Ambulation Prediction After Spinal Cord Injury: What Have We Learned In The Past 10 Years?

November 21st, 2021

Wesley Thornton, PT, DPT, NCS; Rachael Fuller, BA; Sara Hobbs, PT, DPT, NCS; Jeffrey Berliner, DO; Candace Tefertiller, PT, DPT, NCS, PhD; Andrew C. Smith, PT, DPT, PhD

Introduction:

There is a recognized need for accurate and available prognostic variables to determine potential for recovery of ambulation after a person has a sustained a spinal cord injury (SCI). A number of variables hold predictive relationships with ambulation potential after SCI, including time required for surgical decompression,[1] sex assigned at birth,[2] age,[3-5] severity of injury,[3,5-8] American Spinal Injury Association Impairment Scale (AIS),[3,5,8,10,] and lower extremity motor return as assessed by International Standard for the Classification of Spinal Cord Injury (ISNCSCI) examination.[7,11-14] Questions remain about how to best predict functional walking recovery after SCI in the clinical setting. Improving accurate prediction of ambulation would facilitate tailored and individualized therapy protocols for each patient. This knowledge can also aid in anticipating equipment needs, level of attendant care, and potential home modifications upon discharge from rehabilitation and into the future.

Studies that group predictive variables for ambulation post-SCI have been published.[5,15] In 2011, a study from van Middendorp, et al (researchers in Europe) created a clinical prediction rule (CPR) for ambulation prognosis in SCI.[16] This study not only combined many of the reported variables into one CPR, but also used an established SCI outcome measure (Spinal Cord Independence Measure) to define independent ambulation.[16]

For the past decade, much of the research on ambulation prognosis after SCI has been focused on the study and refinement of the van Middendorp-based CPR.[17-22] It is valuable to evaluate clinicians' current ability to predict functional walking by assessing data from the last 10 years since the CPR has been available. (2011 to 2021).

The purpose of this narrative review is to summarize the current state of ambulation prognosis after SCI to inform physical therapist practice.

Objectives:

1. Describe the understanding of the potential to predict ambulation potential following SCI prior to 2011.
2. Describe the current state of the research within the past 10 years (2011-2021) in the prediction of ambulation potential following SCI.
3. Describe contributions that advanced imaging may provide in understanding ambulation potential after SCI.

Target Audience
The primary target audience for this *Current State of the Research* paper is physical therapists and other clinicians working with individuals who have sustained spinal cord injury.

Brief Summary:
Determining functional ambulation prognosis following SCI is a difficult task for clinicians.[23] Previously published literature focused on 1-2 variables to determine which patients may ambulate again, but these studies did not exhaustively capture characteristics that would make a return to walking most likely.[3-9,11-15,24-30] In 2011, a CPR was created that aimed to help clinicians determine ambulation prognosis.[16] For the past ten years this CPR has been both accepted and challenged.[17-22] Recent research suggests that while it is useful, it lacks the optimal capability to predict return to ambulation for those individuals in the middle of the injury severity spectrum (i.e. AIS B and C).[20-21] In our opinion, there is presently no best single measure that can optimally be used for post-SCI ambulation prognosis. Physical therapists working with this patient population will need to continue to rely on multiple prognostic tools (old and new), interdisciplinary communication, and clinical judgement to determine if functional walking is a realistic outcome.

Objective 1: Describe understanding of ambulation potential following SCI up to 2011.

Findings prior to 2011:

Prior to 2011, there was a commonality across studies regarding variables that were most likely to predict a return to walking post-SCI. Below is a review of those variables.

Age:
The older an individual is at the time of sustaining a spinal cord injury, the less likely they are to return to walking.[3-5] Previous research reported that increased age not only negatively impacted one's chances of functional recovery, but also long-term survival post-injury.[25-26,28] When compared to younger people who have similar motor/sensory presentation, the older SCI population tends to have less functional motor return.[3,5,25,28] This includes the likelihood of ambulation recovery.[3-5]

While aging has consistently been found to be a barrier to optimal functional gains post-SCI, the cut-off age for decreased success is not agreed upon. The 2011 CPR used 65 years as a marker,[16] but earlier studies focused on 50 years as the point where age became a negative prognostic factor for a return to walking.[3,5] This discrepancy, along with the knowledge that each SCI and each individual is different, is a reminder that age alone does not determine ambulation prognosis. Future research in this area is certainly warranted.

Spared Sensation Type:
Of the 5 variables making up the 2011 CPR, two of them focus on the sparing of light touch for predicting walking recovery (see Figure 1).[16] Prior to 2011, however, the sparing of pin-prick sensation was associated with a greater prognosis for functional motor return.[9,14,30] This is theoretically due to the anatomical proximity of the lateral spinothalamic and corticospinal tracts.[9] Research on individuals with motor complete/sensory incomplete injuries demonstrated an increased likelihood of a return to walking within a year if sacral and lower extremity pinprick sensation was preserved one-month post-injury.[9,14,30] Clinicians should be aware that the absence of pinprick sensation could be an indicator for limited long-term motor return.

Motor Complete vs Motor Incomplete:
This section is not simply an acknowledgment of the chance of returning to ambulation based on Frankel or AIS classification.[3,5,8-10] It also includes research focusing on specific characteristics that both signal a greater chance of return to walking and place an individual into the "motor incomplete" category. The most prominent of these characteristics is lower extremity motor return.

Studies vary on the amount of motor return required to indicate a positive independent walking prognosis. Lower extremity motor scores (LEMS) ranging from 10-30, (lower scores associated with return to walking requiring assistive devices/orthotics and higher scores associated with independent community ambulation) were found to be impactful in determining who is going to walk again.[7,13-14] Additional findings suggest that knee extension and/or hip flexor strength ≥2/5 (one study 3/5) within two months from time of injury improve chances of walking within a year.[7,11-12]

While it makes sense that increased lower extremity motor return indicates a greater chance of return to walking, these early studies differed on the optimal timepoint for predictive baseline testing. Within these studies, baseline testing used to predict ambulation potential occurred from 72 hours to 6+ months after the initial SCI.[7,11-14]

Injury Classification:

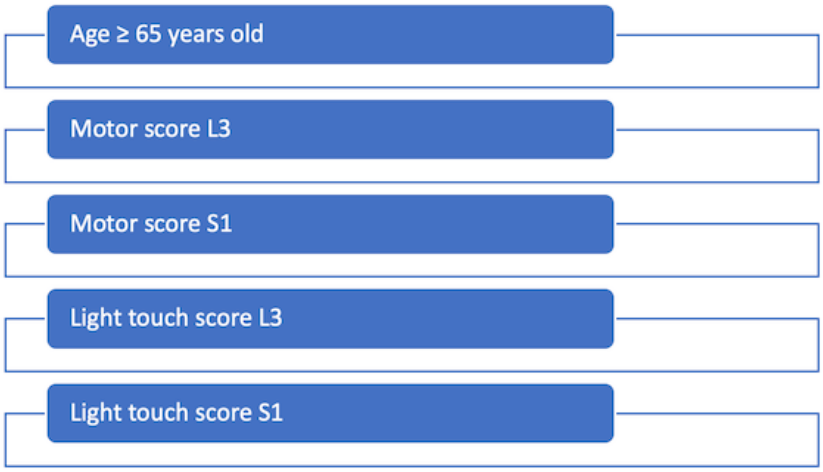
Both anatomical level of injury and injury severity as ambulation predictors were reported prior to 2011.[3,5-8] Studies found that injury levels above T9 in individuals with complete paraplegia are a poor prognosis for return to walking.[6] Complete injuries at T12 and below, as well as incomplete cervical injuries improved chances of ambulation.[3,6-7] Regarding injury severity, several retrospective studies showed the less severe the initial injury classification, the greater the chance of walking 1 year post SCI.[3,5,8]

While some individuals' injury classifications convert from motor complete to motor incomplete status (i.e. AIS A/B to AIS C/D), conversion-to-motor-incomplete as a sole variable is not a strong predictor for a return to functional ambulation.[31-33]

Highlighted in this prior research, that is still an important issue today, is the difficulty in predicting ambulation recovery for patients with tetraplegia classified with an AIS C injury.[3,5] These studies suggest that with this patient subgroup, one should not only consider injury severity, but include other predictive factors such as age and rehabilitation start time.[3,5] Indeed, individuals with AIS C injuries often do not return to walking by discharge from acute inpatient rehabilitation with same success rate as patients with AIS D injuries.[5]

In summary, prior to 2011, work was done to determine building blocks for predicting a return to walking post-SCI. It became evident that key variables exist to determine if someone is going to walk again. In 2011, the van Middendorp CPR (Figure 1) concluded that optimal variables for prediction included age, lower extremity motor scores (L3 and S1), and lower extremity light touch sensation (L3 and S1).[16]

Figure 1: CPR variables for Ambulation Prognosis after traumatic SCI (adapted from Van Middendorp 2011)[16]



Were these findings accurate? Was the van Middendorp CPR useful in improving clinicians' confidence with ambulation prognostication post-SCI?

Objective 2: Describe the current state of the research within the past 10 years (2011 – 2021) in ambulation potential following SCI.

Findings after 2011:

Some studies post-2011 continued to look at specific predictive variables such as age or pin-prick sensation.[33-34] Many studies, however, focused solely on prognostic variables for a return to ambulation centered around either validating or simplifying the 2011 CPR.[17-22]

Validation:

Between 2013 and 2020, multiple studies looked to validate the 2011 CPR. Researchers in the United States, Canada, and Australia attempted to assess the predictive success of the van Middendorp European study by applying it to their own cohorts.[17-21] While some researchers found the CPR to be generalizable in North America, others found discrepancies.[17-21]

In 2016, an Australian research group found similarities between their data and the findings from the European team in 2011.[18] They also found other variables of significance, including severity of injury and length of stay in the ICU. Notably, when removing the data from individuals who died before discharge, this team found that older patients were able to walk again at an even higher rate than younger individuals. These authors suggested further investigation of the 2011 CPR model.[18]

In 2019, the van Middendorp CPR was used to predict walking in individuals with non-traumatic SCI.[19] Studies from 2001 suggested that those with non-traumatic injuries recover function similar to, but not as robust as those individuals with traumatic SCI.[35] When using the CPR as a prognostic tool, this group concluded that the CPR succeeded in predicting ***who would not*** walk following non-traumatic SCI but showed limited accuracy in predicting those who ***would*** walk, particularly those with motor incomplete injury.[19] These findings indicate potential problems in applying the van Middendorp CPR across injury etiologies.

Interesting findings came from two studies in 2019 and 2020 that demonstrated limited predictive accuracy of the van Middendorp CPR when considering the middle AIS classifications.[20-21] Specifically, the van Middendorp CPR demonstrated reduced ability to predict walking for individuals with AIS B or C severities in comparison to those with AIS A or D. This can be viewed as disappointing, given the idea that an optimal prognostic tool should have the greatest clinical utility predicting future ambulation status for AIS B and C levels of severity, as it is in this mid-severity group that outcome is most unclear. One of these studies also reported reduced accuracy with prognosis prediction for older individuals and suggested dropping the age from 65 to 50 years old.[21]

Simplification:

In 2017, amidst other validation studies,[17-21] Hicks, et al attempted to simplify the 5 variable CPR by consolidating into 3 variables (Age, L3 motor, and S1 light touch).[22] Statistical analyses revealed that this model demonstrated similar psychometric properties to the 2011 study, despite using a different outcome measure (Functional Independence Measure vs SCIM). Nevertheless, while creating a more simplified tool for clinicians, the paring down of the 2011 CPR did not address its limited predictive ability with AIS B and C injuries.

Defining "independent ambulation":

The Hicks CPR also highlights another concern regarding walking prognosis. The use of the Functional Independence measure (FIM) as opposed to the SCIM, while valid, creates obscurity in defining independent ambulation. The simplified Hicks CPR focused on level of assistance (e.g. Modified Independence and Complete Independence) to define successful ambulation recovery, but also included those that use a wheelchair part-time.[22] The van Middendorp study focused primarily on independence with indoor ambulation but one major critique is that they included a 4/8 on the indoor mobility portion of the SCIM in their definition of independent walking, which is arguably not functional in the community (*Walks with a walking frame or crutches (swing)*).[16] Perhaps the most ideal way to define independent ambulation is found in a paper published in 2021 where the authors chose item 14 on the SCIM (outdoor mobility > 100 meters) at one-year after SCI.[36] This group used a cutoff score of 6 or greater (walking with one cane, leg orthosis only, or walking without assistive devices) and found L3 and L5 motor + S1 light touch as optimal predictors.[36] Indeed, the lack of clarity in a consistent definition of independent ambulation highlights potential issues in clinical implementation of these CPR tools.

Naturally, research has led to more questions when it comes to SCI walking prognosis. While having tools at a clinicians' exposure may assist in the process of predicting future walking, clinicians must also use their clinical judgement.[23] This is especially true for those individuals with sensory complete injuries that likely have more potential than these original and modified CPRs suggest, as well as those individuals with motor incomplete injuries who have other factors impeding their ability to return to walking despite substantially recovered lower extremity motor function. It is also worthwhile exploring other avenues that might help the healthcare

team identify the potential for spinal cord injury walking recovery. Thus, this paper also aims to summarize imaging findings that may be useful for prognosis.

Objective 3: Describe contributions that imaging may provide in understanding ambulation potential after SCI.

Findings prior to 2011:

Throughout the 1990s and 2000s, analysis of MR (magnetic resonance) imaging was (and continues to be) a promising means for assessing extent of SCI and predicting who might walk again after SCI.[37-41] Qualitatively, the presence of hemorrhage and edema involved with the SCI are observed using MRI.[39] Spinal stenosis and cord compression were established as quantitative measures of the extent of spinal cord injury.[40] Hemorrhage, length of edema, stenosis and canal compromise were indicated as predictive of worse recovery outcomes and decreased chance of ISNCSCI conversion.[37-41] Most importantly, while few studies used these variables to predict who might walk after SCI, they established these measures as reliable, and set the stage for future research.

Findings after 2011:

Researchers advocate for using MR imaging as a first-line due to its high sensitivity in providing canal dimensions as well as visualization of soft-tissue components within the spinal canal.[42] Developments in MRI-based prognostication of walking between 2011 and 2021 confirm this conclusion. Studies assessed ligament damage, gray matter atrophy, and examined implications of midsagittal tissue bridges (thought to be a proxy for axonal sparing).[43-47] Ligamentum Flavum damage and intramedullary edema correlated to poor recovery at follow up,[45] and midsagittal tissue bridge width was predictive of walking ability one-year after injury.[48] Researchers calculated spinal cord damage ratios to measure extent of damage and reported on Diffusion Tensor Imaging (DTI) to assess the microstructural neurodegeneration within cord tissue.[49-54] Smaller damage ratios correlated with greater walking ability and DTI was a strong predictor of AIS classification and walking ability.[49-54] Additionally, a new SCI rating system (specific to MRI) called the BASIC score was developed and found to be correlated with walking ability after SCI.[48,55] Open-source software, the Spinal Cord Toolbox, was developed to help standardize spinal cord imaging and this program allows for template-based analyses.[56,57] This approach can provide estimates of specific areas of spinal cord damage, and damage to the lateral corticospinal tract has shown promise in predicting future motor deficits.[50,58]

There have been significant advancements in MR imaging and its application specific to ambulation prediction. Clinicians can use these quantitative and qualitative MRI measurements along with their published reference values to guide their clinical judgment and provide additional evidence to support their clinical decisions. Clinicians should be aware, however, that MRI will likely not add much more prognostic value as compared to the strongest predictors such as baseline lower extremity motor scores.[48]

Conclusion

Over the past ten years, progress has been made on various fronts to help clinicians better predict who will walk again after sustaining a spinal cord injury. This work continues to revolve around the development of predictive algorithms.[31,33-34,59-60] However, limitations within studies and lack of consensus continue to result in clinicians relying on an incomplete picture when considering ambulation prognosis.

The difficulty with the CPRs above are their limited ability to successfully predict ambulation for those individuals with SCI who are not on the outer boundaries of the severity spectrum. For example, ambulation prognosis continues to be a challenge for an individual with an acute AIS B who has pinprick sensation below the level of injury, or a patient with an acute AIS C injury who has limited lower extremity motor return. Further, a gap in the literature exists on the role that intervention plays in facilitating the potential for return to ambulation in the acute/subacute phase of SCI (i.e. locomotor training timing, type, dosage, duration), especially for this mid-severity group.

Hopefully, ongoing and future research will continue to improve our ability to predict walking recovery after spinal cord injury. However, in our opinion, there is presently no best single measure that can optimally be used for post-SCI ambulation prognosis. Physical therapists working with this patient population will need to continue to rely on multiple prognostic tools (old and new), interdisciplinary communication, and clinical judgement to determine if functional walking is a realistic outcome.

References:

1. Ahuja, Christopher S., Jetan H. Badhiwala, and Michael G. Fehlings. ""Time is spine": the importance of early intervention for traumatic spinal cord injury." Spinal cord 58.9 (2020): 1037-1039.
2. Scivoletto, G., B. Morganti, and M. Molinari, Sex-related differences of rehabilitation outcomes of spinal cord lesion patients. Clin Rehabil, 2004.18(6): p. 709-13.
3. Burns, S.P., et al., Recovery of ambulation in motor-incomplete tetraplegia. Arch Phys Med Rehabil, 1997. 78(11): p. 1169-72.
4. Scivoletto, G., et al., Effects on age on spinal cord lesion patients' rehabilitation. Spinal Cord, 2003. 41(8): p. 457-64.
5. Kay, E.D., A. Deutsch, and L.A. Wuermser, Predicting walking at discharge from inpatient rehabilitation after a traumatic spinal cord injury. Arch Phys Med Rehabil, 2007. 88(6): p. 745-50.
6. Waters, R.L., et al., Recovery following complete paraplegia. Arch Phys Med Rehabil, 1992. 73(9): p. 784-9.
7. Waters, R.L., et al., Motor and sensory recovery following incomplete paraplegia. Arch Phys Med Rehabil, 1994. 75(1): p. 67-72.
8. Scivoletto, G., B. Morganti, and M. Molinari, Neurologic recovery of spinal cord injury patients in Italy. Arch Phys Med Rehabil, 2004. 85(3): p. 485-9.
9. Crozier, K.S., et al., Spinal cord injury: prognosis for ambulation based on sensory examination in patients who are initially motor complete. Arch Phys Med Rehabil, 1991. 72(2): p. 119-21.
10. Kirshblum, S.C. and K.C. O'Connor, Predicting neurologic recovery in traumatic cervical spinal cord injury. Arch Phys Med Rehabil, 1998. 79(11): p. 1456-66.
11. Crozier, K.S., et al., Spinal cord injury: prognosis for ambulation based on quadriceps recovery. Paraplegia, 1992. 30(11): p. 762-7.
12. Waters, R.L., et al., Motor and sensory recovery following complete tetraplegia. Arch Phys Med Rehabil, 1993. 74(3): p. 242-7.
13. Waters, R.L., et al., Prediction of ambulatory performance based on motor scores derived from standards of the American Spinal Injury Association. Arch Phys Med Rehabil, 1994. 75(7): p. 756-60.
14. Gittler MS, McKinley WO, Stiens SA, Groah SL, Kirshblum SC. Spinal cord injury medicine. Rehabilitation outcomes. Arch Phys Med Rehabil 2002; 83(3 Suppl 1): S65-71, S90-.
15. Zorner, B., et al., Clinical algorithm for improved prediction of ambulation and patient stratification after incomplete spinal cord injury. J Neurotrauma, 2010. 27(1): p. 241-52.
16. van Middendorp, J.J., et al., A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: a longitudinal cohort study. Lancet, 2011. 377(9770): p. 1004-10.
17. Malla, External validation study of a clinical prediction rule for ambulation outcomes after traumatic spinal cord injury, in Texas Medical Center Dissertations (via ProQuest). 2013: The University of Texas School of Public Health.
18. van Silfhout, L., et al., Validation of the Dutch clinical prediction rule for ambulation outcomes in an inpatient setting following traumatic spinal cord injury. Spinal Cord, 2016. 54(8): p. 614-8.
19. Sturt, R., et al., Validation of a clinical prediction rule for ambulation outcome after non-traumatic spinal cord injury. Spinal Cord, 2019.
20. Phan, P., et al., Highlighting discrepancies in walking prediction accuracy for patients with traumatic spinal cord injury: an evaluation of validated prediction models using a Canadian Multicenter Spinal Cord Injury Registry. Spine J, 2019. 19(4): p. 703-710.
21. Engel-Haber, E., et al., The effect of age and injury severity on clinical prediction rules for ambulation among individuals with spinal cord injury.Spine J, 2020.
22. Hicks, K.E., et al., A simplified clinical prediction rule for prognosticating independent walking after spinal cord injury: a prospective study from a Canadian multicenter spinal cord injury registry. Spine J, 2017. 17(10): p. 1383-1392.
23. Pelletier-Roy, Rémi, et al. "Clinical judgment is a cornerstone for validating and using clinical prediction rules: a head-to-head study on ambulation outcomes for spinal cord injured patients." Spinal Cord (2021): 1-7.
24. Bohlman, H.H., Acute fractures and dislocations of the cervical spine. An analysis of three hundred hospitalized patients and review of the literature. J Bone Joint Surg Am, 1979. 61(8): p. 1119-42.
25. Penrod, L.E., S.K. Hegde, and J.F. Ditunno, Jr., Age effect on prognosis for functional recovery in acute, traumatic central cord syndrome. Arch Phys Med Rehabil, 1990. 71(12): p. 963-8.
26. DeVivo, M.J., et al., The influence of age at time of spinal cord injury on rehabilitation outcome. Arch Neurol, 1990. 47(6): p. 687-91.

27. Roth, E.J., et al., Traumatic cervical Brown-Sequard and Brown-Sequard-plus syndromes: the spectrum of presentations and outcomes.Paraplegia, 1991. 29(9): p. 582-9.
28. Spivak, J.M., et al., Cervical spine injuries in patients 65 and older. Spine (Phila Pa 1976), 1994. 19(20): p. 2302-6.
29. McKinley, W.O., M.A. Tewksbury, and N.M. Mujteba, Spinal stenosis vs traumatic spinal cord injury: a rehabilitation outcome comparison. J Spinal Cord Med, 2002. 25(1): p. 28-32.
30. Oleson, C.V., et al., Prognostic value of pinprick preservation in motor complete, sensory incomplete spinal cord injury. Arch Phys Med Rehabil, 2005. 86(5): p. 988-92.
31. Lee, B.A., B.E. Leiby, and R.J. Marino, Neurological and functional recovery after thoracic spinal cord injury. J Spinal Cord Med, 2016. 39(1): p. 67-76.
32. van Middendorp, J., Hosman, A., Pouw, M. et al. ASIA impairment scale conversion in traumatic SCI: is it related with the ability to walk? A descriptive comparison with functional ambulation outcome measures in 273 patients. Spinal Cord 47, 555–560 (2009).
33. Scivoletto, Giorgio, et al. "Who is going to walk? A review of the factors influencing walking recovery after spinal cord injury." Frontiers in human neuroscience 8 (2014): 141.
34. Oleson, C.V., et al., Influence of Age Alone, and Age Combined With Pinprick, on Recovery of Walking Function in Motor Complete, Sensory Incomplete Spinal Cord Injury. Arch Phys Med Rehabil, 2016. 97(10): p. 1635-41.
35. McKinley, W.O., et al., Nontraumatic vs. traumatic spinal cord injury: a rehabilitation outcome comparison. Am J Phys Med Rehabil, 2001. 80(9): p. 693-9; quiz 700, 716.
36. Jean S, Mac-Thiong JM, Marie-Christine J, Dionne A, Begin J, Richard-Denis A. Early Clinical Prediction of Independent Outdoor Functional Walking Capacity in a Prospective Cohort of Traumatic Spinal Cord Injury Patients. *Am J Phys Med Rehabil*. 2021;100(11):1034-1041.
37. Flanders AE, Spettell CM, Friedman DP, Marino RJ, Herbison GJ. The relationship between the functional abilities of patients with cervical spinal cord injury and the severity of damage revealed by MR imaging. AJNR Am J Neuroradiol, 1999. 20(5): p. 926-934.
38. Shepard MJ, Bracken MB. Magnetic resonance imaging and neurological recovery in acute spinal cord injury: observations from the National Acute Spinal Cord Injury Study 3. Spinal Cord, 1999. 37(12): p. 833-837.
39. Boldin C, Raith J, Fankhauser F, Haunschmid C, Schwantzer G, Schweighofer F. Predicting neurologic recovery in cervical spinal cord injury with postoperative MR imaging. Spine (Phila Pa 1976), 2006. 31(5): p. 554-559.
40. Fehlings MG, Furlan JC, Massicotte EM, et al. Interobserver and intraobserver reliability of maximum canal compromise and spinal cord compression for evaluation of acute traumatic cervical spinal cord injury. Spine (Phila Pa 1976), 2006. 31(15): p. 1719-1725.
41. Miyanji F, Furlan JC, Aarabi B, Arnold PM, Fehlings MG. Acute cervical traumatic spinal cord injury: MR imaging findings correlated with neurologic outcome--prospective study with 100 consecutive patients. Radiology, 2007. P. 243(3): p. 820-827.
42. Talekar K, Poplawski M, Hegde R, Cox M, Flanders A. Imaging of Spinal Cord Injury: Acute Cervical Spinal Cord Injury, Cervical Spondylotic Myelopathy, and Cord Herniation. Semin Ultrasound CT MR., 2016. 37(5): p. 431-447.
43. Martínez-Pérez R, Paredes I, Cepeda S, et al. Spinal cord injury after blunt cervical spine trauma: correlation of soft-tissue damage and extension of lesion. AJNR Am J Neuroradiol, 2014. 35(5): p. 1029-1034.
44. Huber E, Lachappelle P, Sutter R, Curt A, Freund P. Are midsagittal tissue bridges predictive of outcome after cervical spinal cord injury? Ann Neurol., 2017. 81(5): p. 740-748.
45. Martínez-Pérez R, Cepeda S, Paredes I, Alen JF, Lagares A. MRI Prognostication Factors in the Setting of Cervical Spinal Cord Injury Secondary to Trauma. World Neurosurg., 2017. 101: p. 623-632.
46. Huber E, David G, Thompson AJ, Weiskopf N, Mohammadi S, Freund P. Dorsal and ventral horn atrophy is associated with clinical outcome after spinal cord injury. Neurology, 2018. 90(17): p. e1510-e1522.
47. David G, Seif M, Huber E, et al. In vivo evidence of remote neural degeneration in the lumbar enlargement after cervical injury. Neurology, 2019. 92(12): p. e1367-e1377.
48. Berliner JC, O'Dell DR, Albin SR, et al. The influence of conventional T2 MRI indices in predicting who will walk outside one year after spinal cord injury. J Spinal Cord Med, 2021. p. 1-7.
49. Smith AC, Weber KA, Parrish TB, et al. Ambulatory function in motor incomplete spinal cord injury: a magnetic resonance imaging study of spinal cord edema and lower extremity muscle morphometry. Spinal Cord, 2017. 55(7): p. 672-678.

50. Smith AC, Weber KA 2nd, O'Dell DR, Parrish TB, Wasielewski M, Elliott JM. Lateral Corticospinal Tract Damage Correlates With Motor Output in Incomplete Spinal Cord Injury. Arch Phys Med Rehabil., 2018. 99(4): p. 660-666.
51. Poplawski MM, Alizadeh M, Oleson CV, et al. Application of Diffusion Tensor Imaging in Forecasting Neurological Injury and Recovery after Human Cervical Spinal Cord Injury. J Neurotrauma, 2019. 36(21): p. 3051-3061.
52. Seif M, David G, Huber E, Vallotton K, Curt A, Freund P. Cervical Cord Neurodegeneration in Traumatic and Non-Traumatic Spinal Cord Injury. J Neurotrauma, 2020. 37(6): p. 860-867.
53. Shanmuganathan K, Zhuo J, Bodanapally UK, et al. Comparison of Acute Diffusion Tensor Imaging and Conventional Magnetic Resonance Parameters in Predicting Long-Term Outcome after Blunt Cervical Spinal Cord Injury. J Neurotrauma, 2020. 37(3): p. 458-465.
54. Smith AC, Albin SR, O'Dell DR, et al. Axial MRI biomarkers of spinal cord damage to predict future walking and motor function: a retrospective study. Spinal Cord, 2021. 59(6): p. 693-699.
55. Talbott JF, Whetstone WD, Readdy WJ, Ferguson AR, Bresnahan JC, Saigal R, Hawryluk GW, Beattie MS, Mabray MC, Pan JZ, Manley GT, Dhall SS. The Brain and Spinal Injury Center score: a novel, simple, and reproducible method for assessing the severity of acute cervical spinal cord injury with axial T2-weighted MRI findings. J Neurosurg Spine. 2015;23(4):495-504.
56. de Leener B, Lévy S, Dupont SM, et al. SCT: Spinal Cord Toolbox, an open-source software for processing spinal cord MRI data. *NeuroImage*. 2017;145:24-43.
57. de Leener B, Fonov VS, Collins DL, Callot V, Stikov N, Cohen-Adad J. PAM50: Unbiased multimodal template of the brainstem and spinal cord aligned with the ICBM152 space. *NeuroImage*. 2017;165:170-179.
58. Smith AC, O'Dell DR, Albin SR, Berliner JC, Dungan D, Robinson E, Elliott JM, Carballido-Gamio J, Stevens-Lapsley J, Weber KA. Lateral corticospinal tract and dorsal column damage: predictive relationships with future motor and sensory scores at discharge from acute rehabilitation after spinal cord injury. *Archives of Physical Medicine and Rehabilitation.* 2021. doi: 10.1016/j.apmr.2021.07.792.
59. Belliveau, T., et al., Developing Artificial Neural Network Models to Predict Functioning One Year After Traumatic Spinal Cord Injury. Arch Phys Med Rehabil, 2016. 97(10): p. 1663-1668 e3.
60. Muriel Buri, Lorenzo G. Tanadini, Torsten Hothorn, and Armin Curt. Unbiased Recursive Partitioning Enables Robust and Reliable Outcome Prediction in Acute Spinal Cord Injury. Journal of Neurotrauma. ahead of print. http://doi.org/10.1089/neu.2020.7407