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ARTICLE

Neurological recovery after traumatic spinal cord injury: what is meaningful? A patients' and physicians' perspective

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Abstract

Study design Cross-sectional survey.

Objectives Most studies on neurological recovery after traumatic spinal cord injury (tSCI) assess treatment effects using the American Spinal Injury Association Impairment Scale (AIS grade) or motor points recovery. To what extent neurological recovery is considered clinically meaningful is unknown. This study investigated the perceived clinical benefit of various degrees of neurological recovery one year after C5 AIS-A tSCI.

Setting The Netherlands.

Methods By means of a web-based survey SCI patients and physicians evaluated the benefit of various scenarios of neurological recovery on a scale from 0 to 100% (0% no benefit to 100% major benefit). Recovery to AIS-C and D, was split into C/C+ and D/D+, which was defined by the lower and upper limit of recovery for each grade.

Results A total of 79 patients and 77 physicians participated in the survey. Each AIS grade improvement from AIS-A was considered significant benefit (all $p < 0.05$), ranging from 47.8% (SD 26.1) for AIS-B to 86.8% (SD 24.3) for AIS-D+. Motor level lowering was also considered significant benefit ($p < 0.05$), ranging from 66.1% (SD 22.3) for C6 to 81.7% (SD 26.0) for C8.

Conclusions Meaningful recovery can be achieved without improving in AIS grade, since the recovery of functional motor levels appears to be as important as improving in AIS grade by both patients and physicians. Moreover, minor neurological improvements within AIS-C and D are also considered clinically meaningful. Future studies should incorporate more detailed neurological outcomes to prevent potential underestimation of neurological recovery by only using the AIS grade.

Supplementary information The online version of this article (<https://doi.org/10.1038/s41393-020-0436-4>) contains supplementary material, which is available to authorized users.

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Introduction

The initial severity of spinal cord injury is related to the neurological outcome, where patients with a complete traumatic spinal cord injury (tSCI) may have less neurological recovery than patients with an incomplete tSCI [1, 2].

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Although patients can learn to adapt to their condition over time, late complications such as pressure ulcers, respiratory, cardiovascular, and urinary and bowel complications can cause great morbidity and even mortality [3, 4].

Many studies have investigated the effect of early surgical decompression on neurological recovery in patients with tSCI [5–7]. This effect is often evaluated with an improvement in American Spinal Injury Association Impairment Scale (AIS grade) or motor score points, which are frequently used as primary outcome measures. Whilst some studies define at least one AIS grade improvement as a success [5, 8], others consider at least two AIS grades improvement as a success [6, 7]. It is however unknown whether this improvement in AIS grade or motor score points translates into clinically meaningful recovery from the patients' and physicians' perspective [9].

In order to define clinically meaningful recovery, some studies have evaluated the priorities of neurological recovery in patients with tSCI. The priorities of neurological improvement differ for persons with paraplegia or tetraplegia. Persons with paraplegia have a higher priority of regaining locomotion compared with patients with tetraplegia [10, 11]. Conversely, persons with tetraplegia have a high priority of regaining hand function, which does not necessarily have to coincide with an improvement in AIS grade but could also occur with a decrease in the motor level of injury.

When determining a successful treatment, it is important to define the minimal threshold of recovery that is considered clinically relevant. Since the definition of clinically meaningful recovery after complete cervical tSCI is unclear, we investigated the experienced value of various degrees of neurological recovery by SCI patients and physicians who are involved in treatment of tSCI patients.

Methods

Procedures

We set up a multidisciplinary team of specialists involved in the care of patients with tSCI, consisting of one rehabilitation specialist and one psychologist, who exclusively treat SCI patients, two orthopedic surgeons and two neurosurgeons from level I academic trauma centers. The survey was constructed jointly and tested internally. Approval by the Medical Ethical Research Council was granted.

Participants

The survey was sent to all 138 Dutch neurosurgeons, member of the Dutch Society of Neurological Surgeons, of which 59 were also member of the Dutch Spine Society (DSS). In addition, the survey was sent to all 88 orthopedic

surgeons who are members of the DSS and to 34 rehabilitation specialists who are members of the Dutch-Flemish Spinal Cord Society. The survey was also sent to the members of the Dutch Spinal Cord Injury Association, which were contacted through the monthly newsletter. All participants provided informed electronic consent to participate on the survey.

Survey

The survey was conducted between June 2019 and October 2019 and consisted of three sections. The first section included questions on respondent characteristics (Supplementary 1). The second section of the survey contained five questions regarding a hypothetical case with initially a complete C5 AIS-A tSCI. Patients and physicians were asked to give their opinion on the perceived clinical benefit of neurological recovery in a case where the AIS grade remained the same, i.e., AIS-A, but the level of motor injury lowered to C6, 7, and 8 specifically. The cases were accompanied by a brief description of the consequences of the neurological recovery on motor function, mobility, independence in eating, and independence in making transfers [12, 13]. For each scenario, they were asked to indicate how large the benefit of a lower motor level would be compared with the baseline, e.g., C6 compared with C5, C7 compared with C5, or C8 compared with C5. The magnitude of the difference was measured on a continuous scale where 0% defined no clinical benefit and 100% defined major clinical benefit. A difference of 50% was translated to a moderate benefit.

The third section of the survey consisted of seven similar questions regarding the same hypothetical case but now the scenario was improvement in AIS grade instead of motor level. Because there is a wide variation in functionality within the grades AIS-C and D, we described the situation for the lower and upper limit of recovery for each grade, thus creating a C and C+ grade and a D and D+ grade.

Statistical analysis

Difference in importance between and within AIS grades and motor level improvements were calculated with paired *t*-tests using all responses. Secondly, differences of importance of improvement between physicians and patients were calculated with independent *t*-tests and Welch's *t*-test where appropriate. Levene's test was used to assess equality of variances. Thirdly, subgroup analyses were performed to investigate possible differences in opinion between (1) surgeons and physiatrists, (2) paraplegic and tetraplegic patients, as well as (3) recent SCI (≤ 5 years ago) and long-term SCI (> 5 years ago). *P* values < 0.05 were considered statistically significant. Statistical analyses and data

visualization were conducted using R version 3.6.0 (R Core Team, 2019).

Results

A total of 156 persons participated in the study: 79 patients and 77 physicians. The mean age of patients was 53.9 ± 16.6 years. Most patients were tetraplegic (64.1%). The majority of patients (68.4%) were long-term SCI patients (>5 years). There were 14 rehabilitation specialists, 35 neurosurgeons, 22 orthopedic surgeons and six other physicians of whom two resident neurosurgery, two resident orthopedic surgery, and two physician assistants. The overall response rate of rehabilitation specialists was 41.2%, 25.4% for neurosurgeons, and 25.0% for orthopedic

surgeons. Characteristics of respondents are summarized in Table 1.

AIS improvement

In a range from 0 to 100%, all respondents considered the clinical benefit for recovering from AIS-A to AIS-B 47.8% (SD 26.1), to AIS-C 55.0% (SD 22.2), to AIS-C+ 70.0% (23.5), to AIS-D 81.4% (SD 23.7), and to AIS-D+ 86.8% (SD 24.3, Fig. 1). Every consecutive improvement in AIS grade was perceived as a significant beneficial improvement. Also, neurological recovery within motor incomplete grades AIS-C/ C+ and D/D+ was regarded as significant improvement. The importance of the functional improvement per AIS grade improvement was supported when respondents were asked to compare neurological recovery to AIS-B or C. The benefit associated with the difference in neurological recovery between both grades was regarded 53.9% (SD 23.1), which indicates a moderate difference. When respondents were asked to compare recovery to AIS-C+ or D, the difference between recovering to AIS-C+ or D was regarded 72.5% (SD 25.1), which indicates a more than moderate difference in neurological recovery between the two.

Motor level improvement

The perceived success of neurological recovery increased per motor level gained and was significant for all levels (Fig. 1). The clinical benefit from motor level lowering from C5 to C6 was considered 66.1% (SD 22.3), to C7 74.0% (SD 24.2), and to C8 81.7% (SD 26.0). The difference between recovering to C7 instead of C6 was considered clinically different, i.e., 67.3% (SD 25.1), which indicates a more than moderate difference. The difference between neurological recovery to C8 instead of C7 was considered 69.4% (SD 27.1). The clinical benefit of motor level lowering to C6 scored higher than AIS improvement to AIS-B or C (Fig. 1). In addition, recovery to C7 scored higher than recovery to AIS-C+ or lower and C8 higher than recovery to AIS-D or lower.

Subgroup analysis

We observed a significant difference between patients and physicians for the considered value of all levels of motor improvement (Table 2). Physicians were more positive towards the benefit of motor level lowering (Fig. 2). There was no significant difference for AIS grade improvement between patients and physicians, except for recovery to AIS-D and D+ (Table 2 and Fig. 2). However, the variance in responses was significantly larger in patients compared with physicians for all hypothetical cases of neurological improvement. In patients specifically, there were no significant differences in responses based on their level, severity,

Table 1 Demographical data of survey respondent.

Patients		N = 79
Age (mean (SD))		53.9 (16.6)
Duration SCI (%)	0–5 years	24 (31.6)
	>5 years	52 (68.4)
Education (%)	No education	3 (3.8)
	Prevocational education	17 (21.5)
	High school	19 (24.1)
	University	35 (44.3)
	Other	5 (6.3)
Level of SCI (%)	Paraplegia	28 (35.9)
	Tetraplegia	50 (64.1)
Disability arm/hands in tetraplegic patients (%)	No disability	5 (10.0)
	Slight disability	5 (10.0)
	Moderate disability	6 (12.0)
	Severe disability	15 (30.0)
	Fully disabled	19 (38.0)
Mobility (%)	Wheelchair	69 (88.5)
	Walking aid short distance	1 (1.3)
	Walking aid long distance	7 (9.0)
	Short distance no walking aid	1 (1.3)
	Long distance no walking aid	0 (0.0)
	Other	0 (0.0)
Specialists		N = 77
(%)	Rehabilitation specialist	14 (18.2)
	Neurosurgeon	35 (45.5)
	Orthopedic surgeon	22 (28.6)
	Other	6 (7.8)

SCI spinal cord injury, SD standard deviation.

Importance of improvement

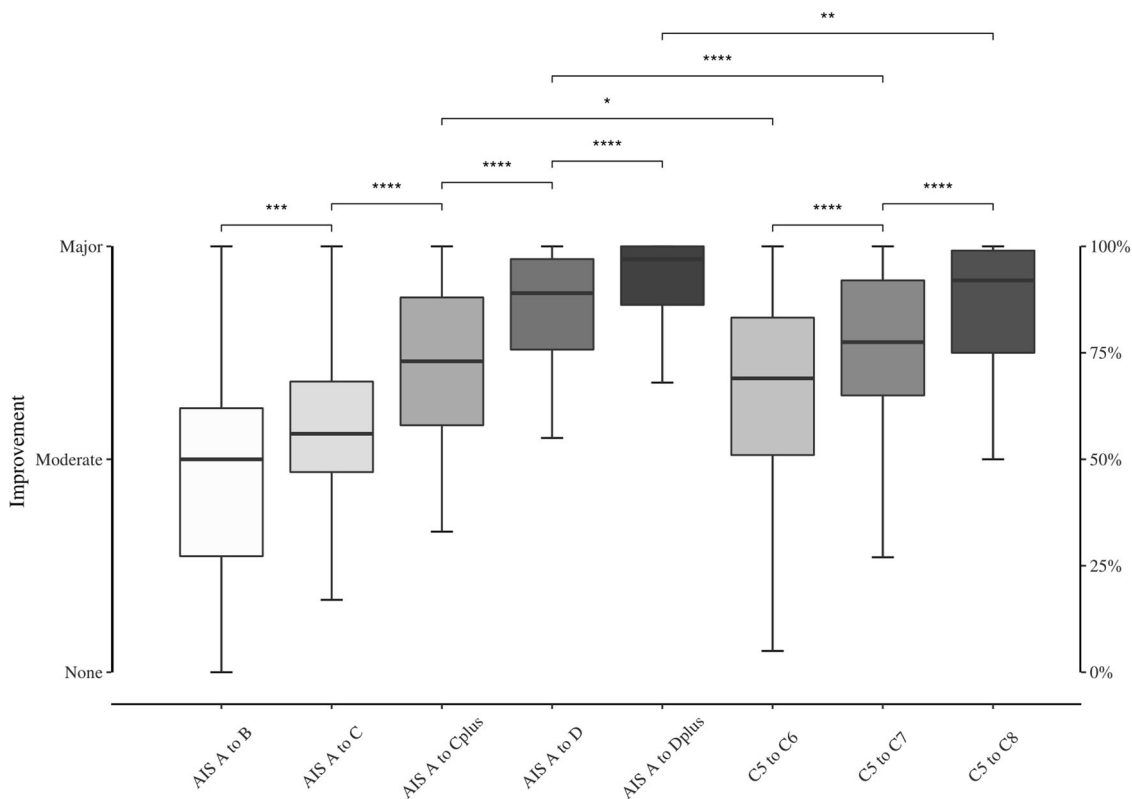


Fig. 1 Importance of improvement. 0 = no benefit, 100 = major benefit. AIS American Spinal Injury Association Impairment Scale, SD standard deviation. Ns = $p > 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

Table 2 Importance of improvement between patients and physicians.

Neurological improvement	Patients	Physicians	P
Perceived benefit of motor level improvement (mean (SD))			
C5 AIS-A → C6	61.3 (27.0)	70.1 (16.7)	0.036
C5 AIS-A → C7	66.5 (30.2)	80.2 (15.1)	0.002
C5 AIS-A → C8	72.9 (34.3)	89.3 (11.6)	0.001
Perceived difference between motor level improvement (mean (SD))			
C5 AIS-A → C7 vs. C6	61.1 (29.5)	72.3 (19.7)	0.018
C5 AIS-A → C8 vs. C7	63.5 (33.6)	74.5 (18.9)	0.032
Perceived benefit of AIS grade improvement (mean (SD))			
C5 AIS-A → B	48.2 (30.6)	47.5 (22.4)	0.896
C5 AIS-A → C	53.3 (27.6)	56.3 (16.9)	0.521
C5 AIS-A → C+	67.9 (31.0)	71.6 (15.3)	0.451
C5 AIS-A → D	75.0 (32.5)	86.4 (11.5)	0.018
C5 AIS-A → D+	78.1 (33.5)	93.5 (9.1)	0.002
Perceived difference between AIS grade improvement (mean (SD))			
C5 AIS-A → AIS-C vs. AIS-B	53.9 (26.8)	53.9 (19.9)	1.000
C5 AIS-A → AIS-D vs. AIS-C+	64.1 (32.1)	79.0 (15.3)	0.004

0 = no benefit, 100 = major benefit.

AIS American Spinal Injury Association Impairment Scale, SD standard deviation.

or duration of SCI. Among physicians, a significant difference was observed between surgeons and physiatrists. Overall rehabilitation specialists were more positive about each type of neurological recovery compared with surgeons (Table 3).

Discussion

This study investigated the perceived success for various degrees of neurological recovery after complete cervical tSCI, both from patients’ and physicians’ perspectives. Not only an improvement in AIS grade, but also lowering of the motor level in complete cervical tSCI has a clinical benefit according to both patients and physicians. Meaningful recovery can therefore be achieved without improving in AIS grade, since regaining complete hand function while remaining AIS-A appeared to be as important as recovering from C5 AIS-A to AIS-D. In particular patients with complete cervical tSCI will recover less likely in AIS grade compared with patients with incomplete injuries [1, 2]. It is unknown whether currently available studies using the AIS grade could potentially underestimate clinically meaningful neurological recovery in these patients.

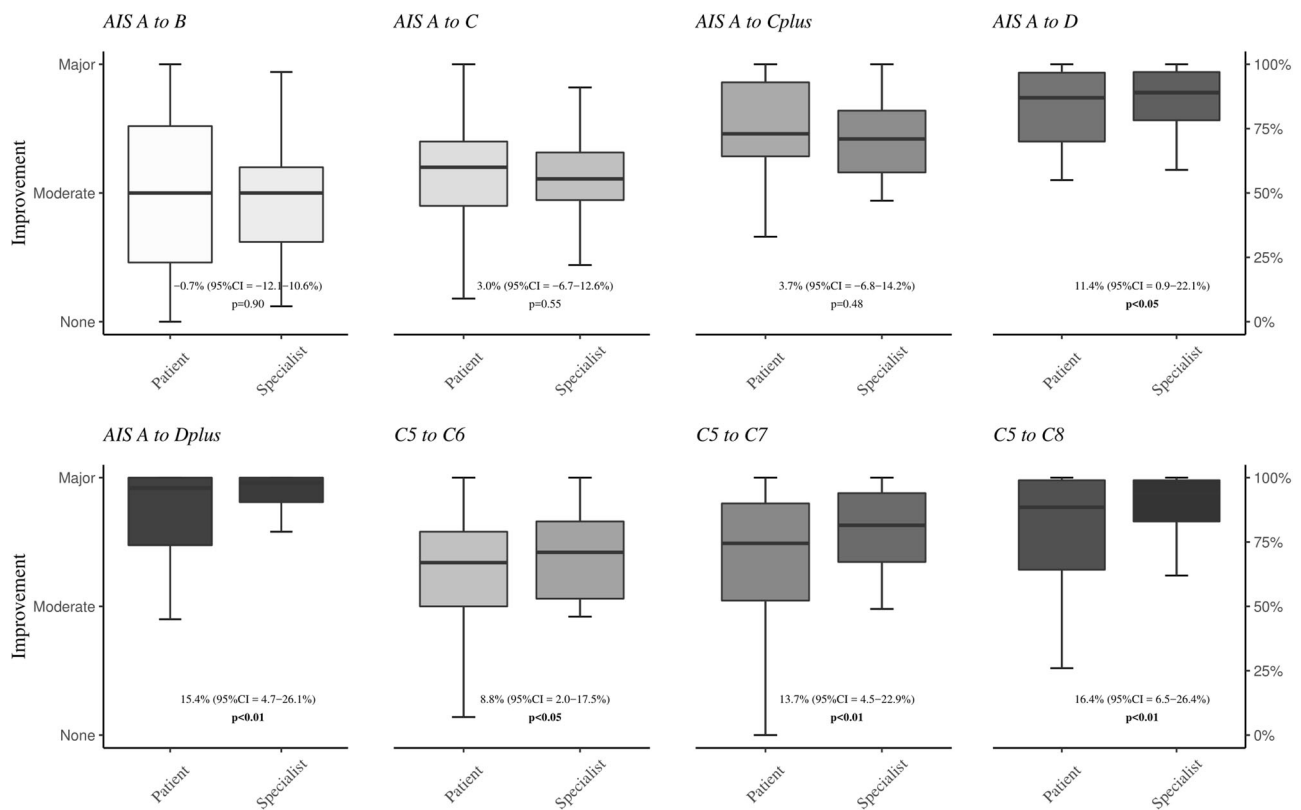


Fig. 2 Importance of improvement between patients and physicians. 0 = no benefit, 100 = major benefit. AIS American Spinal Injury Association Impairment Scale, SD standard deviation, CI confidence interval.

Table 3 Perceived benefit of motor level and AIS grade improvement between surgeons and rehabilitation specialists.

Neurological improvement	Surgeons	Rehabilitation specialists	P
Motor level improvement perceived benefit (mean (SD))			
C5 AIS-A → C6	67.6 (16.4)	78.4 (15.5)	0.033
C5 AIS-A → C7	78.2 (15.5)	87.4 (11.6)	0.045
C5 AIS-A → C8	88.2 (12.1)	93.0 (9.5)	0.175
AIS improvement perceived benefit (mean (SD))			
C5 AIS-A → B	44.6 (22.0)	56.5 (22.2)	0.098
C5 AIS-A → C	54.7 (18.1)	61.2 (11.8)	0.229
C5 AIS-A → C+	70.0 (15.1)	76.3 (15.2)	0.200
C5 AIS-A → D	84.0 (11.3)	94.2 (8.3)	0.004
C5 AIS-A → D+	92.6 (9.9)	96.5 (5.4)	0.183

0 = no benefit, 100 = major benefit.

AIS American Spinal Injury Association Impairment Scale, SD standard deviation.

AIS grade recovery

Most studies in tSCI patients have focused their primary outcomes on AIS grade improvements. While the AIS grade is frequently used to compare treatment effects, the AIS

grade by itself does not take into account whether patients who remained the same AIS grade experienced any motor level lowering or whether the improvement in AIS grade led to functional improvement [14]. In addition, cases have been described in which patients did improve neurologically, but paradoxically worsened in AIS grade [15]. Our study shows that AIS grade improvements are indeed considered meaningful by both patients and physicians. In addition, we found that there may even be substantial clinical benefit from smaller neurological improvements within an AIS grade C and D. This finding is particularly important when using the AIS grade as an outcome measure for recovery in patients with an initial AIS-D, since a ceiling effect in neurological recovery has been suggested that subsequently prevents them from further improvement in AIS grade [16, 17]. It is unclear whether currently available studies using the AIS grade as only outcome measure could potentially underestimate clinically meaningful neurological recovery. Other outcome measures have been developed to identify functional recovery in tSCI patients, such as the Spinal Cord Independence Measure (SCIM) and more recently the Spinal Cord Ability Ruler [18]. However, improvement in SCIM can sometimes be achieved by training, independent of any neurological recovery [19]. Therefore, defining relevant outcomes is crucial for

designing and interpreting study results, especially in tSCI patients, since meaningful neurological recovery in this specific patient population may not always coincide with AIS grade improvement [16, 20].

Motor level recovery

The recovery of functional motor levels in complete cervical tSCI was found to be both as important as improving in AIS grade, in particular when hand function was regained. The importance of the latter has also been confirmed by two other studies. One of those asked 565 tetraplegic patients to compare certain types of neurological recovery and prioritize them for their expected improvement in quality of life [21]. Patients prioritized regaining hand function above improvement in standing function. The level of motor injury did not appear to affect their prioritization, since patients with C4, C5, C6, and C7 motor levels prioritized regaining hand function above standing. Comparably, another study in 151 tSCI patients asked patients to trade-off certain functions against one another [22]. Patients preferred hand function above walking, with an odds ratio of 1.47 (95% CI 1.38–1.57). The importance in motor level lowering in cervical tSCI was also confirmed by another study in complete (AIS-A) cervical tSCI patients [23]. A lowering of at least two motor levels was significantly associated with improvement in functional independence in these patients [24]. The improvement in motor level recovery can be overlooked when only motor score recovery is considered as outcome measure, since this does not necessarily have to correspond with regaining functional strength in certain muscle groups. Only few studies in cervical tSCI patients evaluated motor level recovery in addition to functional neurological recovery [23, 25]. One study in cervical tSCI patients evaluated motor level recovery in patients surgically treated within and after 24 h. When surgical decompression was performed within 24 h only 1/20 (5%) did not improve in motor level, 7/20 (35%) improved one motor level, 11/20 (55%) improved two motor levels, and one patient (5%) improved completely. In contrast, when surgery was performed after 24 h 4/12 (33%) did not improve in motor level, 6/12 (50%) improved one motor level, and 2/12 (17%) improved two motor levels [25]. As patients with complete cervical tSCI are less likely to recover in AIS grade [2, 16], it is important to evaluate whether early surgical decompression might have an impact on lowering of the motor level in these patients, especially since motor level recovery can also have a major impact on the reconstructive possibilities to regain partial hand function. Reconstructions are possible starting at C5 and more possibilities are present at every lower level of injury [26].

Limitations and strengths

This study has several limitations. Firstly, surveys are subject to the respondents' interpretation. As we observed a greater variation in the perceived success between patients compared with physicians, it is unknown whether a variation in interpretation of described neurological recovery played a role, or that actual slightly different opinions exist between patients and physicians. In addition, it is important to keep in mind that the perceived success by a group can be experienced differently by an individual. Secondly, the scenarios described in our survey are an unavoidable simplification of the complex and heterogeneous patterns of neurological recovery that we see in our daily practice. The neurological recovery patterns in this study are limited to only a few scenarios of recovery after a C5 AIS-A tSCI. Frequently, neurological recovery in tSCI will be more heterogeneous and would consist of a combination of motor level lowering and AIS grade recovery. It is unknown whether certain combinations of these recovery patterns are considered more meaningful compared with others. Moreover, our comparison of motor level recovery over AIS grade improvement is impaired as we did not ask to rank their importance, nor did we ask respondent's trade-off questions between them. Nonetheless, this study does show that meaningful recovery may be achieved even without improving in AIS grade according to patients and physicians. This could either be through minor neurological recovery within AIS-C or D or improvement in motor level. These findings put the assessment of outcome in complete tSCI patients into perspective. Currently, multiple questions regarding the optimal management of tSCI patients remain unanswered. Most of them are based on the AIS grade as a primary outcome measure. Only very few have incorporated motor score recovery or even motor level recovery. In addition, other functional recoveries which are prioritized by patients [27], such as bladder and bowel management, sexual functions and autonomic functions, should also be examined. Future studies should therefore be encouraged to further explore the field of such recoveries and incorporate more detailed neurological recoveries in order to improve study designs and interpretation of meaningful neurological recovery.

Conclusion

Motor level lowering in complete cervical tSCI patients is considered clinically meaningful neurological recovery in addition to AIS grade recovery. Moreover, minor neurological improvements within AIS-C and D are also considered valuable recovery. These opinions are shared by both physicians and patients. This study shows that meaningful

recovery may be achieved even without improving in AIS grade. It is unknown whether the currently available studies using the AIS grade as only outcome measure could potentially underestimate clinically meaningful neurological recovery in these patients. Future studies should therefore not only focus on AIS grade improvement or motor score recovery, but should be encouraged to incorporate more detailed neurological and functional outcome measures.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions PVTW was responsible for the study conceptualization, survey creation, data acquisition, analysis and interpretation of data, writing of the paper, and final approval of the manuscript. MWMP contributed to study conceptualization, survey creation, interpretation of data, critical revision of the paper, and final approval of the manuscript. EM was responsible for survey creation, data acquisition, analysis and interpretation of the data, critical revision of the paper, and final approval of the manuscript. JSS contributed to study conceptualization, survey creation, interpretation of data, critical revision of the paper, and final approval of the manuscript. AJFH contributed to study conceptualization, interpretation of data, critical revision of the paper, and final approval of the manuscript. SS contributed to study conceptualization, interpretation of data, critical revision of the paper, and final approval of the manuscript. WPV contributed to study conceptualization, interpretation of data, critical revision of the paper, and final approval of the manuscript. FCO contributed to study conceptualization, interpretation of data, critical revision of the paper, final approval of the manuscript, and study supervision.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics statement We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

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