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Reciprocal association between pain and quality of life after newly acquired spinal cord injury

Maren Westphal[1] · Valerie Carrard[2,3] · Céline Braunwalder[2,4,5] · Caroline Debnar[2,4] · Marcel Post[6,7] · Christine Fekete[2,4] · Mayra Galvis[2,4] · Anke Scheel-Sailer[2,3,4,8]

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Abstract

Purpose Pain is highly prevalent in spinal cord injury (SCI) and a key determinant of quality of life (QoL). This is the first study to examine reciprocal associations between pain and QoL in patients undergoing their first inpatient rehabilitation after SCI.

Methods Longitudinal data, with three measurement time points (1 month and 3 months after SCI onset, and at discharge from inpatient rehabilitation) from the Inception Cohort of the Swiss Spinal Cord Injury Cohort Study. Participants were 381 individuals aged ≥ 16 years with a newly diagnosed traumatic or non-traumatic SCI. 75.1% were male and the average age was 53.2 years. Random intercept cross-lagged panel models were conducted to examine the reciprocal association between pain intensity and QoL, as measured with the International SCI QoL Basic Data Set three individual items (satisfaction with life, physical health, and psychological health) and total score (mean of the three individual items).

Results Both item and total QoL scores increased over time. 1 month: 5.3 (SD = 2.7), 3 months: 5.9 (SD = 2.3), discharge: 6.6 (SD = 2.0). Participants reported relatively low levels of pain intensity that remained stable over the course of inpatient rehabilitation. 1 month: 2.7 (SD = 2.3), 3 months: 2.6 (SD = 2.4), discharge: 2.7 (SD = 2.5). There were no significant cross-lagged associations between QoL and pain intensity across time.

Conclusion Results indicate that pain intensity does not predict changes in QoL during first rehabilitation, and vice versa. Associations between pain intensity and QoL reported by previous studies may be attributable to individual characteristics and timely events that simultaneously influence pain and QoL.

Keywords Quality of life · Pain · Spinal cord injury · Rehabilitation · Cross-lagged panel analysis

Plain English summary

Pain is very common in spinal cord injury (SCI) and associated with lower levels of quality of life. Understanding how the relationship between pain and QoL evolves during first rehabilitation is important for knowing when might be the best time to intervene. The goal of this study was to examine how pain and QoL influence each other in the context of inpatient rehabilitation following SCI using an advanced statistical methodology. Patients experienced improvements in QoL over time and reported relatively low levels of pain intensity that remained stable over the course of inpatient

✉ Maren Westphal
mwestphal@pace.edu

1 Department of Psychology, Pace University, 861 Bedford Rd, Pleasantville, NY 10570, USA

2 Swiss Paraplegic Research, Nottwil, Switzerland

3 Psychiatric Liaison Service, Department of Psychiatry, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland

4 Faculty of Health Sciences and Medicine, University of Lucerne, Lucerne, Switzerland

5 Institute of Complementary and Integrative Medicine, University of Bern, Bern, Switzerland

6 Center of Excellence in Rehabilitation Medicine, UMC Utrecht Brain Center, University Medical Center Utrecht and De Hoogstraat Rehabilitation, Utrecht, The Netherlands

7 Department of Rehabilitation Medicine, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

8 Swiss Paraplegic Centre, Nottwil, Switzerland

rehabilitation. Pain intensity did not predict changes in QoL during first rehabilitation, and neither did QoL predict pain intensity. Findings suggest that QoL may evolve independently of pain during first rehabilitation.

Introduction

Pain is a very common consequence of spinal cord injury (SCI) that is experienced by 70% of individuals with SCI [1], with more than a third reporting severe levels of pain [2]. Pain interferes with daily activities [3], sleep, mood, social relationships, and enjoyment of life [4]. The presence and severity of secondary health issues such as pain also contribute to differences in quality of life (QoL) and mental health in individuals with SCI as compared to the general population [5]. For example, individuals with SCI who experience less frequent or less severe pain have been found to be more similar to the general population with regard to mental health and QoL than those experiencing more frequent or severe pain [6].

Longitudinal research has further established pain as a predictor of QoL and mental health outcomes among individuals with SCI. For example, a longitudinal cohort study of individuals with SCI found strong associations between presence of pain and poor mood and lower global self-related health [7]. Findings from a prospective cohort study conducted in the Netherlands have further shown that pain predicts trajectories of lower life satisfaction [8, 9] and worse mental health as assessed from the start of inpatient rehabilitation for up to 5 years following discharge [10]. Assessing temporal relationships between overall quality of life, pain intensity, and pain interference within 3 months after SCI (baseline) and at 6-, 12-, and 42-months follow-up, a Scandinavian multi-site study found that while QoL increased over time, participants who experienced an increase in pain intensity showed less of an increase in QoL from baseline to the 3.5-year follow-up. Furthermore, changes in QoL score correlated with a change in pain interference [11]. Overall, findings from the Dutch research group's trajectory studies and the Scandinavian study's longitudinal regression analysis suggest that the relationship between pain and satisfaction with QoL is dynamic and warrants a longitudinal measurement approach.

Consistent with a biopsychosocial model of pain and disability [12], longitudinal studies with general and medical populations have shown that individuals with pain or depression face an increased risk for developing the other, resulting in a spiral of pain and depression [13, 14]. Although QoL has been conceptualized typically as an outcome rather than a predictor of pain in individuals with SCI, it is possible that low satisfaction with one's QoL may also affect the experience of pain. For example, a cross-sectional study using structural equation modeling to analyze subjective well-being as a determinant of pain and depression found that individuals with physical disabilities with greater subjective well-being endorsed lower pain intensity. Moreover, subjective well-being had significant direct effects on underlying pain-related mechanisms, such as pain control. pain catastrophizing and pain interference as well as depression [15]. A longitudinal study of psychosocial resources, mental health, and pain trajectories in individuals with SCI found that less anxiety, more social support and higher optimism were associated with more favorable pain trajectories in SCI [16]. These findings suggest that longitudinal interrelations between QoL and pain in SCI may resemble those that have been observed for depression and anxiety and pain in other medical populations [17].

Cross-lagged modeling techniques are particularly well suited for examining longitudinal evolutions of two variables where either variable may potentially serve as predictor and change the trajectory of the other variable [18, 19]. Cross-lagged modeling techniques enable the examination of longitudinal interrelationships between multiple variables simultaneously in a single model [20], thus, they provide a more powerful test of how variables influence each other over time than binary logistic and multiple regression models with a single dependent variable.

To our knowledge, no published study has used cross-lagged panel modeling to examine reciprocal relationships between QoL and pain in SCI patients. Cross-lagged studies with other medical populations highlight the potential of this approach to challenge assumptions about directionality. For example, a cross-lagged study conducted with a chronic pain sample found that depression/anxiety longitudinally predicted pain, whereas neither pain nor pain-related disability predicted depression/anxiety [21]. Similarly, a study using cross-lagged panel analysis with arthritis patients revealed bidirectional associations between pain and symptoms of depression over time as well as a significant impact of depression at baseline on pain symptoms at 6 months, whereas pain did not predict depression [22].

Given that extensive changes in physical functioning and independence occur during first rehabilitation following SCI, understanding temporal relationships between pain and SCI in the inpatient rehabilitation context is important for timely assessment and targeted interventions. Indeed, pain and QOL are formally or informally addressed in every SCI rehabilitation center, but the most opportune time to intervene is unknown. Accordingly, the main purpose of the current study was to examine potential reciprocal associations between pain intensity and QoL, as measured with the International SCI QoL Basic Data Set (QoL-BDS) using both its three individual items (satisfaction with life, physical health, and psychological health) and total score (mean of the three individual items). Assessing different dimensions of QoL

as opposed to employing a unidimensional measure of QoL and its use of a cross-lagged panel design distinguish the present study from similar previous research on QoL and pain. Specifically, the Scandinavian multi-site study [11] used one item to measure QoL (global QoL) and the Dutch research group's trajectory studies on pain and life satisfaction and mental health focused on satisfaction with overall QoL [8, 10].

The present study's two main study objectives were to 1) examine if higher pain intensity would be associated with lower QoL at a subsequent time point, and conversely, lower pain intensity would be associated with higher QoL at a subsequent time point, and 2) if better QoL would be associated with lower pain intensity at a subsequent time point, and conversely, if lower QoL would be associated with greater pain intensity. Based on the above-described findings from previous research, we expected that the relationship between pain and QoL would be bidirectional. Moreover, extending previous research, a third exploratory goal was to examine whether the hypothesized bidirectional relationship between pain and QoL would be specific to satisfaction with physical- or psychological-health related QoL or observable across all three items and the total score.

Methods

Design

This study uses longitudinal data from the Inception Cohort of the Swiss Spinal Cord Injury Cohort Study (SwiSCI), prospectively collected between August 2013 and November 2021. The Inception Cohort of the SwiSCI collects somatic and psychological information among patients with SCI, hospitalized in the four SCI-specialized centres of Switzerland. The present study includes three measurement time points of the SwiSCI's Inception Cohort: 1-month post diagnosis (T1), 3-month post diagnosis (T2), and discharge (T3). SwiSCI was approved by the responsible regional ethics committees of the four participating SCI centres. Details on the study design and ethics approval are given elsewhere [23].

Participants

The sample of the presented study includes Swiss residents aged over 16 years who were admitted to initial rehabilitation in one of the four SCI-specialized centres after newly diagnosed traumatic or non-traumatic SCI. Excluded were persons with SCI due to congenital conditions (e.g., spina bifida), neurodegenerative disorders (e.g., multiple sclerosis), Guillain-Barré syndrome, and those in palliative care [24]. Furthermore, participants who filled in the SwiSCI questionnaires before 2015 were excluded because the pain measure used in the present study was introduced in 2015. Also, patients with a cancer diagnosis were excluded due to their specific pain experience and medication compared to the other participants. Finally, participants who did not fill in the questionnaire in at least two time points were excluded. Figure 1 presents the selection process leading to the final dataset of 381 individuals that completed at least two measurements.

Measures

To assess QoL, we used the International SCI QoL Basic Data Set (QoL-BDS), which was developed and validated for the use in individuals with SCI [25, 26]. Participants are asked to rate their satisfaction with life, with physical health, and with psychological health on an 11-point numeric rating scale from 0 = "completely dissatisfied" to 10 = "completely satisfied" over the past four weeks. For the *QoL total score*, a mean score ranging from 0 to 10 is calculated from the three single items, with a higher mean score indicating higher QoL. The QoL-BDS has shown good internal consistency, convergent, and divergent validity among individuals with SCI undergoing inpatient rehabilitation [27–29] as well as those living in the community [26, 28, 30, 31]. The QoL-BDS has also been found to have acceptable to good test–retest reliability across a two-week interval [28, 30] and replicability and responsiveness in the present study, the internal consistency of the scale was good at all time points (1 month: $\alpha = 0.81$, 3 month: $\alpha = 0.87$, discharge $\alpha = 0.88$).

Pain intensity was assessed with one item of the International SCI Basic Pain Dataset [32], which asks participants to report on past week's average pain intensity of their worst pain problem on a numeric scale ranging from 0 = "no pain" to 10 = "most unpleasant pain imaginable".

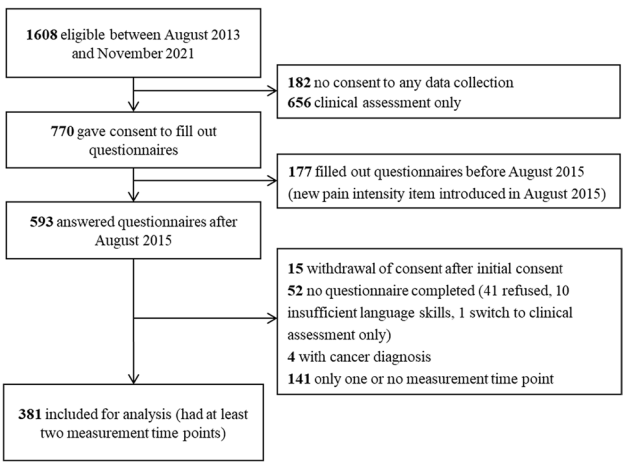

Fig. 1 Participants Flow Chart

Data analysis

Descriptive statistics were performed using STATA version 16 [33]. For categorical variables, number of participants and percentage were reported and mean, standard deviation (SD), median, interquartile range (IQR), skewness, and kurtosis were reported for continuous variables.

Cross-lagged panel models (CLPM) have been used for many years to estimate the reciprocal influences between two variables over time [20]. In a CLPM, three main paths are estimated (see Fig. 2 for graphical representation). First, auto-regressive (AR) paths over time are estimated for the two variables of interest, QoL and pain in our case. AR are regression paths predicting a variable at each time point by the same variable at the previous time point. It enables to account for the fact that the level of, for instance, QoL at a certain time point usually depends on the previous level of this QoL. Second, Co-Movement (CM) are estimated as the correlation between the two variables of interest at each time point. It enables to account for the impact of timely events (e.g., separation or job loss) on QoL and pain at a specific time point. Then, cross-lagged (CL) paths estimate the reciprocal associations between QoL and pain. CL are regression paths modeling the association between pain intensity scores at one time point and the QoL scores at the following time point, and vice versa.

Given that classic CLPMs do not account for time-invariant differences between individuals level of QoL or pain, Hamaker and colleagues proposed the Random Intercept CLPM (RI-CLPM) [20]. The RI-CLPM additionally estimates the impact of time-invariant inter-individual differences by adding (1) a latent variable loading on each time point of the first variable of interest (i.e., RI_{QoL}) that estimates all the time-invariant influences on that variable, (2) a similar latent variable for the second variable of interest (i.e., RI_{Pain}), and (3) a correlation path between these two latent variables (see RIs in Fig. 2). Indeed, these inter-individual differences needs to be accounted for, so that the CL paths relate exclusively to changes within individuals [19]. Otherwise, the AR paths would be inflated and the CL paths of interest would be biased. As asserted by Hamaker et al. once the impacts of past levels (AR paths), timely events (CM paths), and inter-individual differences (RI paths) are accounted for, CL paths will provide unbiased estimate of the reciprocal influences between QoL and pain [20].

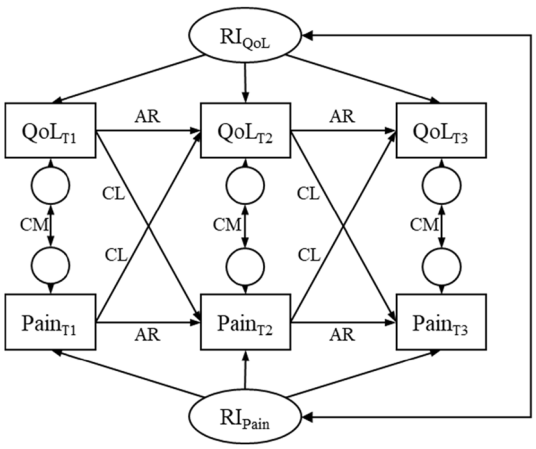

Fig. 2 Random Intercept Cross-lagged Panel Model *Note* Abbreviations: *QoL* quality of life' *AR* auto-regressive paths' *CM* co-movement paths' *CL* cross-lagged paths' *RI* random intercepts

In the present study four separate RI-CLPMs were computed: one for the QoL total score and one for each item of the QoL measure, i.e., satisfaction with life, physical-health, and psychological health separately. Both, traditional CLPMs and RI-CLPMs were estimated, but as expected RI-CLPMs showed better goodness of fit (see Supplementary Table S2). Thus, the following will only present the RI-CLPMs results.

Main analyses were performed using Mplus version 8 [34]. Missing data was addressed with full information maximum likelihood estimation [35]. For sensitivity analysis, models with complete cases (participants without any missing) were additionally run to detect potential bias due to missing values. All data and study analysis codes are available from the last author upon request.

Results

Characteristics of study participants are displayed in Table 1 and correlations between the QOL and pain variables are displayed in Table 2. Participants were predominantly male (75.1%) with an average age of 53.2 years. The most frequent type of SCI was incomplete paraplegia (52.3%) and about 60% experienced a traumatic SCI. On average, QoL slightly increased across time points, with a total score between 5.3 and 6.6 (range 0–10). Satisfaction with physical health at 1 month showed the lowest mean score (4.4, SD = 2.6) and satisfaction with psychological health at discharge had the highest score (7.0, SD = 2.4) of the QoL subscales. Mean pain intensity did not change across time points, i.e., 1 month: 2.7 (SD = 2.3), 3 months: 2.6 (SD = 2.4), and discharge: 2.7 (SD = 2.5). Non-responder analysis indicated that females, older persons, and individuals with complete tetraplegia were slightly underrepresented in the sample (Supplementary Table S1).

Results of the four RI-CLPMs testing the reciprocal association between pain intensity and QoL are presented in Table 3 and Fig. 3. They showed no significant cross-lagged associations between QoL total score or the QoL items and pain intensity across time points, therefore confirming our hypothesis and indicating that a person's change in QoL was

Table 1 Descriptive statistics ($N = 381$)

Variables (missing values in %)	*n* (%)	Mean (SD)	Median (IQR)	Skewness	Kurtosis
Male gender (0)	286 (75.1)				
Age at injury in years (0)		53.2 (16.7)	55 (42–67)		
Lesion severity (2.6)					
Incomplete paraplegia	194 (52.3)				
Complete paraplegia	53 (14.3)				
Incomplete tetraplegia	114 (30.7)				
Complete tetraplegia	10 (2.7)				
Traumatic etiology (0)	230 (60.4)				
QoL total score					
T1 (32.3)		5.3 (2.7)	5.3 (3.7–7.0)	−0.02	2.40
T2 (28.6)		5.9 (2.3)	6.0 (4.3–7.7)	−0.46	2.82
T3 (8.1)		6.6 (2.0)	6.7 (5.3–8.0)	−0.74	3.55
Satisfaction with life					
T1 (32.3)		5.3 (2.7)	5 (3–7)	−0.06	2.18
T2 (23.6)		5.7 (2.6)	6 (4–8)	−0.30	2.36
T3 (4.5)		6.5 (2.3)	7 (5–8)	−0.63	3.01
Satisfaction with physical health					
T1 (32.3)		4.4 (2.6)	4 (2–6)	0.27	2.44
T2 (24.2)		5.1 (2.7)	5 (3–7)	−0.15	2.17
T3 (4.5)		5.9 (2.4)	6 (5–8)	−0.56	2.88
Satisfaction with psychological health					
T1 (32.8)		6.4 (2.5)	7 (5–8)	−0.42	2.44
T2 (23.9)		6.3 (2.6)	7 (4–8)	−0.45	2.31
T3 (5.0)		7.0 (2.4)	7 (5–9)	−0.79	3.09
Pain intensity					
T1 (33.6)		2.7 (2.3)	3 (0–4)	0.41	2.33
T2 (23.1)		2.6 (2.4)	3 (0–5)	0.41	2.09
T3 (4.5)		2.7 (2.5)	3 (0–5)	0.42	2.09

QoL Quality of life, *SD* standard deviation, *IQR* interquartile-range

not associated with his or her pain intensity at a following time point, and vice versa a person's change in pain intensity did not influence his or her QoL at a following time point (Fig. 3).

Further, the analysis revealed several significant AR paths indicating how past levels of pain or QoL influence their own future score. We observed that the intensity of pain reported at T2 significantly influenced pain intensity experienced at T3. For QoL, significant autoregressive paths were observed for satisfaction with physical health (between T1 and T2 as well as between T2 and T3) and for QoL total scores (between T2 and T3).

Results from sensitivity analysis comparing presented results with findings from complete case analysis showed the same findings in all models (Table S3).

Discussion

This is the first longitudinal study that used cross-lagged analysis to investigate the directionality of associations between QoL and pain intensity during initial SCI rehabilitation. The hypothesis of bidirectionality between pain and QoL was not supported. There were no significant cross-lagged associations between pain intensity and QoL across time points, indicating that a person's change in QoL was not related to a person's pain intensity at a previous time point, and vice versa. This may seem to contrast with previous findings indicating that pain at the beginning of the inpatient rehabilitation predicts the course of quality

Table 2 Spearman correlation coefficients between quality of life (QoL) total score, QoL subscales, and pain intensity (N = 381)

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. T1 QoL—total score	–														
2. T2 QoL—total score	0.566	–													
3. T3 QoL—total score	0.570	0.643	–												
4. T1 QoL—Life	0.895	0.465	0.481	–											
5. T2 QoL—Life	0.521	0.919	0.610	0.444	–										
6. T3 QoL—Life	0.543	0.566	0.901	0.480	0.554	–									
7. T1 QoL—Phys	0.863	0.513	0.479	0.693	0.470	0.450	–								
8. T2 QoL—Phys	0.529	0.882	0.555	0.425	0.732	0.493	0.555	–							
9. T3 QoL—Phys	0.480	0.576	0.894	0.406	0.530	0.719	0.446	0.550	–						
10. T1 QoL—Psy	0.821	0.485	0.513	0.604	0.432	0.471	0.531	0.384	0.387	–					
11. T2 QoL—Psy	0.465	0.876	0.557	0.376	0.729	0.468	0.344	0.623	0.461	0.485	–				
12. T3 QoL—Psy	0.512	0.587	0.894	0.410	0.557	0.714	0.394	0.450	0.682	0.522	0.566	–			
13. T1 Pain intensity	−0.172	−0.182	−0.120	−0.143	−0.135	−0.097	−0.115	−0.174	−0.086	−0.186	−0.177	−0.138	–		
14. T2 Pain intensity	−0.111	−0.163	−0.128	−0.072	−0.089	−0.075	−0.076	−0.181	−0.115	−0.140	−0.165	−0.151	0.459	–	
15. T3 Pain intensity	−0.123	−0.144	−0.166	−0.128	−0.125	−0.104	−0.044	−0.110	−0.175	−0.146	−0.151	−0.164	0.505	0.596	–

QoL Quality of life, *Life* Satisfaction with life, *Phys* Satisfaction with physical health, *Psy* Satisfaction with psychological health

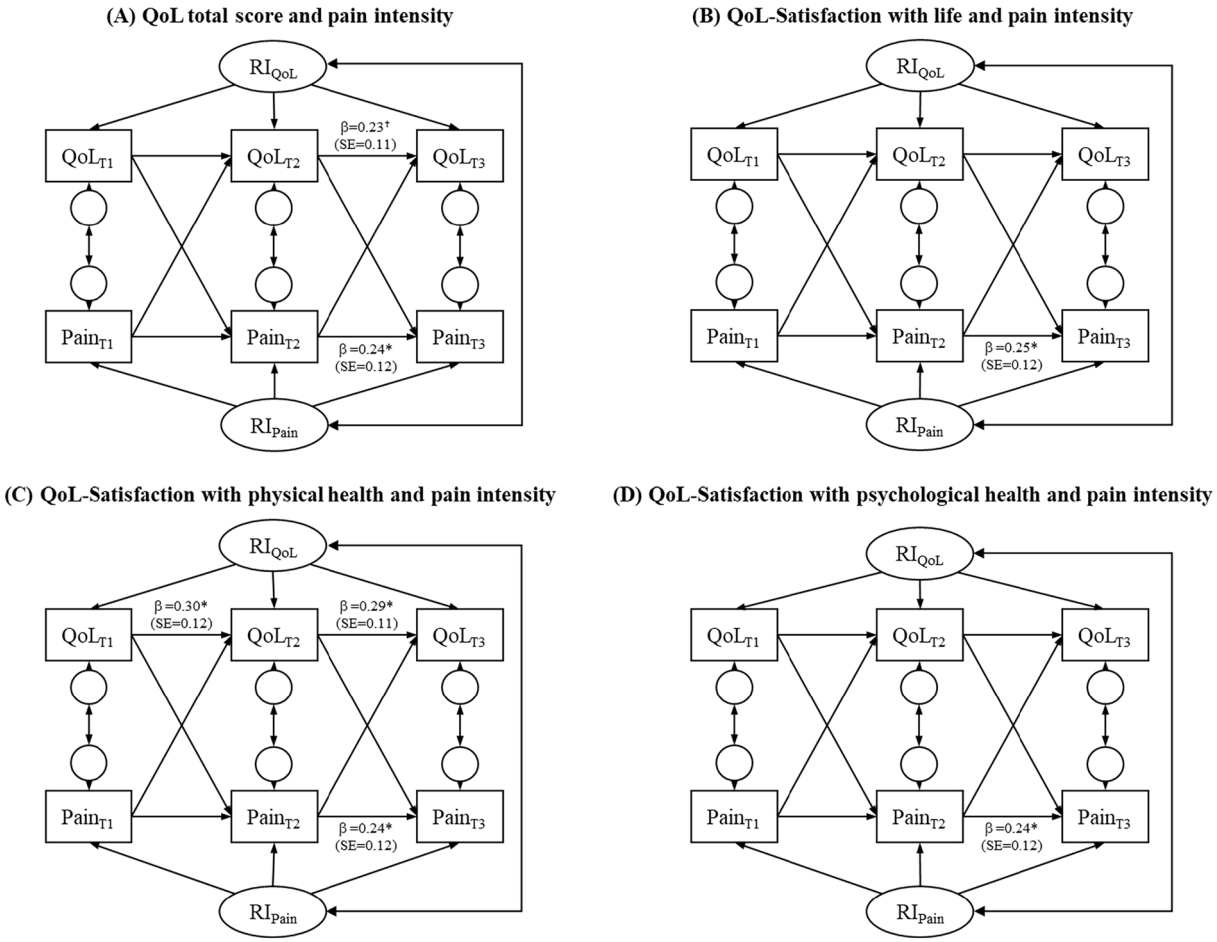

Fig. 3 Random Intercept Cross-lagged Panel Models Estimating the Longitudinal Association between Pain Intensity and QoL *Note* Standardized results of the random intercept cross-lagged panel models estimate the longitudinal association between pain intensity and the four measures of QoL: **A** QoL total score, **B** QoL-Satisfaction with life, **C** QoL-Satisfaction with physical health, and **D** QoL-Satisfaction with psychological health. Coefficients are indicated only for the significant paths (†$p \leq .10$, *$p \leq 0.05$). Abbreviations: *QoL* quality of life, *T1* 1 month post diagnosis, *T2* 3 months post diagnosis, *T3* discharge

of life, operationalized in terms of life satisfaction [8, 10]. However, such studies did not take into account stable inter-individual differences (captured by random intercepts in RI-CLPM) or controlled for the impact of timely events (via observation of co-movement in RI-CLPM). Indeed, inter-individual differences such as personality traits can explain the correlation between QoL and pain observed in other studies. For instance, individuals with high neuroticism tend to experience lower QoL and more pain, while individuals with low neuroticism experience higher QoL and less pain [36, 37]. Similarly, timely event could explain a correlation between QoL and pain. For instance, the discharge from inpatient rehabilitation and return to the community living might simultaneously negatively influence QoL and pain of individuals with SCI as their access to care becomes more limited.

The absence of significant bidirectional effects in the present study converges with the longitudinal findings of a Scandinavian study that found no significant interinfluence of pain and QoL [11]. Using regressions, this study showed that change in pain intensity was not a significant predictor of change in QoL and that change in QoL was not a significant predictor of change in pain intensity. Importantly, changes in the extent to which pain interferes with general activity, mobility and work significantly influenced changes in QoL [11]. Overall, findings highlight the importance of investigating external and internal compensatory factors that may mitigate the impact of pain on QoL. Pain may be better controlled in the inpatient setting as patients have better access to medication (not measured in the current study), physical therapy and psychotherapy, and the environment is designed to be accessible, minimizing barriers to participation. Studies of community-dwelling individuals with SCI suggest that pain negatively affects QoL by restricting participation [2, 38–40] and that pain interference is a more robust predictor of QoL than pain intensity and pain type

Table 3 Autoregressive and cross-lagged associations between QoL and pain intensity: standardized coefficients (β), unstandardized coefficients (B), and standard error (SE) from random intercept cross-lagged panel model ($N = 381$)

	Autoregressive paths				Cross-lagged paths		
	β	B	SE		β	B	SE
QoL total score and pain intensity							
$QoL_{T1} \rightarrow QoL_{T2}$	0.11	0.11	0.14	$QoL_{T1} \rightarrow Pain_{T2}$	0.01	0.01	0.14
$QoL_{T2} \rightarrow QoL_{T3}$	***0.23***	***0.18***	***0.11***	$QoL_{T2} \rightarrow Pain_{T3}$	−0.05	−0.06	0.11
$Pain_{T1} \rightarrow Pain_{T2}$	0.07	0.08	0.20	$Pain_{T1} \rightarrow QoL_{T2}$	−0.20	−0.21	0.14
$Pain_{T2} \rightarrow Pain_{T3}$	**0.24**	**0.27**	**0.12**	$Pain_{T2} \rightarrow QoL_{T3}$	−0.01	−0.01	0.09
QoL-Satisfaction with life and pain intensity							
$QoL_{T1} \rightarrow QoL_{T2}$	0.04	0.04	0.11	$QoL_{T1} \rightarrow Pain_{T2}$	0.09	0.07	0.10
$QoL_{T2} \rightarrow QoL_{T3}$	0.10	0.08	0.11	$QoL_{T2} \rightarrow Pain_{T3}$	−0.05	−0.05	0.09
$Pain_{T1} \rightarrow Pain_{T2}$	0.08	0.09	0.20	$Pain_{T1} \rightarrow QoL_{T2}$	−0.08	−0.10	0.16
$Pain_{T2} \rightarrow Pain_{T3}$	**0.25**	**0.28**	**0.12**	$Pain_{T2} \rightarrow QoL_{T3}$	0.08	0.07	0.11
QoL-Satisfaction with physical health and pain intensity							
$QoL_{T1} \rightarrow QoL_{T2}$	**0.30**	**0.31**	**0.12**	$QoL_{T1} \rightarrow Pain_{T2}$	−0.11	−0.09	0.09
$QoL_{T2} \rightarrow QoL_{T3}$	**0.29**	**0.24**	**0.11**	$QoL_{T2} \rightarrow Pain_{T3}$	−0.10	−0.08	0.07
$Pain_{T1} \rightarrow Pain_{T2}$	0.09	0.10	0.19	$Pain_{T1} \rightarrow QoL_{T2}$	−0.24	−0.33	0.14
$Pain_{T2} \rightarrow Pain_{T3}$	**0.24**	**0.27**	**0.12**	$Pain_{T2} \rightarrow QoL_{T3}$	−0.09	−0.09	0.10
QoL-Satisfaction with psychological health and pain intensity							
$QoL_{T1} \rightarrow QoL_{T2}$	0.01	0.02	0.14	$QoL_{T1} \rightarrow Pain_{T2}$	−0.04	−0.04	0.13
$QoL_{T2} \rightarrow QoL_{T3}$	0.14	0.12	0.11	$QoL_{T2} \rightarrow Pain_{T3}$	−0.03	−0.03	0.09
$Pain_{T1} \rightarrow Pain_{T2}$	0.06	0.06	0.20	$Pain_{T1} \rightarrow QoL_{T2}$	−0.08	−0.09	0.16
$Pain_{T2} \rightarrow Pain_{T3}$	**0.24**	**0.27**	**0.12**	$Pain_{T2} \rightarrow QoL_{T3}$	−0.02	−0.02	0.11

Bold (p-value < 0.05) and italic (p-value < 0.10) results highlight significant findings

Abbreviations: *QoL* quality of life, *Life* satisfaction with life, *Phys* satisfaction with physical health, *Psy* satisfaction with psychological health

[11, 41]. Thus, more longitudinal studies in the context of clinical rehabilitation that focus on pain interference are needed to obtain a better understanding of the relationship between pain and QoL.

Consistent with previous longitudinal studies that have measured QoL in individuals during first rehabilitation [11, 40], we observed an average improvement of QoL over time. For example, a recent international longitudinal study that also used the BDI-QoL found that scores on 'life as a whole', 'physical health' and the total scale significantly increased from inpatient rehabilitation to 12-month follow among individuals with recent onset of spinal cord injury or disease (SCI/SCD) [42]. Similarly, in the present study, both item and total scores increased over time, and the increase was highest for total QoL.

Our results indicate that participants reported relatively low levels of pain intensity and that they remained rather stable through time. Pain stability was also observed in a recent cohort study from the Netherlands that found only a small decrease of pain intensity between admission and discharge from inpatient rehabilitation [43]. The finding that there were no important changes in pain intensity scores over the course of inpatient rehabilitation contrasts with two longitudinal studies that reported a decrease in pain intensity from admission to discharge [44, 45]. The relatively low level of pain observed in our sample might be due to its sampling. Patients were not included in the study if their physicians considered that their physical or mental condition were too poor. Moreover, individuals with especially poor mental or physical health are known to turn down survey participation [46, 47] and individuals with tetraplegia were slightly underrepresented in our sample. Therefore, individuals with especially high pain were unlikely to be included in the present study.

The current study is subject to several limitations. First, a common problem with longitudinal studies is that changes in variables observed at different time points might be due to measurement error rather than reflecting real changes in the outcome variable. For example, changes in personal standards for what constitutes satisfactory QoL following SCI may lead individuals to recalibrate their perceptions of QoL. This response shift can introduce bias, as individuals may interpret and respond to measurement items differently over time [48]. Similarly, changes in the perception and evaluation of pain over time and difficulty recalling past pain episodes may lead to bias in the longitudinal measurement of pain intensity. A related source of bias is fluctuations in pain intensity due to external conditions and mode of assessment (e.g., pain intensity ratings may be different if assessed during or after physical

therapy or in the context of a clinician administered interview compared to self-report) [49].

Second, the small sample size precluded more complex analyses testing for example gender and age differences (i.e., RI-CLPM multi-group comparison). Cross-sectional research indicates that women tend to report more pain compared to men as part of their experience of aging with SCI, highlighting the importance of considering gender and age as a covariate over time [50]. Future studies using larger sample sizes would be needed to differentiate reciprocal associations for different sub-groups. Third, the generalizability of findings from unadjusted analyses might be limited as females, older persons, and individuals with complete tetraplegia were slightly underrepresented in our sample. Finally, it remains unknown if study participation was associated with QoL or pain, or with important variables that were not included in the present study, such as mental health.

Notwithstanding these limitations, the study has multiple methodological strengths that enhance its contributions to the literature on the pain-QoL relationship in SCI. First, it uses a statistical methodology uniquely suited for testing the temporal relationship between pain as a predictor of subsequent QoL, and of QoL as a predictor of subsequent pain while controlling for individual differences and temporal stability of pain and QoL. Second, it uses longitudinal prospective data from a well-defined sample, drawn from the Inception Cohort of the Swiss Spinal Cord Injury Cohort Study (SwiSCI). Third, it uses a measure of QoL that has been validated in individuals with SCI and captures subjective QoL as opposed to imposing a narrower operationalization of QoL such as health-related QoL.

The study's findings have clinical implications. The absence of significant cross-lagged effect indicates that changes in pain are primarily due to individual differences in their own previous scores of pain intensity (auto-regressive paths) suggest that pain interventions may be most effective if administered as early as possible post injury. Similarly, the observation that QoL is also strongly influenced by previous level of QoL points to the benefits of addressing low QoL early in the rehabilitation process. The lack of a bidirectional association in the present study draws attention to the possibility that QoL may evolve independently of pain during this early inpatient stage. In a sense, this finding brings hope for individuals living with SCI and high pain intensity because it implies that they might still experience high QoL. Awareness of this possibility could encourage rehabilitation staff to reflect on assumptions they may hold about the relationship between pain and QoL in SCI that might inadvertently influence their patients' own expectations of QoL after SCI. Qualitative research would be needed to explore beliefs of rehabilitation professionals regarding the pain-QoL link in SCI and examine their potential impact on SCI patients' levels of hope and pessimism regarding the impact of pain on their QoL.

Conclusion

This is the first longitudinal study that used cross-lagged analysis to investigate the directionality of associations between QoL and pain intensity during initial SCI rehabilitation. Controlling for inter-individual differences in and co-movement of pain and QoL, the study showed that pain intensity does not contribute to lower QoL at a later time or vice versa during the inpatient stay. This suggests that longitudinal associations between pain intensity and QoL reported by others may be attributable to personality traits or timely event impacting simultaneously pain and QoL scores. Future longitudinal studies that examine potential compensating factors and a pain interference may inform efforts to increase the well-being of individuals with SCI during the inpatient stay and afterward.

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Data availability Owing to our commitment to SwiSCI study participants and their privacy, datasets generated during the current study are not made publicly available but can be provided by the SwiSCI Study Center based on reasonable request (contact@swisci.ch).

Code availability The analyses' syntax is available from the last author, Anke Scheel-Sailer, upon request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval Ethical approval was granted by the Ethics Committee of Northwest- and Central Switzerland (EKNZ, Project-ID: 11042 PB_2016-02608, approved December 2016). We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed over the course of this research.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Not applicable.

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