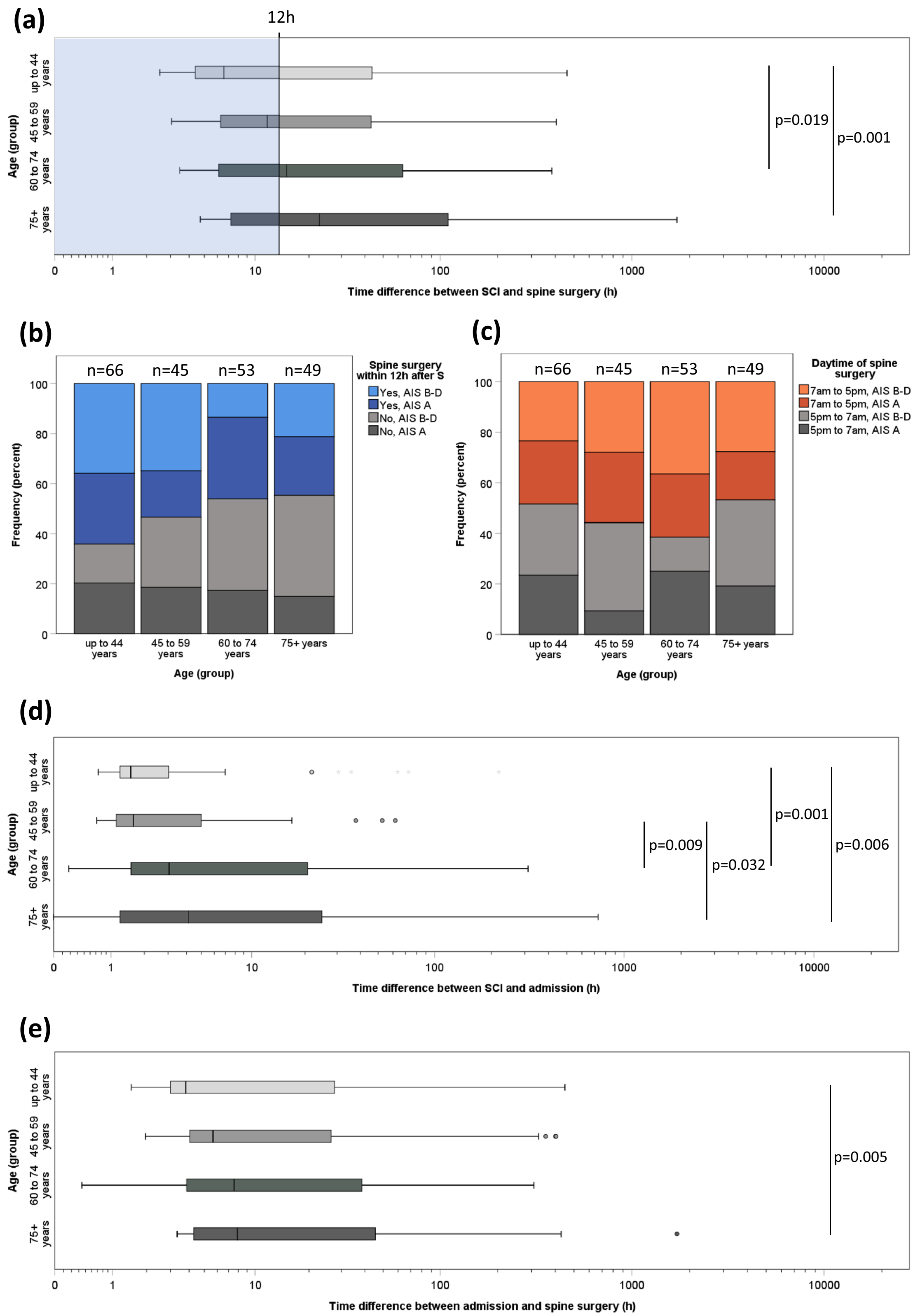
Statistical analysis

For continuous variables, median and quartiles are reported as descriptive measures. Differences between groups were tested using the Kruskal–Wallis test followed by Dunn's post-test for multiple comparison. Categorical variables were reported as absolute and relative frequencies and compared using the Chi-square test. To examine the association of age with primary or secondary referral, natural cubic splines were used in a sensitivity analysis. The neurological recovery was analyzed in the total sample and stratified for baseline AIS into complete SCI (AIS A) and incomplete SCI (AIS B–D) as the AIS represents a major prognostic factor [17] and in order to address interactions between age and AIS. The binary multiple regression models with AIS conversion as outcome variable included the independent variables: age group, gender, CCI, surgery ≤ 12 h after SCI, accompanying TBI, cervical NLI at admission, and, if applicable, AIS at admission. The enrollment period (retrospective vs. prospective) was also included to adjust for differences in data quality and possible variations of the ISNCSCI [18]. Considerations for model development were visualized by means of directed acyclic graphs (Supplementary Fig. 1) using the browser-based application DAGitty (version 3.0).

Table 1 Sociodemographic baseline and injury characteristics by age group

Age group	≤ 44y *n* = 66	45–59y *n* = 45	60–74y *n* = 53	≥ 75y *n* = 49	*p*-value
Age min–max	14.1–44.8	46.1–59.5	61–74.9	75–90.7	_
Age, Median (IQR)	32.5 (25.6–40.9)	53.9 (49.3–57.2)	70.0 (64.0–72.5)	79.6 (77.8–83.2)	_
Gender, female (%)	13 (19.7)	5 (11.1)	15 (28.3)	20 (40.8)	0.006
BMI, Median (IQR)	24.5 (22.2–26.2)	24.8 (24.0–28.2)	27.5 (25.4–30.9)	26.0 (23.7–27.8)	< 0.001
CCI, Median (IQR)	0 (0–0)	0 (0–1)	1 (0–3)	2 (1–4)	< 0.001
Etiology of SCI, falls: traffic: other (%)	15: 28: 23 (22.7: 42.4: 34.8)	18: 16: 11 (40.0: 35.6: 24.4)	40: 10: 3 (75.5: 18.9: 5.7)	40: 8: 1 (81.6: 16.3: 2.0)	< 0.001
AIS, A: B: C: D (%)	31: 7: 4: 22 (48.4: 10.9: 6.3: 34.4)	16: 4: 4: 19 (37.2: 9.3: 9.3: 44.2)	26: 2: 4: 20 (50.0: 3.8: 7.7: 38.5)	18: 1: 13: 15 (38.3: 2.1: 27.7: 31.9)	0.025
Neurological level, c: th: ls (%)	21: 22: 21 (32.8: 34.4: 32.8)	26: 12: 4 (61.9: 28.6: 9.5)	32: 8: 12 (61.5: 15.4: 23.1)	35: 5: 7 (74.5: 10.6: 14.9)	< 0.001
TBI, I°: II°: III° (%)	5: 4: 8 (7.6: 6.1: 12.1)	10: 1: 4 (22.2: 2.2: 8.9)	6: 5: 0 (11.3: 9.4: 0)	7: 0: 1 (14.3: 0: 2.0)	0.016
Additional injuries other than TBI (%)	47 (71.2)	27 (60.0)	21 (39.6)	19 (38.8)	0.001

The age groups as defined by the International SCI Core Dataset [12] were modified in a way that younger age categories were combined to ≤ 44 years. TBI is categorized as mild (I°), moderate (II°), and severe (III°). Abbreviations: AIS = ASIA Impairment Scale, BMI = body mass index, c = cervical, CCI = Charlson comorbidity index, IQR = interquartile range, ls = lumbosacral, TBI = traumatic brain injury, th = thoracic, y = years


(a)
12h
Age (group)
up to 44 years
45 to 59 years
60 to 74 years
75+ years
p=0.019
p=0.001
0
1
10
100
1000
10000
Time difference between SCI and spine surgery (h)
(b)
n=66
n=45
n=53
n=49
Frequency (percent)
100
80
60
40
20
0
Spine surgery within 12h after S
Yes, AIS B-D
Yes, AIS A
No, AIS B-D
No, AIS A
up to 44 years
45 to 59 years
60 to 74 years
75+ years
Age (group)
(c)
n=66
n=45
n=53
n=49
Frequency (percent)
Daytime of spine surgery
7am to 5pm, AIS B-D
7am to 5pm, AIS A
5pm to 7am, AIS B-D
5pm to 7am, AIS A
up to 44 years
45 to 59 years
60 to 74 years
75+ years
Age (group)
(d)
Age (group)
up to 44 years
45 to 59 years
60 to 74 years
75+ years
p=0.009
p=0.032
p=0.001
p=0.006
Time difference between SCI and admission (h)
(e)
Age (group)
up to 44 years
45 to 59 years
60 to 74 years
75+ years
p=0.005
Time difference between admission and spine surgery (h)

◂**Fig. 2** Timing of surgical management by age-subgroups. **a** Time from SCI to first spine surgery. The line indicates the 12 h threshold for the start of spine surgery (cut) based on the trial center's internal guideline. **b** Frequency of spine surgery performed within the 12 h threshold stratified for the baseline AIS. Chi-square test comparing the onset of surgery categories (surgery ≤ 12 h vs. surgery > 12 h) between the age groups (AIS A $p=0.802$; AIS B-D $p=0.003$). **c** Frequency of spine surgery within or without regular working hours (7am–5 pm vs. 5 pm–7am) stratified for the baseline AIS. Chi-square test comparing the daytime of surgery categories between the age groups (AIS A $p=0.376$; AIS B-D $p=0.096$). **d** Time difference between SCI and admission to the trial center. **e** Time from trial center admission to first spine surgery. Bonferroni adjusted p-values of Dunn's post-test after Kruskal–Wallis test are shown in the panels a, d, and e. Abbreviations: AIS = ASIA Impairment Scale, SCI = spinal cord injury

Sensitivity analysis included binary multiple logistic regression models using continuous age and a logarithmic transformation of the time from injury to surgery instead of the respective categorized variables. Natural cubic splines were used for age and injury to surgery time where appropriate (decision based on AIC comparison between models). A two-sided significance level of $\alpha = 0.05$ was used. If not otherwise stated, no adjustment for multiple testing was applied in this exploratory study. All p-values have to be interpreted cautiously. All analyses were performed in the COaT-SCI database version as of 03/18/2019 using the software SPSS (version 26.0) and R (packages 'base,' 'splines,' 'ggeffects' and 'tidyverse'). The study was reported according to the STROBE statement [19] (Supplementary Table 2).

Results

Baseline characteristics

The median age of the study population ($n = 213$) was 58.8 years with an interquartile range (IQR) of 42.0–74.6 and a range of 14.1–90.7 years. When comparing the age groups, '60-74y' and '≥ 75y' included more female patients and had clearly higher BMI and CCI scores compared to '≤ 44y' and '45-59y' (Table 1). Falls were the prevailing etiology of SCI in the groups of older patients, whereas traffic accidents and other types of injury were much more frequent in the '45-59y' and especially in the '≤ 44y' group. A slight disparity in SCI severity across the age groups was attributable to a higher rate of 27.7% motor incomplete AIS C patients in the '≥ 75y' group compared to the younger groups with rates between 6.3% and 9.3% (Table 1). The distribution of the NLI in the age groups shifted with older age toward much higher frequencies of cervical NLI and less frequent thoracic or lumbar NLI. Approximately one third of the '≤ 44y' group had a cervical NLI (32.8%), whereas rates between 61.5% and 74.5% were observed in the older groups (Table 1).

The older patients suffered less frequently TBI or other accompanying injuries. The rate of severe TBI was 12.1% in the '≤ 44y' and 8.9% in the '45-59y' group, but 0.0% in the '60-74y' and 2.0% in the '≥ 75y' group. The rate of other concomitant injuries was also lower in older patients with 71.2% in the '≤ 44y' compared to 38.8% in the '≥ 75y' group (Table1).

Timing of surgical management

The injury to surgery time for decompression and/or stabilization [median (IQR), hours] was clearly shorter in the group '≤ 44y' [6.6 (4.4–47.9)] compared to '60-74y' [15.1 (6.0–63.8)] and particularly to '≥ 75y' [22.8 (7.2–121.3)]. The '45-59y' group had an injury to surgery time of [11.8 (6.3–58.8)] (Fig. 2a). Consequently, the study center's internal guideline to start the first spine surgery ≤ 12 h after SCI could be met in more than half of the cases only in the '≤ 44y' and '45-59y' groups. Shorter injury to surgery time (≤ 12 h) in younger age groups was associated incomplete SCI AIS B-D (Fig. 2B). Frequency of surgeries within or outside regular working hours was similar between the age groups (Fig. 2C).

The time from SCI to study center admission [median (IQR), hours] differed considerably between the age groups '≤ 44y' [1.5 (1.2–3.0)] or '45–60 years' [1.6 (1.1–5.1)] compared to '60-74y' [3.1 (1.5–22.7)] or '≥ 75y' [4.1 (1.2–24.8)] (Fig. 2d). The time from admission to the first spine surgery was substantially longer only in the '≥ 75y' [7.9 (4.3–48.0)] group compared with the '≤ 44y' [3.8 (3.0–31.2)] group (Fig. 2e).

Reasons for delayed spine surgery

The main conditions associated with delayed spine surgery (> 12 h) after SCI were multiple trauma in the '≤ 44y' and '45-59y' groups and secondary referral from other hospitals as well as multimorbidity in the '60-74y' and '≥ 75y' groups (Fig. 3a). Other conditions not observed in the '≤ 44y' group, but relevant for postponed surgery in the '45-59y' and the older groups, were intake of coagulation inhibitors (direct oral anticoagulants $n = 4$; coumarin derivates $n = 4$; antiplatelet drugs $n = 1$) or extended diagnostics in cases with underlying ankylosing spondylitis (Fig. 3a).

In a subgroup analysis, the rate of secondary referrals was higher in the older age groups (Table 2). The median time from injury to admission was considerably longer in patients with secondary referral compared to those in the primary referral groups. Similarly, the injury to surgery time interval was prolonged in the secondary referral compared to

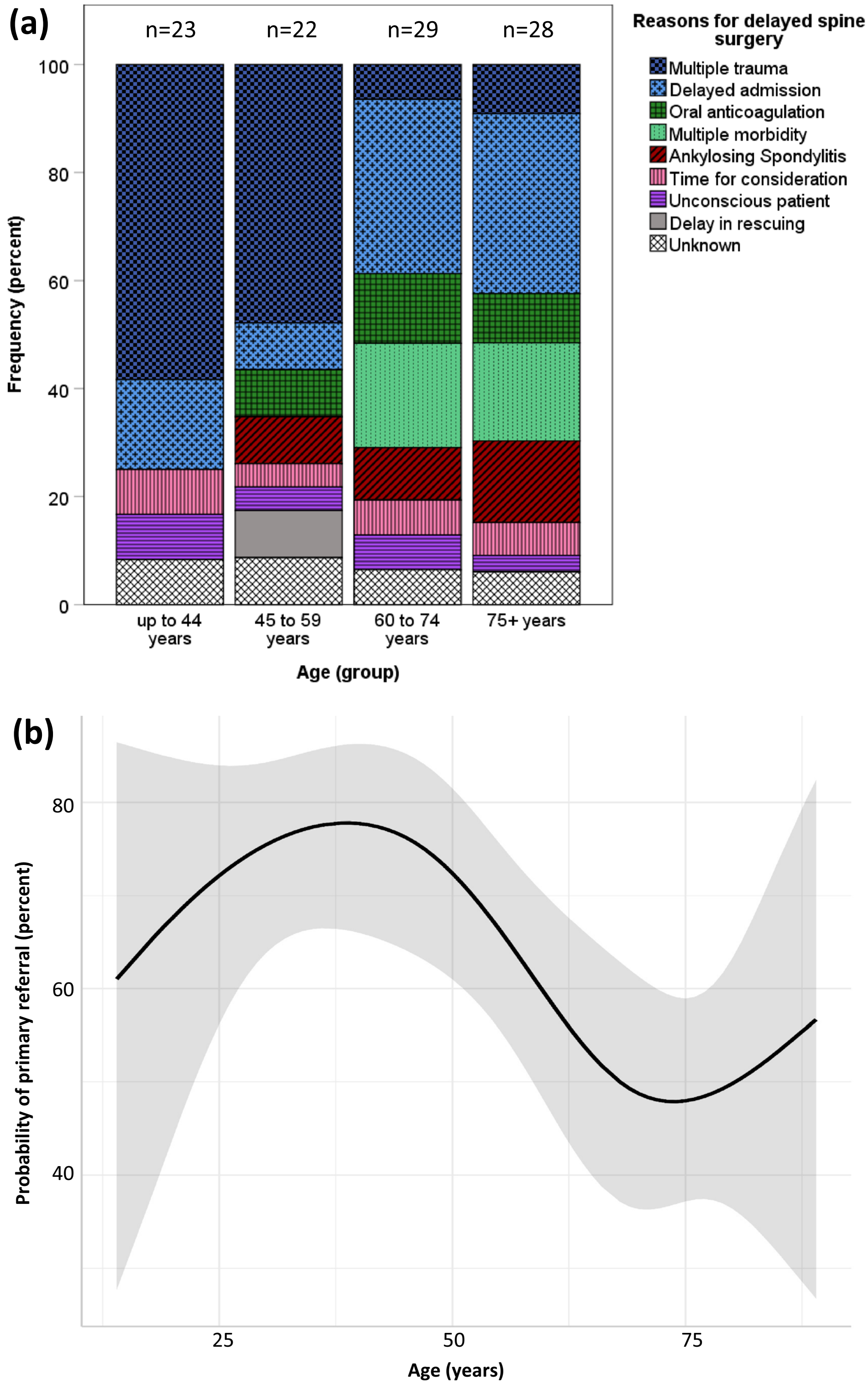


Fig. 3 Reasons for delay in spine surgery and association of age with primary referral. **a** Reasons for surgery performed > 12 h after SCI. Sample size (reasons/patients): total $n = 111/102$, '≤ 44 y' $n = 24/23$, '45–59 y' $n = 23/22$, '60–74 y' $n = 31/29$, '≥ 75y' $n = 33/28$. **b** Estimated probability of primary referral as function in association to patient age based on binary logistic regression using natural cubic splines with 3 degrees of freedom ($n = 213$ patients). Abbreviations: SCI = spinal cord injury

the primary referral groups. However, the median time from trial center admission to surgery was not longer in each age group after secondary referral (Table 2).

Sensitivity analysis using natural cubic splines revealed that patients ≥ 60 years of age were less likely to have a primary referral (45–55% probability) compared with younger age groups (65–75% probability) (Fig. 3b).

Table 2 Timing of surgical management across the age groups comparing primary versus secondary referral

Age groups		≤44y		45–59y		60–74y		≥75y	
		n = 66		*n* = 45		*n* = 53		*n* = 49	
Type of referral, n (%)		Primary	Secondary	Primary	Secondary	Primary	Secondary	Primary	Secondary
		48 (72.7)	18 (27.3)	32 (71.1)	13 (28.9)	24 (45.3)	29 (54.7)	23 (46.9)	26 (53.1)
Hours SCI to admission	Median (IQR)	1.3 (1.1–1.6)	5.2 (3.3–31.8)	1.3 (1.0–1.9)	5.3 (4.7–22.6)	1.5 (1.1–1.8)	6.7 (3.4–38.5)	1.3 (1.0–2.2)	7.2 (4.1–51.1)
	mean (±SD)	*1.5 (0.9)*	*27.2 (52.4)*	*2.4 (3.5)*	*15.7 (20.5)*	*8.6 (21.8)*	*52.8 (94.4)*	*39.2 (152.2)*	*53.1 (97.6)*
Hours SCI to surgery	Median (IQR)	5.2 (4.3–12.1)	17.2 (9.4–155.2)	9.9 (5.6–75.6)	11.8 (9.3–58.8)	6.6 (4.8–23.4)	25.6 (10.9–132.9)	12.2 (5.7–109.9)	27.0 (9.2–135.5)
	mean (±SD)	*45.7 (95.7)*	*92.9 (133.5)*	*73.9 (127.1)*	*38.0 (48.8)*	*24.3 (38.3)*	*87.0 (113.6)*	*163.7 (387.8)*	*86.2 (127.8)*
Hours admission to surgery	Median (IQR)	3.5 (2.9–10.7)	11.0 (9.4–76.6)	6.2 (3.9–73.6)	5.3 (4.1–18.9)	4.7 (3.2–15.4)	13.3 (4.7–44.0)	9.8 (4.8–60.0)	6.6 (4.3–25.4)
	mean (±SD)	*44.2 (95.7)*	*65.7 (113.8)*	*71.5 (126.0)*	*22.2 (35.6)*	*15.7 (22.5)*	*34.1 (59.1)*	*124.5 (360.4)*	*33.1 (57.1)*

Abbreviations: SCI = Spinal Cord Injury, IQR = interquartile range, SD = standard deviation, y = years

Neurological outcome

Comparing the spine surgery categories (surgery ≤ 12 h, surgery > 12 h) in the total sample, AIS conversions were occurring more frequently, when the surgery began ≤ 12 h compared to > 12 h within all four age groups but without clear differences between the age groups (Fig. 4a). After stratification for the AIS at admission, a rather similar pattern of AIS conversions was observed in AIS A (Fig. 4b). In the AIS B–D stratum, a majority of patients with surgery ≤ 12 h after SCI experienced an AIS conversion across all age groups, but particularly the '≤44y' group converted more frequently than the older groups (Fig. 4c).

The analysis of NLI changes in the total sample revealed higher rates of improvement both when the surgery has started ≤ 12 h compared to > 12 h and in the younger compared to the older groups (Fig. 4d). This pattern of NLI changes did not apply to the AIS A stratum (Fig. 4e), but to AIS B–D revealing patterns of NLI improvement (Fig. 4f) very similar to AIS conversions (Fig. 4c).

The adjusted logistic regression model calculated in the total sample demonstrated a higher probability of AIS conversion when the surgery began ≤ 12 h after SCI [OR (95% CI) of 4.22 (1.85–9.65)]. In addition, the baseline AIS was associated with AIS conversion, but only a weak association of age with probability of AIS conversion was observed (Table 3). Sensitivity analysis using natural cubic splines of continuous age and injury to surgery time confirmed these results (Table 4). The adjusted spline curve for probability of AIS conversion declined from 45 to 15% in patients ≤ 40 years and it plateaued at a probability of 10% in patients > 40 years (Fig. 5a). Regarding the injury to surgery time, the adjusted curve indicated the highest probability for AIS conversion at > 20% when the surgery was performed < 20 h after SCI and the probability declined to below 10% when the surgery began > 60 h after SCI (Fig. 5b).

In the AIS A stratum, a clear effect of surgery ≤ 12 h, but not of age on AIS conversions was observed (Table 3). Here, cervical NLI indicated a higher probability for AIS conversion [OR (95% CI), 12.74 (2.12–76.72)]. Sensitivity analysis using age and the injury to surgery interval as continuous variables confirmed these effects (Table 4). In the AIS B–D stratum, the surgery ≤ 12 h status was also associated with a higher probability for AIS conversion [3.00 (1.02–8.88)] and older age indicated a lower prospect to improve ['45-59y,' 0.09 (0.02–0.44); '60-74y,' 0.12 (0.02–0.67); and '≥75y,' 0.10 (0.02–0.61)] compared to the '≤44y' reference group. Significant additional effects in the AIS A–B stratum were also observed for the AIS at admission and the enrollment period (Table 3). Sensitivity analysis using natural cubic spline of age and the log-transformed injury to surgery interval as covariates confirmed the effect of age. The effect of the injury to surgery interval however was weaker when the continuous injury to surgery interval was used instead of the categorical variable (Table 4). The adjusted spline curve for probability of AIS conversion in association with age declined steeply from 80 to 20% in patients < 40 years and it plateaued at a probability between 5 and 20% in patients ≥ 40 years (Fig. 5c).

Discussion

The fact that half of the study population is at least 59 years old and experienced significant delay in spine surgery underlines the importance of rethinking SCI emergency care algorithms for elderly patients [4, 20]. The

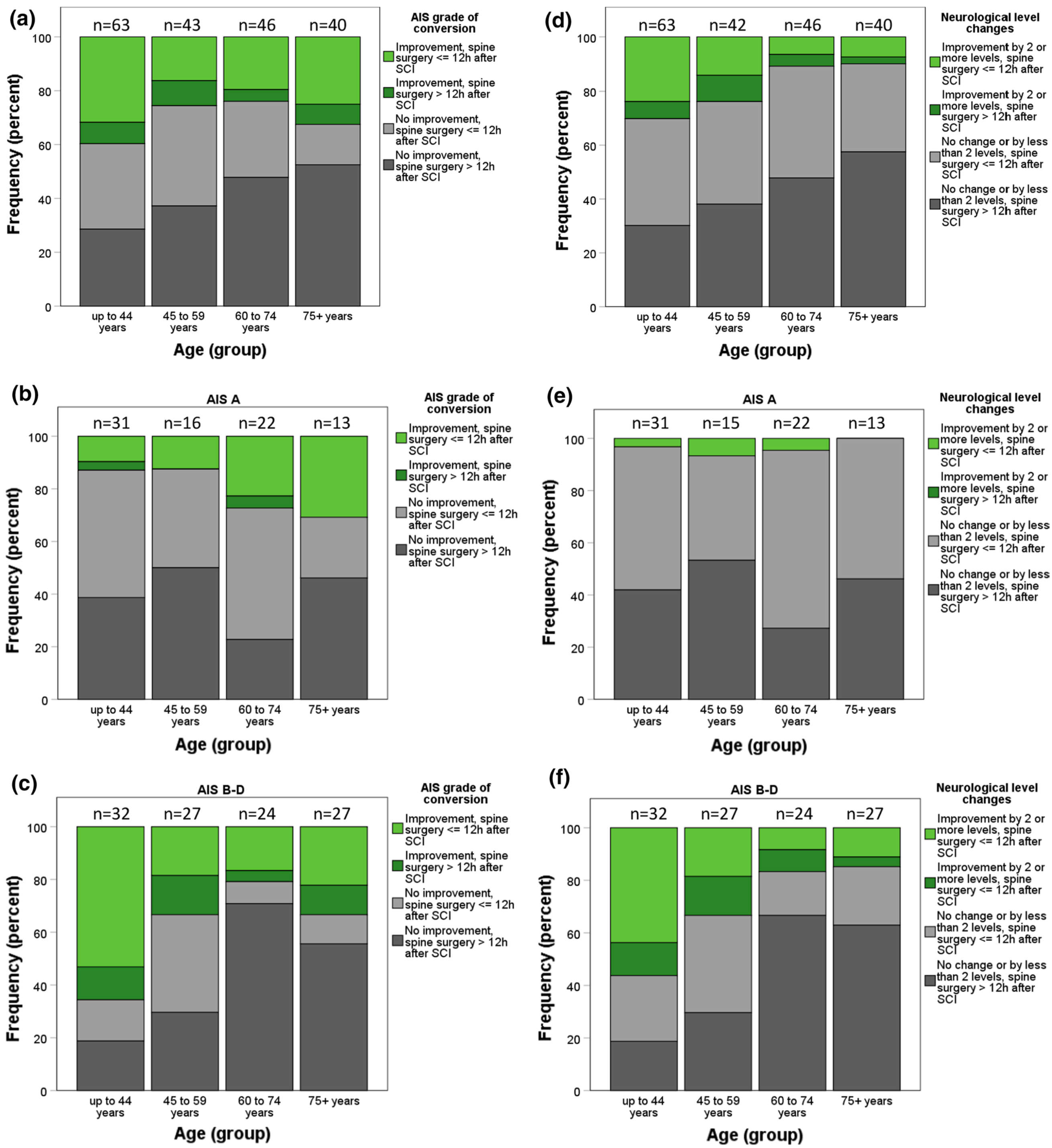


Fig. 4 Neurological recovery in the total sample and stratified for severity of SCI. **a** Pattern of AIS conversion in the total sample. Chi-square test comparing AIS conversion between spine surgery categories (surgery $< = 12$ h, surgery > 12 h) $p < 0.001$. Chi-square test comparing age groups $p = 0.272$. **b** AIS conversion in patients AIS A at baseline. Chi-square test comparing AIS conversion between spine surgery categories $p = 0.021$. Chi-square test comparing AIS conversion between age groups $p = 0.358$ **c** AIS changes in patients AIS B-D at baseline. Chi-square test comparing AIS conversion between spine surgery categories $p < 0.001$. Chi-square test comparing AIS conversion between age groups $p = 0.004$. **d** Pattern of NLI changes by more than two segments in the total sample. Chi-square test comparing NLI changes between spine surgery categories $p = 0.011$. Chi-square test comparing NLI changes between age groups $p = 0.023$. **e** NLI changes in patients AIS A at baseline. Chi-square test comparing NLI changes between spine surgery categories $p = 0.143$. Chi-square test comparing NLI changes between age groups $p = 1$. **f** Frequency of NLI changes for patients AIS B-D at baseline. Chi-square test comparing NLI changes between spine surgery categories $p = 0.004$. Chi-square test comparing NLI changes between age groups $p = 0.002$. Abbreviations: AIS = ASIA Impairment Scale, SCI = spinal cord injury

Table 3 Association of age categories and an injury to surgery time ≤ 12 h with AIS conversion from multiple binary logistic regression models

Total sample (*n* = 191)		
Covariates	Odds ratio (95% CI)	*p*-value
Age group	–	0.158
≤ 44y *(ref)*	1	–
45-59y	0.27 (0.09–0.85)	0.024
60-74y	0.54 (0.18–1.6)	0.264
≥ 75y	0.44 (0.12–1.64)	0.221
Gender *(male, ref: female)*	1.49 (0.61–3.63)	0.383
CCI *(per one point increase)*	0.83 (0.62–1.11)	0.205
AIS admission	–	> 0.001
AIS D *(ref)*	1	–
AIS C	6.35 (1.77–22.81)	0.005
AIS B	4.02 (0.83–19.43)	0.083
AIS A	0.42 (0.18–1.01)	0.052
NLI admission *(cervical, ref: thoracolumbar)*	2.95 (1.23–7.06)	0.015
TBI *(yes, ref: no)*	0.56 (0.22–1.45)	0.231
Surgery within 12 h post injury *(yes, ref: no)*	4.22 (1.85–9.65)	0.001
Enrollment period *(retrospective, ref: prospective)*	0.47 (0.22–1.04)	0.062
		Nagelkerke's $R^2 = 0.39$
AIS A (*n* = 81)		
Covariates	Odds ratio (95% CI)	*p*-value
Age group	–	0.539
≤ 44y *(ref)*	1	–
45-59y	1.25 (0.13–11.84)	0.844
60-74y	1.84 (0.31–10.87)	0.499
≥ 75y	7.16 (0.47–108.2)	0.155
Gender *(male, ref: female)*	2.56 (0.38–17.4)	0.337
CCI *(per one point increase)*	0.51 (0.24–1.08)	0.079
NLI admission *(cervical, ref: thoracolumbar)*	12.74 (2.12–76.72)	0.005
TBI *(yes, ref: no)*	0.26 (0.04–1.72)	0.161
Surgery within 12 h post injury *(yes, ref: no)*	5.56 (0.98–31.63)	0.053
Enrollment period *(retrospective, ref: prospective)*	1.53 (0.33–7.13)	0.586
		Nagelkerke's $R^2 = 0.42$
AIS B–D (*n* = 110)		
Covariates	Odds ratio (95% CI)	*p*-value
Age group	–	0.014
≤ 44y *(ref)*	1	–
45-59y	0.09 (0.02–0.44)	0.003
60-74y	0.12 (0.02–0.67)	0.016
≥ 75y	0.10 (0.02–0.61)	0.013
Gender *(male, ref: female)*	2.91 (0.86–9.91)	0.087
CCI *(per one point increase)*	0.92 (0.64–1.32)	0.634
AIS admission	–	0.002
AIS D (ref)	1	–
AIS C	13.24 (2.93–59.86)	0.001
AIS B	4.05 (0.77–21.37)	0.100
NLI admission *(cervical, ref: thoracolumbar)*	1.74 (0.72–5.84)	0.369

Table 3 (continued)

AIS B–D (*n* = 110)		
Covariates	Odds ratio (95% CI)	*p*-value
TBI *(yes, ref: no)*	0.58 (0.15–2.18)	0.421
Surgery within 12 h post injury *(yes, ref: no)*	3.00 (1.02–8.88)	0.047
Enrollment period *(retrospective, ref: prospective)*	0.17 (0.05–0.56)	0.004
		Nagelkerke's $R^2 = 0.5$

Multiple binary logistic regression models with AIS conversion until discharge as dependent variable in the total sample (top) and stratified for severity of SCI into complete SCI patients AIS A (middle) and incomplete SCI patients AIS B–D (bottom)**.** Coding of the dependent variable AIS conversion (no = 0, yes = 1). Abbreviations: AIS = ASIA Impairment Scale, CCI = Charlson comorbidity index, NLI = neurological level of injury, SCI = spinal cord injury, TBI = traumatic brain injury

result that spine surgery ≤ 12 h after SCI is associated with better neurological outcome across all age groups adds confirmative evidence to previous studies on the timing of decompression and/or stabilization [5]. Older SCI patients suffer fewer multiple injuries, which are the main reason for postponed spine surgery in younger patients. However, missing the study center's aim to start the surgery ≤ 12 h after SCI can be linked with secondary referral to the Level-1 trauma center particularly in elderly patients with incomplete SCI. This generates the hypothesis that the urgency of spine surgery in this group of patients could be underestimated in the pre-hospital setting. This assumption is supported by our observation that, in contrast to younger SCI patients, the majority of elderly patients has secondary referrals and that the delay in admission to the study center is constantly contributing to the prolonged injury to surgery intervals, whereas the delay after admission exposed a more random pattern attributable to pre-existing individual injury or health conditions including multiple pre-morbidities, oral anticoagulation, or ankylosing spondylitis, the latter of which bares diagnostic challenges in the imaging of occult fractures [21] and requires more complex surgical procedures [22].

In incomplete SCI (AIS B–D), the adjusted regression models reveal age effects additional to the effects of the injury to surgery interval. Thus, not only delayed spine surgery, but also biological effects of aging on neuronal plasticity and/or regeneration may contribute to a poorer neurological outcome [23]. That age effects are observed only after incomplete SCI is consistent with a multicenter study, which has demonstrated stronger age effects on functional recovery in AIS B or C rather than in AIS A cohorts [9] and can be explained by the higher potential for intrinsic recovery in incomplete SCI [17, 24] providing a greater margin for functional loss due to outcome modifying factors [25].

Limitations of the study are its monocenter design and that is not population based. In addition, the follow-up ended at discharge from primary SCI care at a median time of 90 days and thus is not standardized. However, the study was conducted in a Level I trauma center with a supra-regional catchment area and a large specialized SCI treatment center allowing for a disease specific assessment of acute healthcare data, which are not available in European multicenter datasets in this detail [26]. Notably, the distribution of neurological baseline and neurological recovery profiles (ISNCSCI) observed in this study is consistent with multicenter studies in Europe and North America [17]. In addition, the demographic structure of the sample regarding age and gender matches recent data from a nationwide German neurotrauma study [2]. Therefore, the sample seems to have sufficient external validity to allow for explorative studies reflecting urban settings in industrialized countries.

Secondary referral to the study center was one of the most frequent reasons for the delay of the first spine surgery in older patients with incomplete SCI in this study, and this delay was associated with worse neurological outcome. Although observational studies are limited in their ability to reveal causal relationships, the study results are relevant for future health services research on how a straight access of elderly SCI patients to a center with specialized 24 h/7d spine surgery service can be achieved and to evaluate effects of initial referral to specialized centers as a target to improve SCI care [27]. Furthermore, since both delayed spine surgery and age can be considered as independent confounders of neurological recovery, the study findings are relevant to the design of clinical trials [28] on neurorestorative therapies.

Table 4 Sensitivity analysis—association of patient characteristics with AIS conversion from multiple binary logistic regression models using natural cubic splines for age and time between SCI and surgery

Total sample (n = 191) (splines for age and time from SCI to surgery)		
Covariates	Odds ratio (95% CI)	*p*-value
Age (years)		
Spline coefficient for Age (df = 2) 1	0.02 (0.00–0.36)	0.009
Spline coefficient for Age (df = 2) 2	0.73 (0.13–4.24)	0.728
Gender *(male, ref: female)*	1.47 (0.59–3.67)	0.406
CCI *(per one point increase)*	0.87 (0.65–1.15)	0.325
AIS admission	–	
AIS D *(ref)*	1	–
AIS C	5.66 (1.68–19.06)	0.005
AIS B	6.27 (1.18–33.21)	0.031
AIS A	0.67 (0.28–1.62)	0.377
NLI admission *(cervical, ref: thoracolumbar)*	2.29 (0.97–5.43)	0.059
TBI *(yes, ref: no)*	0.59 (0.22–1.56)	0.289
Time from SCI to surgery *(hours, log-transformed)*		
Spline coefficient for logarithmised time (df = 2) 1	0.09 (0.01–1.46)	0.091
Spline coefficient for logarithmised time (df = 2) 2	0.002 (0.00–0.26)	0.012
Enrollment period *(retrospective, ref: prospective)*	0.38 (0.17–0.84)	0.017
		Cragg & Uhler's pseudo R^2 = 0.41

AIS A (n = 81) (without splines)		
Covariates	Odds ratio (95% CI)	*p*-value
Age (years)	1.03 (0.99–1.08)	0.165
Gender *(male, ref: female)*	1.77 (0.31–10.08)	0.519
CCI *(per one point increase)*	0.55 (0.27–1.13)	0.102
NLI admission *(cervical, ref: thoracolumbar)*	12.72 (2.19–73.94)	0.005
TBI *(yes, ref: no)*	0.30 (0.05–1.98)	0.210
Time from SCI to surgery *(hours, log-transformed)*	0.44 (0.20–1.00)	0.049
Enrollment period *(retrospective, ref: prospective)*	1.14 (0.28–4.63)	0.858
		Cragg & Uhler's pseudo R^2 = 0.42

AIS B–D (n = 110) (spline for age)		
Covariates	Odds ratio (95% CI)	*p*-value
Age (years)		
Spline coefficient for Age (df = 2) 1	0.0002 (0.00–0.03)	0.001
Spline coefficient for Age (df = 2) 2	0.31 (0.03–3.12)	0.322
Gender *(male, ref: female)*	3.10 (0.88–10.87)	0.077
CCI *(per one point increase)*	0.98 (0.68–1.42)	0.921
AIS admission		
AIS D *(ref)*	1	
AIS C	12.12 (2.83–51.94)	0.001
AIS B	5.84 (1.10–30.87)	0.038
NLI admission *(cervical, ref: thoracolumbar)*	2.03 (0.57–7.26)	0.278
TBI *(yes, ref: no)*	0.71 (0.18–2.82)	0.627
Time from SCI to surgery *(hours, log-transformed)*	0.70 (0.44–1.10)	0.122
Enrollment period *(retrospective, ref: prospective)*	0.14 (0.04–0.49)	0.002
		Cragg & Uhler's pseudo R^2 = 0.54

Multiple binary logistic regression models with AIS conversion until discharge as dependent variable in the total sample (top) and stratified for severity of SCI into complete SCI patients AIS A (middle) and incomplete SCI patients AIS B–D (bottom)**.** Coding of the dependent variable AIS conversion (no = 0, yes = 1). Natural cubic splines were used for age and time from SCI to surgery where appropriate (decision based on AIC comparison between models). For the adjusted cubic spline curves see Fig. 5. Abbreviations: AIC = Akaike information criterion, AIS = ASIA Impairment Scale, CCI = Charlson comorbidity index, df = degrees of freedom, NLI = neurological level of injury, SCI = spinal cord injury, TBI = traumatic brain injury

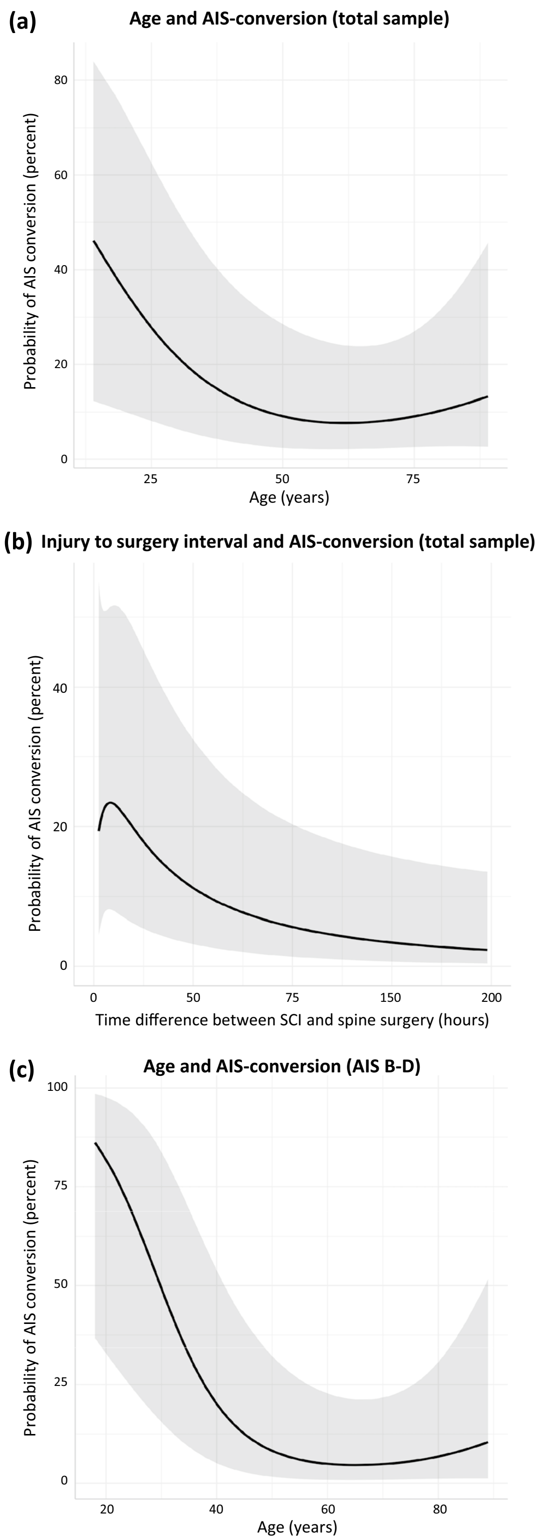


Fig. 5 Estimated probability of AIS conversion using natural cubic splines. The probability of AIS conversion in association with patient age **a** the injury to surgery interval **b** in the total sample ($n=192$) and with patient age in the AIS B-D stratum **c** ($n=110$) was calculated based on multiple binary logistic regression using natural cubic splines with 2 degrees of freedom, adjusted for sex, CCI, AIS at admission, NLI at admission, TBI, time from SCI to surgery (log-transformed) and enrollment period

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Author contributions All authors contributed to the study conception and design. Data were collected by MAK, TLü, AN, EP, JL, MK, and TLi. Source verification of key data was performed by MH. The statistical analysis was performed by TLü, MAK, and UG. The first draft of the manuscript was written by MAK and TLü. All authors contributed on the intellectual content of the final version of the manuscript.

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Availability of data and material The dataset analyzed in the current study is not publicly available due to legal restrictions under the General Data Protection Regulation of the European Union and other applicable national or local privacy regulations but are available from the corresponding author on reasonable request.

Code availability The syntax code used with the statistical software SPSS (version 26.0) and the R script can be provided by the corresponding author upon reasonable request. The code used with the DAGitty online application (version 3.0) is attached to the legend of Supplementary Fig. 1.

Declarations

Conflicts of interest All authors declare that they have no conflicts of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional Ethics Committee of Charité—Universitätsmedizin Berlin (Approval Number EA2/015/15) and with the 1964 Helsinki Declaration and its later amendments and other applicable ethical standards.

Consent to participate If applicable, informed consent for the study participation was obtained from the individual participants prior to the inclusion in the Comparative Outcome and Treatment Evaluation in Spinal Cord Injury (COaT-SCI) study. In case that it was not reasonable to obtain informed consent, only routinely collected clinical care data were used for non-commercial research in accordance with the regulations of the Berlin State Hospital Act in this study.

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