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## Impact of Baseline Magnetic Resonance Imaging on Neurologic, Functional, and Safety Outcomes in Patients With Acute Traumatic Spinal Cord Injury

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# Impact of Baseline Magnetic Resonance Imaging on Neurologic, Functional, and Safety Outcomes in Patients With Acute Traumatic Spinal Cord Injury

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## Abstract

**Study Design:** Systematic review.

**Objective:** To perform a systematic review to evaluate the utility of magnetic resonance imaging (MRI) in patients with acute spinal cord injury (SCI).

**Methods:** An electronic search of Medline, EMBASE, the Cochrane Collaboration Library, and Google Scholar was conducted for literature published through May 12, 2015, to answer key questions associated with the use of MRI in patients with acute SCI.

**Results:** The literature search yielded 796 potentially relevant citations, 8 of which were included in this review. One study used MRI in a protocol to decide on early surgical decompression. The MRI-protocol group showed improved outcomes; however, the quality of evidence was deemed very low due to selection bias. Seven studies reported MRI predictors of neurologic or functional outcomes. There was moderate-quality evidence that longer intramedullary hemorrhage (2 studies) and low-quality evidence that smaller spinal canal diameter at the location of maximal spinal cord compression and the presence of cord swelling are associated with poor neurologic recovery. There was moderate-quality evidence that clinical outcomes are not predicted by SCI lesion length and the presence of cord edema.

**Conclusions:** Certain MRI characteristics appear to be predictive of outcomes in acute SCI, including length of intramedullary hemorrhage (moderate-quality evidence), canal diameter at maximal spinal cord compression (low-quality evidence), and spinal cord swelling (low-quality evidence). Other imaging features were either inconsistently (presence of hemorrhage, maximal canal compromise, and edema length) or not associated with outcomes. The paucity of literature highlights the need for well-designed prospective studies.

## Keywords

spinal cord injury, magnetic resonance imaging, risk factors, neurologic outcomes, functional outcomes

## Introduction

Imaging of the spine is an essential part of the early management of the polytrauma patient.<sup>1</sup> Most major trauma centers have a variety of imaging modalities available for acute spinal trauma. The choice of modality is determined by the need to evaluate bony, ligamentous, soft tissue, and neural elements. In the acute setting, imaging should provide a rapid and accurate assessment of spinal stability, as well as guide clinical management. Current trauma protocols rely heavily on computed tomography (CT),<sup>1</sup> as it allows for efficient evaluation of the head, body, and spine and identifies most injuries. High-quality

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imaging, however, cannot replace a good clinical examination, but rather should supplement and confirm findings of the primary and secondary trauma survey.

### *Magnetic Resonance Imaging*

Magnetic resonance imaging (MRI) is not routinely used for initial evaluation of the trauma patient. MRI is usually performed after initial clinical and radiological (CT or X-rays) evaluations, when further delineation of neural structures, such as the spinal cord, nerve roots, or brachial plexus, is required due to the presence of a neurological deficit or the suspicion of a structural problem such as a ligamentous injury. Conventional MRI, including T1- and T2-weighted imaging, provides excellent views of the soft tissue and can readily identify features of spinal cord compression such as intervertebral disc herniation and epidural hematoma.<sup>1,2</sup> Although CT is often able to detect pre- and paravertebral soft tissue swelling, MRI provides a more reliable detection of traumatic injury. Short-tau inversion recovery sequences produce fat-suppressed images that better delineate ligamentous injuries, which can cause mechanical instability of the spinal column. T2-weighted MRI is ideal for demonstrating intramedullary spinal cord edema and hemorrhage; high signal intensity indicates edema, while a focus of acute hemorrhage has low, heterogeneous signal intensity.<sup>3</sup> Gradient echo (GRE) and susceptibility weighted imaging (SWI) are highly sensitive for hemorrhage and can also identify microhemorrhage consistent with cord contusions.

The use of MRI for the initial evaluation of trauma patients is limited largely by long scanning times. Although monitoring is available in many MRI suites, it is not advised to keep trauma patients supine and flat for extended periods of time as a result of pain and hemodynamic instability. Critically ill trauma patients may also have concomitant head and chest injuries that may result in increased intracranial pressure and decreased ventilation during MRI acquisition.<sup>4</sup> The use of a small number of specific sequences with appropriate coils can reduce scanning time. Current guidelines for the use of MRI in acute spine trauma are based on limited available data.<sup>1</sup>

The primary goal of this study was to perform a systematic review of the literature to (1) assess MRI features that may affect clinical decision making and outcomes in patients with acute SCI; (2) determine if baseline MRI characteristics can predict neurologic, functional, and patient-reported outcomes; (3) evaluate the safety of MRI in this population; and (4) characterize the cost-effectiveness of MRI in acute SCI.

To accomplish this goal, we aimed to answer the following key questions (KQ) in adult patients with acute traumatic SCI:

**KQ1:** How does MRI influence management strategy(ies), such as surgical timing and approach, and/or neurologic, functional, patient-reported, and safety outcomes?

**KQ2:** Do spinal cord lesion characteristics, pattern, and length identified on baseline MRI predict neurologic, functional, patient-reported, and safety outcomes?

**KQ3:** Do spinal cord characteristics identified on diffusion tensor imaging (DTI) predict neurologic, functional, patient-reported, and safety outcomes?

**KQ4:** Is there evidence to suggest that baseline MRI is cost-effective in patients with acute SCI?

## **Materials and Methods**

### *Electronic Literature Search*

We conducted a systematic search of PubMed/MEDLINE, EMBASE, the Cochrane Collaboration Library, and Google Scholar for literature published through May 12, 2015. Citations with abstracts of human studies were considered for inclusion, with no other limits (including language) applied to the search. Reference lists of included studies as well as pertinent reviews were systematically checked to identify additional articles. A summary of the search strategy is presented in the supplemental material (available in the online version of the article).

The search strategy included the use of controlled vocabulary (MeSH terms) as well as keywords. Terms specific to traumatic spinal cord injuries and central cord syndrome as well as those related to MRI and DTI were used. For KQ1, we sought to identify comparative studies that assessed if presurgical MRI influenced management strategies and, consequently, neurologic, functional, patient-reported, and safety outcomes. For KQ1 and KQ4, we only included studies that compared specific treatment strategies (eg, emergency decompressive surgery), outcomes (KQ1), or cost-effectiveness data (KQ4) between groups that did and did not receive presurgical MRI. For KQ2 and KQ3, we attempted to identify prospective or retrospective cohort studies that evaluated lesion characteristics, pattern, and/or length on conventional MRI (KQ2) or DTI (KQ3) as predictors of neurologic change/recovery (eg, Frankel grade, American Spinal Injury Association [ASIA] impairment scale [AIS]), functional outcomes (eg, Functional Impairment Measure [FIM]), patient-reported outcomes (eg, pain), and safety (eg, complications and adverse events). For KQ4, we sought comparative full-economic studies that evaluated the cost-effectiveness of presurgical MRI in patients with acute SCI. Meeting abstracts/proceedings, white papers, editorials, narrative reviews, case reports, nonclinical and animal studies, and studies with less than 10 subjects in total (KQ2 and KQ3) or per group (KQ1 and KQ4) were excluded. Studies on patients with cord compression/spinal cord injuries due to degenerative disease (eg, cervical spondylotic myelopathy, spinal stenosis), tumor, or hematoma were also excluded. The PICO (Patients, Intervention, Comparator and Outcomes) and PPO (Patients, Prognostic Factors and Outcomes) tables provide additional information on inclusion/exclusion criteria (Tables 1 and 2).

### *Data Extraction*

The full texts of potential articles were reviewed by 2 independent investigators (DJF, ACS) to obtain the final collection of

**Table 1.** PICO Table Summarizing Inclusion and Exclusion Criteria for Key Questions 1 and 4.

Study Component	Inclusion	Exclusion
Patient	<ul style="list-style-type: none"> <li>• Adult patients with acute traumatic spinal cord injury (complete or incomplete)</li> <li>• Adult patients with central cord syndrome</li> </ul>	<ul style="list-style-type: none"> <li>• Pediatric patients &lt;18 years old</li> <li>• Pregnancy</li> <li>• Penetrating injuries to spinal cord</li> <li>• Cord compression/injury due to tumor, hematoma, degenerative disease (eg, CSM, spinal stenosis)</li> <li>• Patients without neurologic deficit following trauma</li> <li>• &lt;80% of study population with a diagnosis of acute spinal cord injury and/or central cord syndrome</li> <li>• Studies that utilized low-resolution MRI (&lt;1.0 Tesla)</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Baseline MRI was performed</li> </ul>	
Comparator	<ul style="list-style-type: none"> <li>• No baseline MRI was performed</li> </ul>	
Outcomes	<ul style="list-style-type: none"> <li>• Treatment strategies               <ul style="list-style-type: none"> <li>• Surgical</li> <li>• Nonsurgical</li> </ul> </li> <li>• Neurologic change/recovery (eg, Frankel grade, ASIA Motor/Sensory score, ASIA Impairment Scale [AIS] grade)               <ul style="list-style-type: none"> <li>• Change in neurologic grade</li> <li>• Change in motor scores</li> <li>• Change in sensation</li> </ul> </li> <li>• Functional change/recovery (eg, FIM)               <ul style="list-style-type: none"> <li>• Change in functional score</li> <li>• Change in ambulation</li> </ul> </li> <li>• Survival</li> <li>• Patient-reported outcomes</li> <li>• Safety outcomes               <ul style="list-style-type: none"> <li>• Complications, adverse events</li> <li>• Postinjury medical complications</li> </ul> </li> <li>• Incremental cost-effectiveness ratio (ICER) (<i>KQ4 only</i>)</li> </ul>	<ul style="list-style-type: none"> <li>• Synthesized cost with effectiveness or utility measure not reported (<i>KQ4 only</i>)</li> </ul>
Study design	<ul style="list-style-type: none"> <li>• KQ1: Studies that evaluate treatment strategies and neurologic, functional, patient-reported, and/or safety outcomes in patients who underwent presurgical MRI compared to those who did not</li> <li>• KQ4: Studies that evaluate the cost-effectiveness of treatment strategies and neurologic, functional, patient-reported, and/or safety outcomes in patients who underwent presurgical MRI compared to those who did not</li> <li>• Focus will be on studies with the least potential for bias (RCTs and nonrandomized comparative studies)</li> </ul>	<ul style="list-style-type: none"> <li>• No multivariate analysis of primary outcome(s) of interest</li> <li>• Case reports</li> <li>• Studies of &lt;10 subjects per group</li> <li>• Nonclinical studies</li> <li>• Animal studies</li> </ul>
Publication type	<ul style="list-style-type: none"> <li>• Studies with abstracts in peer-reviewed journals</li> </ul>	<ul style="list-style-type: none"> <li>• White papers</li> <li>• Abstracts, conference proceedings</li> <li>• Editorials, letters to editor</li> <li>• Articles identified as preliminary reports with results published in later versions</li> <li>• Narrative reviews</li> <li>• Duplicate publications of the same study which do not report on different outcomes</li> <li>• Multiple studies on the same patient population</li> <li>• Single reports from multicenter trials</li> </ul>

Abbreviations: ASIA, American Spinal Injury Association; CSM, cervical spondylotic myelopathy; FIM, Functional Impairment Measure; KQ, key question; MRI, magnetic resonance imaging; RCT, randomized controlled trial.

included studies. From the included articles, the following data was extracted: study design; patient demographics; inclusion and exclusion criteria; baseline population/disease characteristics; follow-up duration and the rate of follow-up (if reported or calculable); baseline MRI characteristics and assessment;

timing of MRI in relation to injury and intervention (if applicable); treatment groups (KQ1); reported information on specific treatment decisions (KQ1); neurological, functional, safety, and quality of life outcomes (KQ1, KQ2, and KQ3); prognostic factors evaluated (KQ2 and KQ3); association

**Table 2.** PPO Table Summarizing Inclusion and Exclusion Criteria for Key Questions 2 and 3.

Study Component	Inclusion	Exclusion
Patient	<ul style="list-style-type: none"> <li>• Adult patients with acute traumatic spinal cord injury (complete or incomplete)</li> <li>• Adult patients with central cord syndrome</li> </ul>	<ul style="list-style-type: none"> <li>• Pediatric patients &lt;18 years old</li> <li>• Pregnancy</li> <li>• Penetrating injuries to spinal cord</li> <li>• Cord compression/injury due to tumor, hematoma, degenerative disease (eg, CSM, spinal stenosis)</li> <li>• Patients without neurologic deficit following trauma</li> <li>• &lt;80% of study population with a diagnosis of acute spinal cord injury and/or central cord syndrome</li> <li>• Studies that utilized low-resolution MRI (&lt;1.0 Tesla)</li> </ul>
Prognostic factor	<ul style="list-style-type: none"> <li>• Primary factor               <ul style="list-style-type: none"> <li>• Spinal cord lesion characteristics on MRI (eg, spinal cord compression, spinal canal compromise; KQ2)</li> <li>• Spinal cord lesion pattern and/or length on MRI (eg, hematoma, edema; KQ2)</li> <li>• Spinal cord lesion characteristics on diffusion tensor imaging (DTI) MRI (KQ3)</li> </ul> </li> <li>• Secondary (potentially confounding) factors:               <ul style="list-style-type: none"> <li>• Timing of MRI after injury</li> <li>• Age</li> <li>• Patient comorbidities</li> <li>• Neurologic status (eg, Frankel grade, ASIA Impairment Scale [AIS] grade)</li> <li>• Treatment strategies</li> </ul> </li> </ul>	
Outcomes	<ul style="list-style-type: none"> <li>• Neurologic change/recovery (eg, Frankel grade, ASIA Motor/Sensory score, AIS grade)               <ul style="list-style-type: none"> <li>• Change in neurologic grade</li> <li>• Change in motor scores</li> <li>• Change in sensation</li> </ul> </li> <li>• Functional change/recovery (eg, FIM)               <ul style="list-style-type: none"> <li>• Change in functional score</li> <li>• Change in ambulation</li> </ul> </li> <li>• Survival</li> <li>• Patient-reported outcomes</li> <li>• Safety outcomes               <ul style="list-style-type: none"> <li>• Complications, adverse events</li> </ul> </li> </ul>	
Study design	<ul style="list-style-type: none"> <li>• Studies that evaluate the ability of lesion characteristics, pattern, and/or length on MRI to predict outcomes</li> <li>• Focus will be on studies with the least potential for bias (prospective and retrospective cohort studies)</li> </ul>	<ul style="list-style-type: none"> <li>• No multivariate analysis of primary outcome(s) of interest</li> <li>• Did not control for baseline neurologic function in analysis</li> <li>• No longitudinal follow-up</li> <li>• Case reports</li> <li>• Studies of &lt;10 subjects</li> <li>• Nonclinical studies</li> <li>• Animal studies</li> <li>• White papers</li> <li>• Abstracts, conference proceedings</li> <li>• Editorials, letters to editor</li> <li>• Articles identified as preliminary reports with results published in later versions</li> <li>• Narrative reviews</li> <li>• Duplicate publications of the same study which do not report on different outcomes</li> <li>• Multiple studies on the same patient population</li> <li>• Single reports from multicenter trials</li> </ul>
Publication type	<ul style="list-style-type: none"> <li>• Studies with abstracts in peer-reviewed journals</li> </ul>	

Abbreviations: ASIA, American Spinal Injury Association; CSM, cervical spondylotic myelopathy; FIM, Functional Impairment Measure; MRI, magnetic resonance imaging.

between prognostic factors and reported outcomes (KQ2 and KQ3); and cost-effectiveness data (KQ4).

### Study Quality and Overall Strength of Body of Literature

Each article was independently critically appraised and evaluated for risk of bias by at least 2 reviewers (DJF, ACS) using criteria set by *The Journal of Bone and Joint Surgery, American Volume*<sup>5</sup> for prognostic and therapeutic studies, and modified to delineate criteria associated with methodological quality and risk of bias based on recommendations made by the Agency for Healthcare Research and Quality (AHRQ).<sup>6</sup> This appraisal system accounts for features of methodologic quality and important sources of bias by combining epidemiologic principles with characteristics of study design.<sup>7,8</sup> (See Supplemental Material for study ratings; available in the online version of the article.) Any disagreement among the reviewers was resolved through discussion.

The overall quality (strength) of the body of evidence with respect to each outcome was determined based on precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group<sup>9,10</sup> and recommendations made by AHRQ.<sup>6</sup> Additional qualitative analysis was performed according to AHRQ-required (risk of bias, consistency, directness, precision) and additional domains (dose-response, strength of association, publication bias).<sup>11</sup> In general, *risk of bias* was determined when evaluating each individual article as described above.

For outcomes related to KQ1, the initial quality of the overall body of evidence was considered “High” for randomized controlled trials and “Low” for observational studies. The body of evidence could be downgraded 1 or 2 levels based on the following criteria: (1) risk of bias (study limitations), (2) inconsistency of results, (3) indirectness of evidence, (4) imprecision of the effect estimates (eg, wide confidence intervals), or (5) failure to provide an a priori statement of subgroup analyses. The body of evidence for observational studies could be upgraded 1 or 2 levels (if no serious risk of bias) based on the following criteria: (1) large magnitude of effect, (2) dose-response gradient, or (3) if all plausible biases would decrease the magnitude of an apparent effect. For KQ2 and KQ3, the initial quality of the evidence was considered “High” if the majority of prognostic studies had low or moderately low risk of bias, and “Low” if the majority had moderately high or high risk of bias. The body of evidence could be downgraded 1 or 2 levels based on the following criteria: (1) inconsistency of results, (2) indirectness of evidence, (3) imprecision of the effect estimates (eg, wide confidence intervals, small sample size), or (4) failure to provide an a priori statement of subgroup analyses. The body of evidence could be upgraded based on the criteria specified above. Two senior systematic review methodologists rated and discussed the overall quality of evidence.

The final overall strength of the body of literature expresses (1) our confidence that the effect size lies close to the true effect and (2) the extent to which the effect is believed to be stable based on the adequacy of or deficiencies in the body of

evidence.<sup>10</sup> An overall strength of “High” means that we are very confident that the true effect lies close to that of the estimated effect. A “Moderate” rating means that we are moderately confident in the effect estimate; the true effect is likely to be close to the estimated effect, but there is a possibility that it is substantially different. An overall strength of “Low” means that our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate. Finally, a rating of “Very Low” means that we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimated effect. In addition, this rating may be used if there is no evidence or it is not possible to estimate an effect.

### Data Synthesis and Analysis

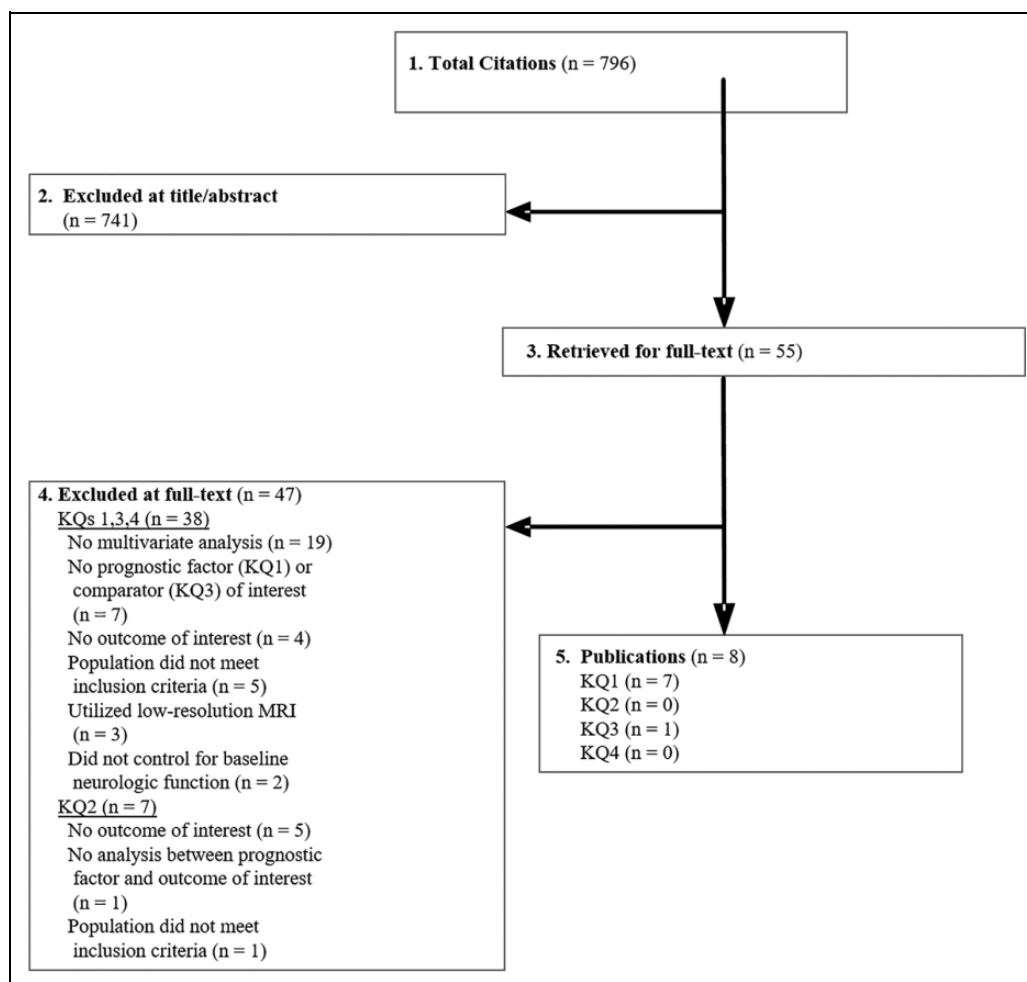
For KQ1, results and comparative statistics regarding treatment decisions and neurologic outcomes were reported. For KQ2, there was variability in the measurement and reporting of prognostic factors and outcomes. To operationalize outcomes and discern patterns of association, we combined outcomes into 2 categories: *neurologic* and *functional*. The latter category included 2 patient-reported outcomes (self-reports of manual dexterity and dysesthetic pain) that may ultimately affect function. Furthermore, authors generally did not report the magnitude of association (eg, effect size estimates with confidence intervals) between predictive characteristics and outcomes, but rather presented *P* values and/or stated whether there was a significant association. We reported the association between the prognostic factor and the specific outcome (no association, association with a negative outcome, or association with a positive outcome).

## Results

### Study Selection

The literature search yielded 796 potentially relevant citations that were evaluated against a priori inclusion/exclusion criteria (Tables 1 and 2; Figure 1). After title/abstract review, 741 were excluded, most of which reported on bony fractures or other acute trauma without SCI. Review of the reference lists of included studies as well as relevant reviews did not yield any additional relevant citations. Among the 55 remaining articles, 47 were excluded after review by 2 reviewers. The primary reasons for exclusion were (1) failure to control for confounding factors (especially baseline neurologic status) via multivariate analysis or other statistical methods and (2) the lack of longitudinal information on neurologic or functional recovery.

For studies evaluating the impact of MRI on clinical decision making, the primary reason for exclusion was the lack of a comparison group with patients that did not receive MRI (KQ1). Additional reasons for exclusion were (1) the absence of outcomes of interest (KQ1, KQ2), (2) the lack of a multivariate analysis or other statistical methods to control for



**Figure 1.** Flow chart showing results of literature search.

important confounders (particularly baseline neurologic status; KQ2), and (3) no assessment of MRI prognostic factors (KQ2, KQ3). We identified a single study for KQ1 that compared treatment decisions and neurological outcomes between patients with and without pretreatment MRI; 7 studies for KQ2 that evaluated important MRI predictors of outcomes; and no studies relevant for either KQ3 or KQ4. Details of excluded articles are provided in the Supplemental Material (available in the online version of the article).

### ***The Influence of Baseline MRI on Treatment Strategy(ies) and SCI Outcomes***

One prospective cohort study<sup>12</sup> (moderately high risk of bias) evaluated the effect of pretreatment MRI on neurological outcome (Frankel grade). Table 3 summarizes the characteristics of this study, while Table 4 reports the influence of a baseline MRI on neurologic outcomes.

Papadopoulos et al reported on 91 consecutive patients suffering from traumatic closed cervical (C1-T1) SCI.<sup>12</sup> Sixty-six (72.5%; protocol group) acute SCI patients were managed according to a decision-making protocol (MRI-protocol group)

in which the MRI results were used to decide on emergency surgical decompression. This study reported that MRI resulted in no adverse events in all 66 patients and identified ongoing cord compression in 34/66 (51.5%) patients receiving MRI, leading to surgical treatment (mean 9.6 hours after hospital arrival, 13.4 hours postinjury). MRI also identified anterior spinal cord compression (disc herniation, epidural hematoma, malalignment, or bone fragments) in 16/66 patients (24.2%), leading to an anterior surgical approach. The remaining 25 patients (27.5%; reference group) were not managed according to the protocol because of a contraindication to performing MRI, the need for an emergent surgical procedure, or “specific surgeon bias regarding the futility of emergent treatment.” These criteria for group assignment indicate a strong potential for selection bias. The MRI-protocol group was 68.2% (45/66) male with a mean age of  $32 \pm 2.1$  (range 2-92) years, while the reference group was 76.0% (19/25) male with a mean age of  $42 \pm 4.8$  (range 2-89) years. The neurologic follow-up interval for patients in the protocol group was on average  $31.6 \pm 3.6$  (range 2-92) months, while patients in the reference group had a mean follow-up of  $36.2 \pm 5.7$  (range 2-96) months. Unfortunately, details regarding management for the reference group



**Table 3.** KQ1 Characteristics of Studies Evaluating the Impact of MRI on Clinical Decision Making and Neurologic, Functional, Pain, and/or Safety Outcomes Compared to No MRI.

Study	Demographics	Baseline Population Definition and Characteristics	Treatment Groups	Baseline MRI Characteristics and Timing	Outcome Measures Evaluated <sup>a</sup>
Papadopoulos (2002) Prospective cohort Risk of bias: Moderately high	<i>Protocol group:</i> N = 66 Sex: 68.2% (45/66) male Mean age: 32 ± 2.1 (2-92) years F/U: 31.6 ± 3.6 (2-92) months F/U %: NR <i>Reference group:</i> N = 25 Sex: 76.0% (19/25) male Mean age: 42 ± 4.8 (2-89) years F/U: 36.2 ± 5.7 (2-96) months F/U %: NR	<i>Population:</i> 91 consecutive patients suffering from traumatic closed cervical (C1-T1) SCI who received acute care. Patients were either managed by a treatment protocol (protocol group) or were part of a reference group. <i>Admitting Frankel score</i> <u>Protocol group</u> • Frankel Grade A: 57.6% (38/66) • Frankel Grade B: 18.2% (12/66) • Frankel Grade C: 13.6% (9/66) • Frankel Grade D: 10.6% (7/66) <u>Reference group</u> • Frankel Grade A: 64.0% (16/25) • Frankel Grade B: 16.0% (4/25) • Frankel Grade C: 0.0% (0/25) • Frankel Grade D: 20.0% (5/25)	<ul style="list-style-type: none"> <li>• <i>Protocol group (n = 66):</i> Patients with cervical spinal malalignment causing suspected SCC were placed in skeletal traction. Once optimal spinal alignment was achieved, patients underwent MRI. Patients with MRI-documented SCC underwent emergency surgical decompression and spinal column stabilization. Patients without SCC were treated with either surgery for internal spinal column stabilization within 24-48 hours or placed in a definitive external orthosis.</li> <li>• <i>Reference group (n=25):</i> Reference group patients were treated outside of the protocol because of contraindication to MRI, the need for an emergent surgical procedure, or admitting surgeon preferences.</li> </ul>	<i>MRI characteristics:</i> T1- and T2-weighted MR imaging of the cervical spine was performed with 1.5-Tesla scanner (protocol group only) <i>MRI assessment:</i> NR <i>MRI timing with regard to injury:</i> Mean time from injury to MRI was 7.7 ± 0.4 hours <sup>b</sup> (for protocol group only) <i>MRI timing with regard to intervention:</i> Mean time from injury to operative decompression was 12.6 ± 1.3 hours <sup>b</sup>	<i>Neurologic</i> <ul style="list-style-type: none"> <li>• Frankel grade at last follow-up</li> </ul> <i>Potential confounding factors</i> <u>Demographic</u> <ul style="list-style-type: none"> <li>• Age</li> <li>• Sex</li> </ul> <u>Clinical</u> <ul style="list-style-type: none"> <li>• Mechanism of injury</li> <li>• Admitting injury level</li> <li>• Admitting Injury Severity Score</li> <li>• Admitting Frankel grade</li> </ul>

Abbreviations: F/U, follow-up; MRI, magnetic resonance imaging; NR, not reported; SCC, spinal cord compression; SCI, spinal cord injury.

<sup>a</sup>Only reported outcome measures related to study question.

<sup>b</sup>Reported as mean ± standard error.

**Table 4.** The Impact of Baseline MRI on Treatment Strategies and Neurologic, Functional, and Safety Outcomes in Patients With Acute Spinal Cord Injury.

Author (Year)	Risk of Bias	Outcome Measures	Follow-up Duration (Months)	Protocol Group (N = 66)	Reference Group (N = 25)	P Value
Papadopoulos (2002)	Moderately high	Frankel grade improvement (last follow-up)	2-92	NR	NR	P < .006 <sup>a</sup>
						Protocol > Reference <sup>b</sup>

Abbreviations: MRI, magnetic resonance imaging; NR, not reported.

<sup>a</sup>P value reported by the authors based on results of multivariate regression analysis that accounted for potential confounders (age, sex, mechanism of injury, admitting injury level, admitting Injury Severity Score, admitting Frankel grade).

<sup>b</sup>Patients in the Protocol group improved 7/10 of a Frankel grade more than patients in the Reference group.

were not reported, and thus no direct comparisons could be made between the groups regarding the impact of MRI on treatment decisions.

The effect of acquiring a baseline MRI (and treatment protocol) was evaluated in a linear regression analysis that adjusted for baseline Frankel grade, age, sex, mechanism of injury, admitting injury level, and admitting Injury Severity Score. Patients in the MRI-protocol group, on average, had

an improved Frankel grade compared to those in the reference group (0.7 of a Frankel grade,  $P < .006$ ). Fifty percent of the MRI-protocol group experienced an improvement in Frankel grade, compared to 24% of the reference group. Eight patients (12%) in the MRI-protocol group improved from a motor-complete injury to independent ambulation, whereas no patients in the reference group patients achieved this improvement.

### **Spinal Cord Lesion Characteristics, Pattern, and Length Identified on Baseline MRI as Predictors of SCI Outcomes**

Table 5 summarizes the characteristics of the included prognostic studies. Of these, 4 prospective cohort studies<sup>13-16</sup> and 1 retrospective cohort study<sup>17</sup> were considered to have moderately low risk of bias, and 2 retrospective cohort studies<sup>18,19</sup> were considered to have moderately high risk of bias. All studies controlled for baseline neurologic status in multivariate models and followed populations for the primary outcome(s) of interest. One included study (Selden et al) reported the importance of baseline neurological status and various MRI findings in predicting neurological outcomes; however, model details were not provided and results were only assumed to be multivariate.

Across studies, there was variability in the reporting and measurement of prognostic factors and outcomes. Adjusted effect sizes and/or confidence intervals describing the magnitude of association between the predictive factor(s) and outcome were rarely reported. Only a single study<sup>17</sup> reported a follow-up of >80% of subjects. One study<sup>13</sup> compared findings in patients with complete SCI to those with incomplete SCI and also performed a post hoc subgroup analysis in only patients with complete SCI.

Across the included studies, the majority of the patient population was male (65.5% to 87.5%) with a wide range of mean ages (29-58 years). Four studies limited their population to patients with cervical SCI.<sup>13,14,18,19</sup> MRI was performed within 3 days of injury in most studies, with one reporting a median of 8 days (range 5-12 days). The timing from MRI to intervention was inconsistently reported. Follow-up time ranged from 1 to 74 months.

### **MRI Predictors of Neurologic Recovery**

The association between MRI features and neurological outcomes was reported in 6 studies. For evidence synthesis, the following measures were considered together: AIS grade, Frankel grade, ASIA Motor score, motor function score, upper/lower extremity motor function and minimally useful function, pin prick score, and light touch score (see Table 6). A detailed table of associations is provided in the supplemental material (available in the online version of the article).

The association between neurological outcomes and the presence of intramedullary spinal cord hemorrhage (defined, in the acute period, as a region of decreased signal intensity surrounded by a thin rim of high signal intensity on T2-weighted images) was investigated in 5 studies, each of which used a different assessment measure. Based on multivariate analysis, 2 studies found no association,<sup>13,15</sup> while 3 studies reported that the presence of hemorrhage is predictive of worse neurologic recovery.<sup>14,18,19</sup> In the study by Selden et al, intra-axial hematoma was present in all Frankel grade A patients, none of whom experienced a change in Frankel grade at follow-up.<sup>19</sup>

Longer rostro-caudal intramedullary hematoma length was associated with worse neurologic recovery in 2 studies.<sup>13,19</sup> Boldin et al reported that each millimeter increase in hematoma length increased the risk of retaining a complete SCI; patients with complete SCI tended to have a longer hematoma length (median 10.5 mm, range 4-15 mm) than those with incomplete injuries (median 4 mm, range 2-9 mm) and did not exhibit a change in AIS grade at follow-up. This study also reported that 5 patients with a hemorrhage length less than 4 mm demonstrated improvements on the AIS grade at follow-up, suggesting that a length less than 4 mm may be predictive of positive outcomes.<sup>13</sup> Based on a single study, cord compression from extra-axial hematoma was not associated with poorer neurologic recovery in multivariate analysis.<sup>19</sup>

The association between maximal canal compromise (MCC) and neurologic recovery was inconsistent across 2 studies. One study<sup>14</sup> found no association, while the other<sup>17</sup> reported that a lower MCC is predictive of a worse neurologic recovery. Maximum spinal cord compression (MSCC) was not associated with neurologic recovery across 3 studies.<sup>14,17,19</sup>

The association between neurological outcomes and MRI evidence of cord edema (defined as a region of high signal intensity on T2-weighted images) was evaluated in 3 studies, each of which used a different assessment measure. Presence of cord edema was not associated with neurologic recovery in all 3 studies.<sup>13-15</sup> Longer edema lesion length, however, was predictive of a worse neurologic recovery in 2 studies.<sup>13,18</sup> In a third study, a significant association was observed between edema lesion length and neurologic recovery following univariate analysis but not following what appears to be multivariate analysis (authors do not provide details of multivariate analysis and cautious interpretation is advised).<sup>19</sup>

Two studies reported no association between SCI lesion length and neurologic recovery.<sup>14,17</sup> Cord swelling (defined as an increased spinal cord diameter) was predictive of worse neurological outcomes in one study;<sup>14</sup> a second study indicated no association between length of cord swelling and neurologic recovery.<sup>19</sup> Finally, single studies suggested no association between the following MRI radiographic factors and neurologic recovery: smaller diameter within swollen length of the cord, soft-tissue injury, preinjury stenosis, disk herniation, cord contusion, rostral point of edema, and worse baseline pin prick, light touch, and motor function scores.

### **MRI Predictors of Functional Recovery**

The association between MRI features and functional outcomes was reported in 2 studies.<sup>16,17</sup> For evidence synthesis, the following measures of functional recovery were considered together: FIM Motor score, functional dependence (dichotomous variable based on FIM score), and self-reported measures of manual dexterity and dysesthetic pain (see Table 6). A detailed table of associations is provided in the supplemental material (available in the online version of the article).

In a single study, lower MCC was significantly associated with worse FIM score, but not with patient-reported measures

**Table 5.** KQ2 Characteristics of Studies Discussing MRI Predictors of Neurologic, Functional, Pain, and/or Safety Outcomes.

Study	Demographics	Baseline Population Definition and Characteristics	Baseline MRI Characteristics and Assessment	MRI Timing: Injury and Intervention	Prognostic Factors Evaluated	Outcome Measures Evaluated <sup>a</sup>
Aarabi (2011) Retrospective cohort Risk of bias: Moderately low	N = 42 Sex: 83.3% (35/42) male Mean age: 58.3 (32-87) years F/U: Mean 29.1 ± 27 months F/U %: 85.7% (42/49)	Population: Patients with acute traumatic CCS Intervention: Patients chose early or late (w/in 6 weeks of injury) decompression surgery; surgical technique was influenced by imaging studies SCI Severity (ASIA Impairment scale) • C: 21.4% (9/42) • D: 78.6% (33/42)	MRI characteristics: T2-weighted MR images were retrieved for 40 of 42 patients. CT scans (42/42 patients) of the cervical spine were obtained with coronal, sagittal, and axial reformatting. MRI assessment: All images were measured independently by 2 radiologists and the senior author in a blinded fashion.	MRI timing with regard to injury: Imaging studies were obtained prior to surgery. MR images were obtained, on average, 5.8 hours after admission, and CT images were obtained, on average, 2.3 hours after admission. MRI timing with regard to intervention: MRI and CT were obtained prior to surgery; timing was NR. Median time from injury to operation was 2.8 days.	<b>Radiographic</b> • Percentage of MCC <sup>b</sup> • Percentage of MSCC <sup>b</sup> • Sagittal diameter of stenotic spinal canal at the point of MSCC (mm) • Length of parenchymal damage (signal change on MRI; mm)  <b>Secondary (potential confounding) factors</b> <u>Demographic</u> • Age <u>Clinical</u> • Mechanism of injury • Admission ASIA motor score • Number of stenotic skeletal segments (1, 2, ≥3) • Surgical technique (front, back, circumferential decompression) • Time delay from injury to surgery	<b>Neurologic</b> • Follow-up ASIA motor score <i>Function and Pain</i> • Follow-up FIM score • Manual dexterity level <sup>b</sup> • Dysesthetic pain level <sup>b</sup>  Safety NR

(continued)

Table 5. (continued)

Study	Demographics	Baseline Population Definition and Characteristics	Baseline MRI Characteristics and Assessment	MRI Timing: Injury and Intervention	Prognostic Factors Evaluated	Outcome Measures Evaluated <sup>a</sup>
Boldin (2006) Prospective cohort Risk of bias: Moderately low	N = 29 Sex: 65.5% (19/29) male Mean age: 43.5 ± 18.1 (18-86) years F/U: Median 35 (24-65) months F/U %: NR	Population: Patients with closed cervical SCI and neurologic deficit Intervention: All patients were treated operatively within 2-9 (mean: 4.3) hours after injury by closed or open reduction and ventral stabilization. SCI Severity (ASIA Impairment scale) • A: 27.6% (8/29) • B: 37.9% (11/29) • C: 27.6% (8/29) • D: 6.9% (2/29) • E: 0% (0/29)	MRI characteristics: T1- and T2-weighted MR images were obtained using a 1.5-Tesla superconducting MR scanner with a surface coil, 3-mm slice thickness for T1 and 2-mm thickness for T2 images. MRI assessment: NR	MRI timing with regard to injury and intervention: MR was performed within 5-12 (median: 8) days after injury. MR imaging was obtained after intervention.	Radiographic • Cord edema • Intramedullary hemorrhage • Edema lesion length • Hemorrhage lesion length Secondary (potential confounding) factors <u>Clinical</u> • Baseline ASIA impairment grade	Neurologic • Follow-up ASIA impairment grade Function and Pain NR Safety NR
Flanders (1996) Retrospective cohort Risk of bias: Moderately high	N = 104 Sex: 87.5% (91/104) male Mean age: 34 (17-70) years F/U: Mean ≥ 12 months F/U %: 58.1% (104/179)	Population: Patients with cervical SCI Intervention: Closed reduction, subluxation, or both SCI Severity (ASIA Impairment scale) • A: 41.3% (43/104) • B: 22.1% (23/104) • C: 26.9% (28/104) • D: 9.6% (10/104) • E: 0% (0/104)	MRI characteristics: Sagittal T1- and T2-weighted MR images were acquired using a 1.5-Tesla superconducting unit to obtain sagittal spin-echo sequences MRI assessment: All images were given a quality rating of satisfactory <sup>c</sup> or incomplete; if unsatisfactory or incomplete, patients were excluded from analyses. All spinal cord trauma locations were recorded by a single neuroradiologist who was blinded to the clinical status of each subject.	MRI timing with regard to injury and intervention: MRI was performed within 72 hours of injury before or after surgical stabilization.	Radiographic • Presence of hemorrhage • Rostral point of edema • Edema lesion length Secondary (potential confounding) factors <u>Clinical</u> • Initial ASIA motor score	Neurologic • Upper extremity motor function <sup>d</sup> • Lower extremity motor function <sup>d</sup> • Upper extremity muscles with minimally useful function <sup>d</sup> • Lower extremity muscles with minimally useful function <sup>d</sup> Function and Pain NR Safety NR

(continued)

**Table 5.** (continued)

Study	Demographics	Baseline Population Definition and Characteristics	Baseline MRI Characteristics and Assessment	MRI Timing: Injury and Intervention	Prognostic Factors Evaluated	Outcome Measures Evaluated <sup>a</sup>
Miyanji (2007) Prospective cohort Risk of bias: Moderately low	N = 100 Sex: 79% (79/100) male Mean age: 45 (17-96) years F/U: Mean 7.3 (1-35) months F/U %: NR	Population: Consecutive patients with cervical spine trauma Intervention: NR SCI Severity • Complete (ASIA grade A): 26% (26/100) • Incomplete (ASIA grade B, C, D): 51% (51/100) • Normal (ASIA grade E): 22% (22/100) • Unknown: 1% (1/100)	MRI characteristics: Sagittal T1- and T2-weighted MR imaging examinations were performed using a 1.5-Tesla magnet and standardized MR imaging protocols for the acutely injured. MRI assessment: All images were analyzed by a spine fellow board-certified in orthopedic surgery with 7 years experience; this individual was blinded to the patients' clinical and neurologic data.	MRI timing with regard to injury: MR images were obtained within 24-48 (median: 24) hours of injury MRI timing with regard to intervention: NR	Radiographic • MCC <sup>e</sup> • MSCC <sup>e</sup> • Intramedullary hemorrhage • Cord edema • Cord swelling • Soft-tissue injury <sup>e</sup> • Preinjury stenosis • Disk herniation • SCI lesion length <sup>e</sup> Secondary (potential confounding) factors <u>Clinical</u> • Baseline ASIA motor score • Baseline ASIA impairment scale (severity of SCI)	Neurologic • Last follow-up ASIA motor score Function and Pain NR Safety NR
Selden (1999) Retrospective cohort Risk of bias: Moderately high	N = 55 Sex: 65.5% (36/55) male Mean age: 29.2 (2-92) years F/U: Mean 18.5 (1-74) months F/U %: NR	Population: Patients with traumatic closed cervical (C1-T1) myelopathy Intervention: Patients with MRI-documented spinal cord compression underwent immediate surgical decompression and fusion. Patients without spinal cord compression underwent urgent surgery for spinal column stabilization within 48 hours. SCI Severity (Initial Frankel grade) • A: 58.2% (32/55) • B: 16.4% (9/55) • C: 14.5% (8/55) • D: 10.9% (6/55)	MRI characteristics: Sagittal and axial T1- and T2-weighted MR images were obtained using a 1.5-Tesla scanner. MRI assessment: All images were interpreted by an attending neuroradiologist who was blinded to the clinical status of the patients.	MRI timing with regard to injury: MR images were obtained within 21 (mean 7.8) hours of injury. MRI timing with regard to intervention: All MRIs were obtained prior to intervention. Emergency interventions occurred at a mean time of 13.6 hours after injury, and urgent interventions occurred at a mean time of 28.7 hours after injury.	Radiographic • Maximal cross-sectional diameter within swollen length of the cord • Spinal cord compression • Length of cord swelling • Length of cord edema • Length of cord hematoma Secondary (potential confounding) factors <u>Clinical</u> Admission Frankel grade	Neurologic • Follow-up Frankel grade Function and Pain NR Safety NR

(continued)

Table 5. (continued)

Study	Demographics	Baseline Population Definition and Characteristics	Baseline MRI Characteristics and Assessment	MRI Timing: Injury and Intervention	Prognostic Factors Evaluated	Outcome Measures Evaluated <sup>a</sup>
Shepard (1999) Prospective cohort (secondary analysis of data collected prospectively in a RCT)	N = 191 Sex: 84.8% (162/ 191) male Age (years) • 14-22: 25.6% (49/191) • 23-34: 28.3% (54/191) • 35-50: 21.5% (41/191) • >50: 24.6% (47/ 191) F/U: Mean 6 weeks F/U %: NR	Population: Patients randomized in the National Acute Spinal Cord Injury Study (NASCIS) 3 who had MR imaging within 72 hours of injury. The purpose of the RCT was to evaluate the efficacy and safety of methylprednisolone infused over 48 hours, or tirilazad mesylate administered every 6 hours for 48 hours with 24 hours of methylprednisolone. Intervention: Spinal surgery was performed within 3 days in 45.0% (86/191) of patients. Extent of Injury (determined by neurologic and radiologic exams) Complete: 39.3% (75/191) Incomplete: 45.5% (87/191) Normal: 15.2% (29/191)	MRI characteristics: Sagittal and axial T1- and T2-weighted MR imaging with 3-5 mm slices. Technical information on the MR imaging unit was not provided. MRI assessment: Results of MR images were transcribed from the MRI report onto the NASCIS forms by study neurosurgical nurses, or were read directly from the image onto the NASCIS forms by the neurosurgeon associated with NASCIS 3.	MRI timing with regard to injury: MR images were obtained within 72 hours of injury; 51.8% (99/ 191) received MRI within 9 hours of injury, and 48.2% (92/ 191) received MRI > 9 hours after injury. MRI timing with regard to intervention: NR	Radiographic • Cord edema • Hemorrhage • Contusion Secondary (potential confounding) factors Clinical • Drug protocol (randomized group) • Extent of injury (complete/ incomplete) • Spinal cord surgery (yes/ no) • Baseline pin prick score <sup>f</sup> • Baseline light touch score <sup>f</sup> • Baseline motor function score <sup>f</sup>	Neurologic • Pin prick score <sup>f</sup> • Light touch score <sup>f</sup> • Motor function score <sup>f</sup> Function and Pain NR Safety NR

(continued)

**Table 5.** (continued)

Study	Demographics	Baseline Population Definition and Characteristics	Baseline MRI Characteristics and Assessment	MRI Timing: Injury and Intervention	Prognostic Factors Evaluated	Outcome Measures Evaluated <sup>a</sup>
Wilson (2012) Prospective cohort (combined 2 prospectively collected databases with similar data elements) Risk of bias: Moderately low	N = 376 Sex: 78.2% (294/376) male Mean age: 43.2 ± 16.9 years F/U: NR 17.6% (66/376); 12 months 82.4% (310/376); Overall 54.0% (376/696)	<i>Population:</i> Patients who were prospectively enrolled in the North American Clinical Trials Network SCI registry or the Surgical Timing in Acute Spinal Cord Injury Study multicenter cohort study. <i>Intervention:</i> Decisions surrounding surgery, including timing, were made by the attending spine surgeon in each case. Mean time to decompressive surgery post-injury was 76.1 (± 338.9) hours. <i>SCI Severity (ASIA Impairment scale)</i> • A: 36.2% (136/376) • B: 16.8% (63/376) • C: 15.4% (58/376) • D: 31.7% (119/376)	<i>MRI characteristics:</i> T1- and T2-weighted images were obtained using standard protocols. <i>MRI assessment:</i> Images were read by a site-specific neuroradiologist.	<i>MRI timing with regard to injury:</i> MR images were obtained within 3 days of injury. <i>MRI timing with regard to intervention:</i> NR	<i>Radiographic</i> • MRI signal characteristics consistent with edema or hemorrhage <i>Secondary (potential confounding) factors</i> <u>Demographic</u> • Age <u>Clinical</u> • Initial ASIA motor score (<50 or >50) • Initial ASIA impairment scale grade	<i>Neurologic</i> NR <i>Function and Pain</i> • FIM motor score <sup>s</sup> • Functional independence (dichotomized variable) <sup>s</sup> Safety NR

Abbreviations: ASIA, American Spinal Injury Association; CCS, central cord syndrome; CT, computed tomography; F/U, follow-up; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; NR, not reported; MR, magnetic resonance; MRI, magnetic resonance imaging; NASCIS, National Acute Spinal Cord Injury Study; NR, not reported; SCI, spinal cord injury.

<sup>a</sup>Only reported outcome measures related to study question.

<sup>b</sup>Aarabi (2011):  $MCC = \{1 - Di/[1/2(Da + Db)]\} \times 100$ , where Di is the midsagittal diameter of the spinal canal at the point of maximum compression, Da is the diameter of the spinal canal one segment above the highest level of spinal stenosis, and Db is the diameter of the spinal canal one segment below the lowest level of spinal stenosis.  $MSCC = \{1 - di/[1/2(da + db)]\} \times 100$ , where da is the diameter of the spinal cord at a normal segment above the highest level of spinal stenosis, and di is the diameter of the spinal cord at the level of maximum stenosis. *Manual dexterity level* was defined as the patient's own perception of dexterity and skill in the following tasks: (1) using a keyboard, (2) playing a musical instrument, (3) buttoning his/her shirt, (4) grooming, and (5) writing. *Dyesthetic pain level* was a subjective rating on a 0 to 10 analog scale.

<sup>c</sup>Flanders (1996): Satisfactory quality rating was defined on a sagittal T1-weighted spin echo (or the combination of sagittal T2-weighted fast spin-echo acquisition and sagittal gradient-echo) sequence.

<sup>d</sup>Flanders (1996): *Extremity motor function* was assessed by testing key individual muscles in the upper and lower extremities. Each muscle received a score of 0 to 5 for a total possible motor index score of 50 for upper extremity function and 40 for lower extremity function. *Minimally useful motor function* in an individual muscle was defined as a score of 3 or better on the 5-point manual muscle test. A score of 3 represents the ability for active movement with a full range of motion against gravity.

<sup>e</sup>Miyajiri (2007): *MCC/MSCC* was defined as described by Fehlings MG, Rao SC, Tator CH, et al. The optimal radiologic method for assessing spinal canal compromise and cord compression in patients with cervical spinal cord injury. Part II: results of a multicenter study. *Spine*. 1999;24(6):605-613. *Soft-tissue injury* was defined as an increased signal intensity of the perivertebral tissues on T2-weighted images. *Spinal cord lesion length* was defined as the distance between the most cephalic and the most caudal extent of the cord signal intensity change on T2-weighted images.

<sup>f</sup>Shepard (1999): *Pin prick/light touch* score was determined as follows: 29 spinal cord segments were tested bilaterally for response to pin prick and light touch, each of which were scored at 1 = absent, 2 = dysfunctional, and 3 = normal. Sensory scores ranged from a total score of 87 (normal response) to a score of 29 (no response in any segment). Responses for the right side were summed, unless some cord segments could not be tested, in which case responses for the left side were used. *Motor function* score was determined by bilaterally measuring fourteen muscle roots, with 0 = no contraction, 1 = flicker/trace of contraction, 2 = active movement without antigravity, 3 = active movement with antigravity, 4 = active movement against resistance, and 5 = normal. The responses for the right side were summed and ranged from 0 to 70.

<sup>g</sup>Wilson (2012): The *FIM motor* score consists of 13 items that assess function across 4 different domains of self-care, sphincter control, transfers, and locomotion. The performance level for each item is strictly defined and ranges in value from 1 to 7, where 1 indicates complete dependence in an activity, and a score of 6 or greater indicates that a patient is capable of performing that activity independently, without supervision or help. The result is a discrete outcome variable with a minimum value of 13 and a maximum value of 91, with a larger value implying superior function. *Functional dependence* was a dichotomous variable defined as having achieved/not achieved ≥ 6 for all 13 FIM score items.

**Table 6.** Association Between MRI and Other Factors and Neurologic, Functional, and Pain Outcomes.

Potential Prognostic Factors	Outcome Measures <sup>a</sup>	
	Neurologic Recovery <sup>b</sup>	Functional and Pain Recovery <sup>c</sup>
<b>Radiographic</b>		
Lower MCC	O (Miyanji)/– (Aarabi)	O/– (Aarabi)
Lower MSCC	O (Aarabi, Miyanji, Selden)	O (Aarabi)
Smaller spinal canal diameter at MSCC (mm)	– (Aarabi)	O (Aarabi)
Smaller diameter within swollen length of cord	O (Selden)	
Longer SCI lesion length (mm)	O (Aarabi, Miyanji)	O/– (Aarabi)
Cord edema	O (Boldin, Miyanji, Shepard)	
Intramedullary hemorrhage or intra-axial hematoma	O (Boldin, Shepard)/– (Miyanji, Flanders, Selden)	
Edema or hemorrhage		O (Wilson)
Cord swelling	– (Miyanji)	
Soft-tissue injury <sup>d</sup>	O (Miyanji)	
Preinjury stenosis	O (Miyanji)	
Disk herniation	O (Miyanji)	
Cord contusion	O (Shepard)	
Longer edema lesion length	O (Boldin, Selden)/– (Flanders)	
Rostral point of edema	O (Flanders)	
Longer hemorrhage lesion or cord hematoma length	– (Boldin, Selden) <sup>e</sup>	
Longer cord swelling length	O (Selden)	
<b>Secondary (potentially confounding) factors</b>		
<i>Demographic</i>		
Older age	O (Aarabi)	O/–/+ (Aarabi, Wilson)
<i>Clinical</i>		
Lower ASIA Impairment Score (Admission)	O (Boldin, Miyanji)	– (Wilson)
Lower ASIA Motor Score (Admission)	– (Aarabi, Miyanji, Flanders)	O/– (Aarabi)
ASIA Motor Score ≤ 50		– (Wilson)
Lower Frankel Score (Admission)	– (Selden)	
Worse baseline pin prick score <sup>†</sup>	O (Shepard)	
Worse baseline light touch score <sup>†</sup>	O (Shepard)	
Worse baseline motor function score <sup>†</sup>	O (Shepard)	
Mechanism of injury	O (Aarabi)	O (Aarabi)
Number of stenotic skeletal segments	O (Aarabi)	O (Aarabi)
Surgical technique (front, back, circumferential decompression)	O (Aarabi)	O (Aarabi)
Time delay after injury until surgery	O (Aarabi)	O (Aarabi)

Abbreviations: ASIA, American Spinal Injury Association; FIM, Functional Independence Measure; MCC, maximum canal compromise; MRI, magnetic resonance imaging; MSCC, maximum spinal cord compression; NS, not significant; SCI, spinal cord injury.

(O) = no association; (–) = association with a negative outcome; (O/–) = no association in one publication **or** with one outcome, association with a negative outcome in a second publication or with another outcome; (O/–/+) = no association in one publication or with one outcome, association with a negative outcome in a second publication or with another outcome, association with a positive outcome in a third publication or with another outcome.

<sup>a</sup>Results presented as reported by the authors based on multivariate regression analyses, adjusted for baseline neurologic status.

<sup>b</sup>Neurologic recovery: ASIA Impairment Scale grade, Frankel grade, ASIA Motor score, motor function score, upper/lower extremity motor function and minimally useful function, pin prick score, light touch score. Motor function score was determined by bilaterally measuring 14 muscle roots, with 0 = no contraction, 1 = flicker/trace of contraction, 2 = active movement without antigravity, 3 = active movement with antigravity, 4 = active movement against resistance, and 5 = normal. The responses for the right side were summed and ranged from 0 to 70. Extremity motor function was assessed by testing key individual muscles in each of the upper and lower extremities. Each muscle received a score of 0 to 5 for a total possible motor index score of 50 for upper extremity function and 40 for lower extremity function. Minimally useful motor function in an individual muscle was defined as a score of 3 or better on the 5-point manual muscle test. A score of 3 represents the ability for active movement with a full range of motion against gravity. Pin prick/light touch score was determined as follows: 29 spinal cord segments were tested bilaterally for response to pin prick and light touch, each of which were scored at 1 = absent, 2 = dysfunctional, and 3 = normal. Sensory scores ranged from a total score of 87 (normal response) to a score of 29 (no response in any segment). Responses for the right side were summed, unless some cord segments could not be tested, in which case responses for the left side were used.

<sup>c</sup>Functional recovery: FIM Motor Score, functional dependence, manual dexterity, dysesthetic pain. Functional dependence was a dichotomous variable defined as having achieved/not achieved ≥6 for all 13 FIM score items. Manual dexterity level was defined as the patient's own perception of dexterity and skill in the following tasks: (1) using a keyboard, (2) playing a musical instrument, (3) buttoning his/her shirt, (4) grooming, and (5) writing. Dysesthetic pain level was a subjective rating on a 0 to 10 analog scale.

<sup>d</sup>Miyanji (2007): Soft-tissue injury was defined as an increased signal intensity of the perivertebral tissues on T2-weighted images.

<sup>e</sup>When length of hematoma was added to the statistical model, the only significant predictor in the model was length of hematoma.



of manual dexterity and dysesthetic pain.<sup>17</sup> MSCC and the spinal canal diameter at MSCC were not predictive of any measure of functional recovery.<sup>17</sup> There was no association between SCI lesion length and FIM score; however, a longer SCI lesion length was related to worse manual dexterity and dysesthetic pain.<sup>17</sup> Finally, based on a single study, MRI signal characteristics consistent with edema or hemorrhage are not important predictors of functional outcomes.<sup>16</sup>

### **Spinal Cord Lesion Characteristics, Pattern, and Length Identified on Baseline Diffusion Tensor Imaging MRI as Predictors of SCI Outcomes**

No studies were identified that assessed the association between DTI characteristics and outcomes.

### **Cost-Effectiveness of Baseline MRI in Patients With Acute SCI**

No full economic analyses were identified that assessed the cost-effectiveness or cost utility of MRI in patients with acute SCI.

### **Evidence Summary**

For KQ1, the overall quality of evidence was “Very Low” that patients who received a baseline MRI had an average improvement of 0.7 in Frankel grade compared to those who did not receive an MRI. Definitive conclusions are not possible from this study due to risk of bias (selection bias), lack of precision, and lack of data regarding the outcome of interest; specifically, details on the impact of MRI on clinical decision making were not reported (Table 7).

For KQ2, Tables 8 and 9 summarize the overall quality of evidence for prognostic factors. There is “Moderate” quality evidence that longer intramedullary hemorrhage and “Low” quality evidence that smaller spinal canal diameter at MSCC are associated with decreased neurologic recovery. There is “Moderate” evidence that lower MSCC, longer SCI lesion length, and cord edema are not associated with worse neurologic recovery. There is inconsistent evidence that presence of hematoma (“Low”), greater edema lesion length (“Very Low”), cord swelling (“Low”), and MCC (“Low”) are predictive of worse neurologic recovery. MCC was the only significant predictor of worse functional outcome (“Low”). There is substantial heterogeneity across these studies with respect to the prognostic factors evaluated as well as in definitions and methods of measurement. Furthermore, there is variability in the measures used to evaluate outcomes, limiting our ability to synthesize findings across studies. In most instances, effect sizes and confidence intervals were not provided, preventing the evaluation of precision and magnitude of effect.

The following list summarizes the findings from the included prognostic studies (Tables 8 and 9):

- *Longer hemorrhage length (“Moderate Evidence”)*: Two studies observed an association between longer hemorrhage length and worse neurologic recovery. Of these, one reported substantially longer hematoma length in ASIA A patients (no change in Frankel grade by follow-up) than in ASIA B, C, D patients (lower Frankel grades at follow-up); adjusted estimates were available only for patients with complete SCI.
- *Hemorrhage (“Low Evidence”)*: Three studies reported an association between the presence of hemorrhage on MRI and worse neurologic recovery; 2 other studies found no association. Each used different measures of neurologic outcome.
- *Cord edema*: Three studies reported no association between cord edema and neurologic function; each used different measures of neurologic outcome (“Moderate Evidence”). Based on a single study, rostral point of edema was not predictive of neurologic outcomes (“Very Low Evidence”).
- *Longer edema lesion length (“Very Low Evidence”)*: A single study reported an association between longer edema lesion length and worse neurologic recovery; 2 other studies found no association.
- *Lower MSCC*: There is no association between MSCC and either neurologic recovery (“Moderate Evidence”) or functional recovery (“Low Evidence”). Three studies reported no association with neurologic recovery. MSCC and the spinal canal diameter at MSCC were not predictive of functional outcomes in one study.
- *Lower MCC*: One study reported an association between lower MCC and worse neurologic recovery; another study found no association (“Low Evidence”). Lower MCC was associated with worse FIM scores but not with manual dexterity or dysesthetic pain in one study (“Low Evidence”).
- *SCI lesion length*: Two studies reported no association between SCI lesion length and neurologic recovery (“Moderate Evidence”). Based on a single study, SCI lesion length was not associated with FIM score (“Low Evidence”); however, a longer SCI lesion length was predictive of worse manual dexterity and dysesthetic pain (“Low Evidence”).
- *Cord swelling (“Low Evidence”)*: A single study reported an association between cord swelling and worse neurologic recovery.
- *Length of cord swelling (“Very Low Evidence”)*: A single study reported no association between length of cord swelling and neurologic recovery.

There were no studies that assessed DTI MRI characteristics as predictors of SCI outcome (KQ3) or the cost-effectiveness of MRI (KQ4); there is therefore insufficient evidence to draw conclusions for these questions.

**Table 7.** Quality (Strength) of Evidence Summary for Studies Evaluating the Impact of MRI on Treatment Decisions and Clinical Outcomes.

*Question 1: How does MRI influence management strategy(ies), such as surgical timing and approach, and/or neurologic, functional, patient-reported, and safety outcomes?*

Outcome	Studies; N; Follow-up	Risk of Bias <sup>a</sup>	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Conclusions/Effect Size
Neurologic	1 Prospective cohort (Papadopoulos, 2002) N = 91 2-96 months	Serious risk of bias <sup>a</sup>	No serious inconsistency	No serious indirectness	Serious risk of imprecision	Undetected	Very Low	Patients with traumatic closed cervical SCI who received a baseline MRI achieved a significant Frankel grade improvement compared to those who did not ( $P < .006$ ); however, there is little confidence in the estimate of effect and no strong conclusions can be made. Furthermore, it is not clear if 7/10 of a Frankel grade constitutes a clinically meaningful change. The influence of MRI on treatment strategy was not directly assessed.
Functional, patient-reported, safety	NR						Insufficient	No studies were identified that assessed the influence of baseline MRI on functional, patient-reported, or safety outcomes.

*Question 4: Is there evidence to suggest that baseline MRI is cost-effective in patients with acute SCI?*

Outcome	Studies; N; Follow-up	Risk of Bias <sup>a</sup>	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence
Cost-effectiveness of baseline MRI	NR						Insufficient

Abbreviations: MRI, magnetic resonance imaging; SCI, spinal cord injury.

<sup>a</sup>Serious risk of bias: The majority of studies violated 2 or more criteria of a good-quality cohort (see the supplemental material for details; available online at <http://journals.sagepub.com/home/gsi>).

No studies were identified that assessed the cost-effectiveness of baseline MRI in patients with acute SCI.

**Table 8.** Quality (Strength) of Evidence Summary for MRI Predictors of Neurological Recovery<sup>a</sup>.

Prognostic Factor	Studies; N; Follow-up	Inconsistency	Indirectness	Imprecision	Overall Quality of Evidence	Conclusions, Effect Size
Lower MCC	1 Prospective cohort (Miyanji, 2007); 1 Retrospective cohort (Aarabi, 2011) N = 142 13.7 months	Inconsistent	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	Results were inconsistent across 2 studies with moderately low risk of bias. A large prospective study reported no association between MCC and neurological outcomes (no effect estimates or <i>P</i> values provided, Miyanji), while a second study demonstrated an association between a lower MCC and worse ASIA motor scores ( <i>P</i> = .02, no effect size estimates or confidence intervals were provided, Aarabi).
Lower MSCC	1 Prospective cohort (Miyanji, 2007); 2 Retrospective cohorts (Aarabi, 2011; Selden, 1999) N = 197 15.1 months	No serious inconsistency	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Moderate	Three studies (2 with moderately low risk of bias, 1 with moderately high risk of bias) reported no association between lower MSCC and neurologic recovery. None of these studies provided effect size estimates or confidence intervals.
Smaller spinal canal diameter at MSCC (mm)	1 Retrospective cohort (Aarabi, 2011) N = 42 12 months	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	In one small study with moderately low risk of bias, smaller spinal canal diameter at MSCC was associated with worse neurologic recovery (ASIA motor score, <i>P</i> = .02; no effect sizes or confidence intervals provided).
Smaller diameter within swollen length of cord	1 Retrospective cohort (Selden, 1999) N = 55	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	A single study with moderately high risk of bias reported no association between diameter within swollen length of cord and neurologic recovery; no effect sizes or confidence intervals were provided.
Longer SCI lesion length (mm)	1 Prospective cohort (Miyanji, 2007); 1 Retrospective cohort (Aarabi, 2011) N = 142 13.7 months	No serious inconsistency	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Moderate	Two studies with moderately low risk of bias reported no association between longer SCI lesion length and neurologic recovery; no effect size estimates or confidence intervals were provided in either study.
Cord edema	3 Prospective cohorts (Miyanji, 2007; Shepard, 1999; Boldin, 2006) N = 320 6.3 months	No serious inconsistency	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Moderate	Three studies with moderately low risk of bias reported no association between cord edema and neurologic recovery. Only one of these provided an adjusted effect size at 6 weeks. Change in motor score (−3.34, <i>P</i> = .06) and light touch recovery (−3.41, <i>P</i> = .05) suggest reduced neurologic function and a negative association; however, these results were borderline insignificant. Furthermore, change in pin prick recovery (−2.46, <i>P</i> = .16) was not statistically significant (Shepard).

(continued)

**Table 8.** (continued)

Prognostic Factor	Studies; N; Follow-up	Inconsistency	Indirectness	Imprecision	Overall Quality of Evidence	Conclusions, Effect Size
Intramedullary hemorrhage or intra-axial hematoma	3 Prospective cohorts (Boldin, 2006; Miyanji, 2007; Shepard, 1999); 2 Retrospective cohorts (Flanders, 1996; Selden, 1999) N = 479 6 weeks to 17.4 months	Inconsistent	No serious indirectness	Serious risk of imprecision <sup>d</sup>	Low	Across 5 studies (3 with moderately low risk of bias, 2 with moderately high risk of bias), presence of hemorrhage or hematoma was inconsistently associated with worse neurologic recovery. In 3 studies (Miyani, $P = .002$ ; Selden, $P < .001$ ; Flanders, $P < .001$ ), hematoma or hemorrhage was significantly predictive of worse neurologic recovery; none of these studies provided adjusted effect sizes or confidence intervals. Two other studies reported no association with outcome: (1) one provided adjusted effect estimates for neurologic recovery at 6 weeks (change in motor score: $-2.7$ , $P = .29$ , pin prick recovery: $0.63$ , $P = .79$ , light touch recovery: $-0.93$ , $P = .69$ (Shepard)) and (2) the other did not provide a $P$ value on a subanalysis of patients with ASIA A injuries (Boldin).
Cord swelling	1 Prospective cohort (Miyanji, 2007) N = 100 7.3 months	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	In one study with moderately low risk of bias, the association between cord swelling and neurologic recovery (ASIA motor score) was borderline insignificant ( $P = .054$ ) in a multivariate model that included hemorrhage; no effect size estimates or confidence intervals were provided.
Soft-tissue injury <sup>b</sup>	1 Prospective cohort (Miyanji, 2007) N = 100 7.3 months	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	A single study reported no association between soft tissue injury and worse neurologic recovery (ASIA motor score); no $P$ value, effect size estimates or confidence intervals were provided.
Preinjury stenosis	1 Prospective cohort (Miyanji, 2007) N = 100	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	A single study reported no association between preinjury stenosis and worse neurologic recovery (ASIA motor score); no $P$ value, effect size estimates or confidence intervals were provided.
Disk herniation	1 Prospective cohort (Miyanji, 2007) N = 100	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	A single study reported no association between disc herniation stenosis and worse neurologic recovery (ASIA motor score); no $P$ value, effect size estimates or confidence intervals were provided.

(continued)

**Table 8.** (continued)

Prognostic Factor	Studies; N; Follow-up	Inconsistency	Indirectness	Imprecision	Overall Quality of Evidence	Conclusions, Effect Size
Cord contusion	1 Prospective cohort (Shepard, 1999) N = 191	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Low	A single study reported no association between the presence of cord contusion and neurological recovery at 6 weeks (change in motor score: -0.36, pin prick recovery: -3.35, or light touch recovery: -1.38; confidence intervals were not provided).
Longer edema lesion length	1 Prospective cohort (Boldin, 2006); 2 Retrospective cohorts (Selden, 1999; Flanders, 1996) N = 188 17.4 months	Inconsistent	No serious indirectness	Serious risk of imprecision <sup>e</sup>	Very Low	Across 3 studies (1 prospective study with moderately low risk of bias and 2 retrospective studies with moderately high risk of bias), longer edema length was inconsistently associated with worse neurologic recovery. A single retrospective study reported that longer edema lesion length was associated with decreased extremity function ( $P = .03$ for decreased upper and lower extremity function, $P < .01$ for lower extremity muscles with useful function) but not with decreased upper extremity muscles with useful function (Flanders). A second retrospective study also reported no association between edema lesion length and neurologic recovery ( $P = .071$ ) (Selden). In the third study, longer edema length was the only predictor of retaining complete SCI in patients with or without hemorrhage. Specifically, each mm increase in edema length increased the risk of retaining a complete SCI (1.15, 95% CI 1.03 to 1.29); however, this variable was no longer predictive following the addition of hematoma length to a multivariate model in 8 patients with ASIA A injury.
Rostral point of edema	1 Retrospective cohort (Flanders 1996) N = 104 Mean: $\geq 12$ months	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Very Low	A single retrospective study with moderately high risk of bias reported no association between rostral point of edema and decreased upper or lower extremity motor function; no effect size estimates or confidence intervals were provided.

(continued)

**Table 8.** (continued)

Prognostic Factor	Studies; N; Follow-up	Inconsistency	Indirectness	Imprecision	Overall Quality of Evidence	Conclusions, Effect Size
Longer hemorrhage lesion or cord hematoma length	1 Prospective cohort (Boldin, 2006); 1 Retrospective cohort (Selden, 1999) N = 84 24.2 months	No serious inconsistency	No serious indirectness	Serious risk of imprecision <sup>e</sup>	Moderate	Across 2 studies (one prospective study with moderately low risk of bias and one retrospective study with moderately high risk of bias), longer hemorrhage length was associated with worse neurological outcome. In the retrospective study, no effect size estimates or confidence intervals were provided ( $P = .028$ ). In the small prospective study, longer hemorrhage length was associated with risk of retaining a complete SCI in a subgroup multivariate model in 8 patients with ASIA A at baseline (OR 1.81 (1.09, 3.02), $P = .02$ ) (Boldin).
Longer cord swelling length	1 Retrospective cohort (Selden, 1999) N = 55 18.5 months	Inconsistency unknown <sup>c</sup>	No serious indirectness	Serious risk of imprecision <sup>b</sup>	Very Low	A single retrospective study with moderately high risk of bias reported no association between length of cord swelling and neurologic recovery.
Adverse events and Safety outcomes	NR					

Abbreviations: ASIA, American Spinal Injury Association; DTI, diffusion tensor imaging; FIM, Functional Independence Measure; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; MRI, magnetic resonance imaging; NR, no reported studies; SCI, spinal cord injury.

<sup>a</sup>Neurologic recovery: ASIA Impairment Scale grade, Frankel grade, ASIA Motor score, motor function score, upper/lower extremity motor function and minimally useful function, pin prick score, light touch score. *Motor function score* was determined by bilaterally measuring fourteen muscle roots, with 0 = no contraction, 1 = flicker/trace of contraction, 2 = active movement without antigravity, 3 = active movement with antigravity, 4 = active movement against resistance, and 5 = normal. The responses for the right side were summed and ranged from 0 to 70. *Extremity motor function* was assessed by testing key individual muscles in each of the upper and lower extremities. Each muscle received a score of 0 to 5 for a total possible motor index score of 50 for upper extremity function and 40 for lower extremity function. *Minimally useful motor function* in an individual muscle was defined as a score of 3 or better on the 5-point manual muscle test. A score of 3 represents the ability for active movement with a full range of motion against gravity. *Pin prick/light touch score* was determined as follows: 29 spinal cord segments were tested bilaterally for response to pin prick and light touch, each of which were scored at 1 = absent, 2 = dysfunctional, and 3 = normal. Sensory scores ranged from a total score of 87 (normal response) to a score of 29 (no response in any segment). Responses for the right side were summed, unless some cord segments could not be tested, in which case responses for left side were used.

<sup>b</sup>No adjusted effect size estimates and/or no confidence intervals reported.

<sup>c</sup>Single study; consistency across studies cannot be assessed for this outcome.

<sup>d</sup>Downgrade for imprecision: Small sample size for subgroup analysis (8 out of 9 patients with ASIA A) in one study (Boldin) and inability to assess precision as effect sizes and confidence intervals were not provided in 4 of the 5 studies.

<sup>e</sup>Downgrade for imprecision: Small sample size for subgroup analysis (8 out of 9 patients with ASIA A) in one study (Boldin) and inability to assess precision in the other study as effect sizes and confidence intervals were not provided.

## Discussion

Magnetic resonance imaging has revolutionized the ability of clinicians to determine the location of traumatic injury in the spinal cord as well as identify disruptions in tissues that constitute the spinal canal. The purpose of this systematic review was to assess the role of MRI in clinical decision making and outcome prediction.

### *The Role of MRI to Assist Clinical Decision Making (KQ1)*

MRI is widely used by many clinicians in the context of acute SCI to assist with clinical decision making. Unfortunately, our

review only identified a single study (very low evidence) to address this question. In the study by Papadopoulos et al, the authors indicated that MRI findings influenced the timing of surgery with 34/66 (52%) receiving emergency surgery due to ongoing spinal cord compression and 16/66 (24%) undergoing anterior surgery due to the presence of anterior cord compression. As a result, the authors concluded that “emergency MRI provided an essential tool for the accurate diagnosis of spinal cord compression and directly influenced (our) initial clinical management in the majority of protocol patients.” Unfortunately, details regarding the surgical management of the reference group (no MRI) were not reported, making it impossible to draw firm conclusions about the utility of MRI in decision

**Table 9.** Quality of Evidence Summary for MRI Predictors of Functional Recovery and Pain<sup>a</sup>.

Prognostic Factor	Studies; N; Follow-up	Inconsistency	Indirectness	Imprecision	Overall Quality of Evidence	Conclusions, Effect Size
Lower MCC	I Retrospective cohort (Aarabi, 2011) N = 42 29.1 months	Inconsistency unknown <sup>b</sup>	No serious indirectness	Serious risk of imprecision <sup>c</sup>	Low	In one small retrospective cohort study with moderately low risk of bias, lower MCC was associated with worse FIM score at follow-up ( $P = .02$ ) but not with manual dexterity ( $P = .10$ ) or dysesthetic pain ( $P = .24$ ); no effect size or confidence intervals were reported.
Lower MSCC		Inconsistency unknown <sup>b</sup>	No serious indirectness	Serious risk of imprecision <sup>c</sup>	Low	In one small retrospective cohort study with moderately low risk of bias, lower MSCC was not associated with worse FIM score ( $P = .47$ ), manual dexterity ( $P = .10$ ), or dysesthetic pain ( $P = .20$ ); no effect size or confidence intervals were reported.
Smaller spinal canal diameter at MSCC (mm)		Inconsistency unknown <sup>b</sup>	No serious indirectness	Serious risk of imprecision <sup>c</sup>	Low	In one small retrospective cohort study with moderately low risk of bias, smaller spinal canal diameter at MSCC was not associated with worse FIM score ( $P = .10$ ), manual dexterity ( $P = .25$ ), or dysesthetic pain ( $P = .42$ ); no effect size or confidence intervals were reported.
Longer SCI lesion length (mm)		Inconsistency unknown <sup>b</sup>	No serious indirectness	Serious risk of imprecision <sup>c</sup>	Low	In one small retrospective cohort study with moderately low risk of bias, longer SCI lesion length was associated with worse manual dexterity ( $P = .002$ ) and dysesthetic pain ( $P = .04$ ) but not with worse FIM score ( $P = .16$ ); no effect size or confidence intervals were reported.
MRI signal characteristics consistent with edema or hemorrhage	I Prospective cohort (Wilson, 2012) N = 376 6-12 months	Inconsistency unknown <sup>b</sup>	No serious indirectness	Serious risk of imprecision <sup>d</sup>	Low	In one prospective cohort study with moderately low risk of bias, MRI characteristics consistent with edema or hemorrhage were not associated with FIM score ( $P = .19$ ; no effect size or confidence interval provided) or functional independence at 12 months (OR 0.75; no confidence interval provided; $P = .54$ ).

Abbreviations: FIM, Functional Independence Measure; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; MRI, magnetic resonance imaging; OR, odds ratio; SCI, spinal cord injury.

<sup>a</sup>FIM = Functional dependence was a dichotomous variable defined as having achieved/not achieved  $\geq 6$  for all 13 FIM score items.

<sup>b</sup>Single study; consistency across studies cannot be assessed for this outcome.

<sup>c</sup>No adjusted effect size estimates or no confidence intervals reported, therefore cannot assess precision.

<sup>d</sup>No confidence interval for the odds ratio was reported, therefore cannot assess precision.

making. A direct comparison, however, was made in terms of outcome; specifically, patients who received an MRI (and treatment based on MRI results) exhibited an additional improvement of 0.7 in Frankel grade compared to those in the reference group. This study had moderately high risk of bias, including evidence of strong selection bias. The authors assigned patients to the reference group (no MRI) due to a contraindication to MRI, another emergent surgical procedure, or based on “perceived futility of treatment” by the attending physician. These criteria for group assignment likely introduce a systematic bias in subsequent treatment decisions. Thus, the results of this single study are not sufficient to confidently

suggest that MRI is beneficial in improving decision making. No other studies were identified that specifically evaluated differences in treatment decisions, such as surgical timing and approach, between subject groups with and without pretreatment MRI. As a result, the overall quality of evidence for KQ1 was very low. This lack of evidence suggests that a profound knowledge gap exists and that future methodologically rigorous comparative studies are needed.

Additional lines of indirect evidence have suggested that MRI can accurately identify specific clinical entities that may be important in clinical decision making. A large number of studies have demonstrated MRI to be useful in identifying ongoing

spinal cord compression, ligamentous injury, disc herniation, and vertebral artery injury.<sup>2</sup> These factors may influence surgical timing, approach, and need for instrumentation. However, the vast majority of studies on this topic did not meet our inclusion criteria as they did not (1) provide information on longitudinal follow-up, (2) compare decision-making choices between patients with and without MRI, or (3) provide estimates of effect on clinical outcomes that adjusted for baseline neurological status. Our approach was to focus on studies that evaluated the effect of MRI on treatment decisions and subsequent outcomes; unfortunately, only one study satisfied the inclusion criteria for this key question. The systematic review by Bozzo et al<sup>2</sup> synthesized a broader pool of studies in the context of acute SCI and developed a weak recommendation (based on weak evidence) for the use of MRI to direct clinical management. However, this systematic review had a number of methodological weaknesses and was rated as poor to moderate quality with a score of 5/11 on the AMSTAR scale (see supplemental material, available in the online version of the article). Furthermore, many of the individual studies (1) either did not report the timing of MRI relative to injury or surgical intervention or reported a broad range of acquisition timing (0-14 days) and/or (2) did not report adjusted estimates of effect on recovery at later follow-up. To better characterize the benefits of MRI, there is a need for future research in the form of well-designed prospective studies that compare the impact of MRI on patient management and outcomes to alternate strategies (eg, no use of MRI).

### *Conventional MRI for Prognostication (KQ2)*

Existing evidence suggests that certain MRI characteristics are important predictors of outcomes in acute SCI, including length of intramedullary hemorrhage and the canal diameter at the level of MSCC. Other imaging characteristics may also be useful for prognostication, such as alternative measures of canal stenosis, presence of hemorrhage, and longer edema length; however, findings related to these predictors were inconsistent. Substantial heterogeneity exists with respect to the reporting and measurement of MRI features and clinical outcomes and limits our ability to synthesize findings across studies.

Prognostic studies included in this review identified that length of intramedullary hemorrhage (moderate-quality evidence), spinal canal diameter at the location of MSCC (low-quality evidence), and baseline neurological status are important predictors of outcome. Longer hemorrhage length was independently predictive of worse neurologic outcomes in 2 studies, particularly in patients with complete (AIS A) injuries. In addition, 3 of 5 studies reported that the presence of hemorrhage is associated with worse neurological outcomes, while 2 other studies observed an insignificant association (low-quality evidence). Overall, hemorrhage (length and presence) appears to be a predictor of worse outcomes; however, this finding must be interpreted with caution due to the inconsistency of results across studies. One small study suggested that length of hemorrhage greater than 4 mm is predictive of poor prognosis,<sup>13</sup> and that each millimeter increase in

hematoma length increases the risk of retaining complete impairment (AIS A); these results need to be confirmed in larger prospective studies with a priori hypotheses. Similarly, the finding that decreased canal diameter at the location of MSCC is associated with worse neurologic outcome also needs to be replicated in a larger cohort. Two additional MRI features were inconsistently associated with outcomes (MCC and greater edema lesion length) and therefore also warrant further study. Other MRI characteristics were not statistically associated with clinical outcomes; however, the level of evidence was either low or very low, suggesting that future research may yield different results.

These prognostic studies were largely exploratory, investigated numerous MRI features, and had variable definitions of what constitutes SCI lesion, hemorrhage, edema, and swelling. For example, several studies categorized any abnormal T2-weighted signal as a "lesion," whereas another study combined edema and hemorrhage together in a single variable (edema = 1 point, hemorrhage = 2 points).<sup>11</sup> Heterogeneity in imaging protocols and the use of nonstandardized techniques for geometric measurements such as MCC, MSCC, hemorrhage length, and edema length are also potential confounders. Moreover, none of the included studies reported interrater reliability of these methods. Clinical outcomes varied across studies, with many studies reporting on coarse outcomes such as AIS or Frankel grade, rather than more sensitive measures of recovery such as International standards for neurological classification of spinal cord injury (ISNCSCI) motor/sensory scores and Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP).<sup>16</sup> The timing of baseline MRI also varied greatly in the reviewed studies and ranged from hours after hospital admission to 14 days postinjury. The magnitude of effect for associations and corresponding confidence intervals were also not provided in most studies. All of these factors prevented data pooling and synthesis and the development of firm evidence-based conclusions. Given these variations in study design, there remain significant knowledge gaps regarding the association between intramedullary abnormalities in the spinal cord and neurologic, functional, patient-reported, and safety outcomes. Overall, in interpreting the current literature, we have identified that length of hemorrhage (moderate evidence) and decreased canal diameter at the location of MSCC (low evidence) are important predictors of worse neurologic outcomes.

The MRI features extracted from conventional MRI, such as length of hemorrhage, tend to be relatively crude methods for determining the extent of tissue compromise. Computing volume of affected tissue and identifying the location of the pathology in the compromised spinal cord (dorsal vs ventral grey matter and/or specific white matter columns) could further improve prognostic performance. Conventional MRI may have only modest prognostic utility due to its inability to distinguish recoverable from nonrecoverable tissue injury. For example, edema alone, whether limited or extensive, is recoverable. On the other hand, contusion, which may have a MRI signal indistinguishable from edema on T2-weighted images, indicates a more advanced injury condition in which there is permanent loss of neurons. The studies included in this review did



not utilize GRE or SWI sequences that are more sensitive for identifying contusion and microhemorrhages. The results of this review highlight the limitations of the traditional T1- and T2-weighted sequences for detecting more specific patterns of injury and quantifying reversible and irreversible components of damage. These findings confirm the need to further develop advanced MRI techniques that can provide a more detailed view of injury to the spinal cord parenchyma, including DTI, SWI, functional MRI, MR spectroscopy, perfusion imaging, and other sequences sensitive to demyelination, such as magnetization transfer and myelin water fraction.<sup>17,18</sup> However, these advanced MRI methods will inevitably be more time consuming and cannot yet be reliably implemented in a clinical setting due to technical challenges; these include the need for improved signal-to-noise ratio, high field strength (3 T or greater), and complex data analysis that is highly labor intensive. Furthermore, these advanced MRI methods would need to be cost-effective and widely available before they are able to be adopted clinically.

### *The Role of DTI in Prognostication (KQ3)*

No articles were identified that assessed the predictive value of DTI in patients with acute SCI; this constitutes an important knowledge gap. Furthermore, there remains a lack of standardization for spinal cord DTI acquisition. All of these issues present an opportunity for future multicenter studies to evaluate the value and practicality of DTI as a prognostic tool in acute SCI. Since certain quantitative metrics derived from DTI appear to correlate with important microstructural features such as axonal integrity,<sup>17</sup> a standardized approach to DTI that can consistently interpret diffusion changes in the SCI zone, as well as remotely in the spinal cord, may offer powerful predictive information following SCI.

### *Cost-Effectiveness of MRI in Acute SCI (KQ4)*

There are no studies that evaluate the cost-effectiveness of MRI using full economic analyses. Our search did identify one conference abstract that investigated the same cohort as Papadopoulos et al.<sup>19</sup> This abstract by Selden et al (1999) reported that the MRI-protocol group had a significantly shorter intensive care unit and hospital length of stay and decreased duration of ventilator support, resulting in an estimated savings of \$50 300 per case. However, details of the cost estimates were not included, and the authors did not perform a full economic analysis. Thus, a substantial knowledge gap exists regarding the cost-effectiveness of MRI in the early evaluation of patients with SCI, suggesting a strong need for further investigation.

### *Knowledge Gaps and Limitations*

This review has identified several knowledge gaps regarding the role of MRI in clinical decision making and outcome prediction in patients with acute SCI. For each of the key questions addressed, well-designed studies are required to clearly define

the role of MRI, the appropriate methodology of conventional as well as advanced MRI (such as DTI), as well as the cost-effectiveness of these strategies. This future research will help generate clinical practice guidelines that outline the best utility for MRI in SCI.

This systematic review has several limitations. First, although we performed a thorough electronic literature search in several major databases and also manually searched reference lists, it is possible that some relevant studies were missed. We focused this review only on the highest quality studies available that directly addressed the key questions and restricted our inclusion criteria to those that compared MRI versus no MRI for KQ1 and KQ4, and those that performed multivariate analysis for KQ2 and KQ3. As a result, our review included a small number of studies and provides only a limited summary of the research that has occurred to date. However, we felt justified in this approach and believe that broader inclusion criteria would have resulted in the inclusion of lower level evidence and additional heterogeneity.

## **Conclusions**

The overall body of evidence regarding the utility of MRI in acute SCI is limited. It has been established that MRI accurately detects potentially important clinical entities such as cord compression, disc herniation, and ligamentous injury; however, no comparative studies were identified that link MRI with decisions such as surgical approach and timing. Furthermore, only very low quality evidence exists linking the use of MRI in acute SCI to clinical outcomes. It appears that MRI, in addition to baseline neurological status, is useful for prognostication; specifically, moderate-quality evidence suggests that longer intramedullary hemorrhage and low-quality evidence indicates that smaller spinal canal diameter at MSCC are associated with poor neurologic recovery. No literature was identified that investigated DTI as a prognostic tool or assessed the cost-effectiveness of MRI in acute SCI. The paucity of literature in each of these areas highlights the need for well-designed prospective multicenter studies and full economic analyses to better understand the utility and cost-effectiveness of MRI in acute SCI.

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## Supplemental Material

The supplemental material is available in the online version of the article.

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