



**CONGRESS OF NEUROLOGICAL SURGEONS SYSTEMATIC REVIEW AND
EVIDENCE-BASED GUIDELINES ON THE EVALUATION AND TREATMENT OF
PATIENTS WITH THORACOLUMBAR SPINE TRAUMA: HEMODYNAMIC
MANAGEMENT**

Sponsored by: Congress of Neurological Surgeons (CNS) and the Section on Disorders of the Spine and Peripheral Nerves in collaboration with the Section on Neurotrauma and Critical Care

Endorsed by: Joint Guidelines Committee of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS)

Sanjay S. Dhall, MD,¹ Andrew T. Dailey, MD,² Paul A. Anderson, MD,³ Paul M. Arnold, MD,⁴ John H. Chi, MD, MPH,⁵ Kurt M. Eichholz, MD,⁶ James S. Harrop, MD,⁷ Daniel J. Hoh, MD,⁸ Sheeraz Qureshi, MD, MBA,⁹ Craig H. Rabb, MD,¹⁰ P. B. Raksin, MD,¹¹ Michael G. Kaiser, MD,¹² and John E. O'Toole, MD, MS¹³

1. Department of Neurological Surgery, University of California, San Francisco, San Francisco, California

2. Department of Neurosurgery, University of Utah, Salt Lake City, Utah

3. Department of Orthopedics and Rehabilitation, University of Wisconsin, Madison, Wisconsin

4. Department of Neurosurgery, University of Kansas School of Medicine, Kansas City, Kansas
5. Department of Neurosurgery, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts
6. St. Louis Minimally Invasive Spine Center, St. Louis, Missouri
7. Departments of Neurological Surgery and Orthopedic Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania
8. Lillian S. Wells Department of Neurological Surgery, University of Florida, Gainesville, Florida
9. Department of Orthopaedic Surgery, Weill Cornell Medical College, New York, New York
10. Department of Neurosurgery, University of Utah, Salt Lake City, Utah
11. Division of Neurosurgery, John H. Stroger, Jr. Hospital of Cook County and Department of Neurological Surgery, Rush University Medical Center, Chicago, Illinois
12. Department of Neurosurgery, Columbia University, New York, New York
13. Department of Neurological Surgery, Rush University Medical Center, Chicago, Illinois

Correspondence:

Sanjay S. Dhall, MD

Associate Professor, Department of Neurological Surgery

University of California, San Francisco

Director of Spinal Neurotrauma, San Francisco General Hospital

505 Parnassus Avenue

San Francisco, CA 94143-0112

Email: sanjaydhall@gmail.com

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Abbreviations

AISA – American Spinal Injury Association Spinal Injury grade

BP – blood pressure

MAP - mean arterial blood pressure

SCI - spinal cord injury

TLSCI - thoracolumbar spinal cord injury

No part of this article has been published or submitted for publication elsewhere.

ABSTRACT

Background: Thoracolumbar spinal cord injuries (TLSCIs) have been studied less than cervical spinal cord injuries. Much of the management of TLSCI has been extrapolated from cervical spinal cord injuries studies, including the management of blood pressure.

Objective: The task force attempted to answer the question: Does the active maintenance of arterial blood pressure after injury affect clinical outcomes in patients with thoracic and lumbar fractures?

Methods: The task force members identified search terms/parameters and a medical librarian implemented the literature search, consistent with the literature search protocol (see Appendix I), using the National Library of Medicine PubMed database and the Cochrane Library for the period from January 1, 1946, to March 31, 2015.

Results: The task force selected 19 articles for full-text review. Of these, 18 were rejected for not meeting inclusion criteria or for being off topic. The majority of rejected articles did not include TLSCI or did not provide separate analysis of thoracolumbar injuries. One manuscript was selected for inclusion in this systematic review.

Conclusion: There is insufficient evidence to recommend for or against the use of active maintenance of arterial blood pressure after thoracolumbar spinal cord injury. However, considering published data from pooled (cervical and thoracolumbar) spinal cord injury patient populations, clinicians may choose to maintain mean arterial blood pressures >85 mm Hg in an attempt to improve neurological outcomes.

RECOMMENDATIONS

Question

Does the active maintenance of arterial blood pressure after injury affect clinical outcomes in patients with thoracic and lumbar fractures?

Recommendations

There is insufficient evidence to recommend for or against the use of active maintenance of arterial blood pressure after thoracolumbar spinal cord injury.

Level of Evidence: Grade Insufficient

However, in light of published data from pooled (cervical and thoracolumbar) spinal cord injury patient populations, clinicians may choose to maintain mean arterial blood pressures >85 mm Hg in an attempt to improve neurological outcomes.

Consensus Statement by the Workgroup

INTRODUCTION

Goals and Rationale

This clinical guideline was created to improve patient care by outlining the appropriate information-gathering and decision-making processes involved in the evaluation and treatment of patients with thoracolumbar spine trauma. The surgical management of these patients often takes place under a variety of circumstances and by various clinicians. This guideline was created as an educational tool to guide qualified physicians through a series of diagnostic and treatment decisions to improve the quality and efficiency of care.

Thoracolumbar spinal cord injuries (TLSCIs) have historically had a relatively lower incidence and thus have been studied less often than other spinal cord injuries (SCIs). Much of the management of TLSCI has been extrapolated from cervical SCI studies, including the management of blood pressure (BP).^{1,2} The task force attempted to answer the question: Does the active maintenance of arterial BP after injury affect clinical outcomes in patients with thoracic and lumbar fractures? While the application of mean arterial BP (MAP) goals to TLSCI is becoming more frequent in trauma centers, it is worthy of study as there is some risk of complication, particularly in older and more frail populations.

METHODS

The guidelines task force initiated a systematic review of the literature and evidence-based guideline relevant to the diagnosis and treatment of patients with thoracolumbar trauma. Through objective evaluation of the evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the

diagnosis and treatment of adult patients with thoracolumbar injury. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods used in this systematic review can be found in the [introduction and methodology chapter](#).

Literature Search

The task force members identified search terms/parameters, and a medical librarian implemented the literature search, consistent with the literature search protocol (see Appendix I), using the National Library of Medicine PubMed database and the Cochrane Library (which included the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effect, the Cochrane Central Register of Controlled Trials, the Health Technology Assessment Database, and the National Health Service Economic Evaluation Database) for the period from January 1, 1946 to March 31, 2015, using the search strategies provided in Appendix I.

RESULTS

The literature search yielded 1100 abstracts. Task force members reviewed all abstracts yielded from the literature search and identified the literature for full-text review and extraction, addressing the clinical questions, in accordance with the literature search protocol (Appendix I). Task force members identified the best research evidence available to answer the targeted clinical questions. When level I, II, and/or III literature was available to answer specific questions, the task force did not review level IV studies.

The task force selected 19 articles for full-text review. Of these, 18 were rejected for not meeting inclusion criteria or for being off topic. The majority of rejected articles did not include TLSCI

or did not provide separate analysis of these injuries. One manuscript was selected for inclusion in this systematic review (Appendix II).

Inclusion/Exclusion Criteria

Articles were retrieved and included only if they met specific inclusion/exclusion criteria. These criteria were also applied to articles provided by guideline task force members who supplemented the electronic database searches with articles from their own files. To reduce bias, these criteria were specified before conducting the literature searches.

Articles that do not meet the following criteria were, for the purposes of this evidence-based clinical practice guideline, excluded. To be included as evidence in the guideline, an article had to be a report of a study that:

- Investigated patients with thoracolumbar injuries;
- Included patients ≥ 18 years of age;
- Enrolled $\geq 80\%$ of thoracolumbar injuries (studies with mixed patient populations were included if they reported results separately for each group/patient population);
- Was a full article report of a clinical study;
- Was not an internal medical records review, meeting abstract, historical article, editorial, letter, or commentary;
- Appeared in a peer-reviewed publication or a registry report;
- Enrolled ≥ 10 patients per arm per intervention (20 total) for each outcome;
- Included only human subjects;
- Was published in or after 1946;

- Quantitatively presented results;
- Was not an in vitro study;
- Was not a biomechanical study;
- Was not performed on cadavers;
- Was published in English;
- Was not a systematic review, meta-analysis, or guideline developed by others*;
- Was a case series (therapeutic study) where higher level evidence exists.

Rating Quality of Evidence

The guideline task force used a modified version of the North American Spine Society's (NASS) evidence-based guideline development methodology. The NASS methodology uses standardized levels of evidence (Appendix III) and grades of recommendation (Appendix IV) to assist practitioners in easily understanding the strength of the evidence and recommendations within the guidelines. The levels of evidence range from level I (high-quality randomized controlled trial) to level IV (case series). Grades of recommendation indicate the strength of the recommendations made in the guideline based on the quality of the literature. Levels of evidence have specific criteria and are assigned to studies before developing recommendations. Recommendations are then graded based upon the level of evidence. To better understand how levels of evidence inform the grades of recommendation and the standard nomenclature used within the recommendations. see Appendix IV.

*The guideline task force did not include systematic reviews, guidelines, or meta-analyses conducted by others. These documents are developed using different inclusion criteria than those specified in this guideline; therefore, they may include studies that do not meet the inclusion criteria specific in this guideline. In cases where these types of documents' abstract suggested relevance to the guideline's recommendations, the task force searched their bibliographies for additional studies.

Guideline recommendations were written using a standard language that indicates the strength of the recommendation. “A” recommendations indicate a test or intervention is “recommended”; “B” recommendations “suggest” a test or intervention; “C” recommendations indicate a test or intervention or “is an option.” “Insufficient evidence” statements clearly indicate that “there is insufficient evidence to make a recommendation for or against” a test or intervention. Task force consensus statements clearly state that “in the absence of reliable evidence, it is the task force’s opinion that” a test or intervention may be considered. Both the levels of evidence assigned to each study and the grades of each recommendation were arrived at by consensus of the workgroup employing up to 3 rounds of voting when necessary.

In evaluating studies as to levels of evidence for this guideline, the study design was interpreted as establishing only a potential level of evidence. For example, a therapeutic study designed as a randomized controlled trial would be considered a potential level I study. The study would then be further analyzed as to how well the study design was implemented and significant shortcomings in the execution of the study would be used to downgrade the levels of evidence for the study’s conclusions (see Appendix V for additional information and criteria).

Revision Plans

In accordance with the Institute of Medicine’s standards for developing clinical practice guidelines and criteria specified by the National Guideline Clearinghouse, the task force will monitor related publications after the release of this document and will revise the entire document and/or specific sections “if new evidence shows that a recommended intervention

causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.”³ In addition, the task force will confirm within 5 years from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with thoracolumbar trauma.

DISCUSSION

While there have been numerous articles that have addressed the use of MAP goals in TLSCI, only 1 study provided a separate analysis of these patients apart from cervical SCI. Vale et al⁴ retrospectively studied blood pressure management in acute spinal cord injury in both cervical and thoracolumbar injuries. Of the total 77 patients, 29 had TLSCI. Of the 21 TLSCI patients with American Spinal Injury Association Spinal Injury (AIS) grade A injuries, 7 improved by ≥ 1 ASIA grade at 1 year of follow-up. Two patients improved to AIS D, 3 to AIS C, and 2 to AIS B. Of the 5 AIS B patients, all improved by ≥ 1 AIS grade at 1 year of follow-up; 2 improved to AIS D, 2 to AIS C, and 1 to AIS B. The study also showed that TLSCI patients with incomplete injuries were more likely to recover than complete, and 88% of these regained the ability to walk (level III evidence).

Hawryluk et al⁵ retrospectively studied vital sign data every minute and the relationship of MAP goals and short-term (discharge) neurologic outcome. Of the 100 patients, 24 had thoracic or TLSCI. The authors found that higher average MAP values correlated with improved neurologic function at discharge. The authors evaluated a new device that records vital sign data for spinal

cord injury. Analysis was performed at 1-minute time points. This study showed that patients above the threshold had greater recovery. Thoracolumbar trauma patients were broken out in a group of 24 patients (meets inclusion criteria). There was no comparison group. This study showed AIS grade improvements. Although the authors concluded that a relationship existed between degree of improvement and maintenance of BP, this treatment group was combined with cervical patients and not evaluated separately for thoracolumbar trauma patients. Therefore, this study was excluded from the evidentiary table.

Question

Does the active maintenance of arterial blood pressure after injury affect clinical outcomes in patients with thoracic and lumbar fractures?

Recommendations

There is insufficient evidence to recommend for or against the use of active maintenance of arterial blood pressure after thoracolumbar spinal cord injury.

Level of Evidence: Grade Insufficient

However, in light of published data from pooled (cervical and thoracolumbar) spinal cord injury patient populations, clinicians may choose to maintain mean arterial blood pressures >85 mm Hg in an attempt to improve neurological outcomes.

Level of Evidence: Consensus Statement by the Workgroup

Future Research

This guideline highlights the need for higher-quality prospective observational data, such as would be provided by a multicenter prospective SCI registry. While randomized controlled trials

may initially sound ideal, it may be difficult to conduct such a trial in SCI patients given many clinicians' possible lack of equipoise regarding MAP goals and the risk of neurologic deterioration.

Conclusions

While the use of MAP goals to maintain spinal cord perfusion after traumatic SCI has become common practice in many high-volume trauma centers, the scientific data supporting this practice are mainly derived from cervical SCI studies.^{1,2} These data have been used to justify similar management in TLSCI. While such a practice appears to be a reasonable option, the medical evidence specifically for patients with TLSCI is lacking.

Potential Conflicts of Interest

The task force members were required to report all possible conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Committee, including potential COIs that are unrelated to the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chairs reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chairs are given latitude to approve nominations of Task Force members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs. The conflict of interest findings are provided in detail in the companion [introduction and methods manuscript](#).

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a multidisciplinary physician volunteer task force and serves as an educational tool designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Disclosures

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the Section on Disorders of the Spine and Peripheral Nerves in collaboration with the Section on Neurotrauma and Critical Care, which received no funding from outside commercial sources to support the development of this document.

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REFERENCES

1. Inoue T, Manley GT, Patel N, Whetstone WD. Medical and surgical management after spinal cord injury: vasopressor usage, early surgeries, and complications. *J Neurotrauma* 2014;31:284-291.
2. Readdy WJ, Whetstone WD, Ferguson AR, et al. Complications and outcomes of vasopressor usage in acute traumatic central cord syndrome [published online ahead of print Jul 31]. *J Neurosurg Spine* 2015.
3. Ransohoff DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. *JAMA* 2013;309:139-140.
4. Vale FL, Burns J, Jackson AB, Hadley MN. Combined medical and surgical treatment after acute spinal cord injury: results of a prospective pilot study to assess the merits of aggressive medical resuscitation and blood pressure management. *J Neurosurg* 1997;87:239-246.
5. Hawryluk GW, Whetstone WD, Saigal R, et al. Mean arterial blood pressure correlates with neurological recovery following human spinal cord injury: analysis of high frequency physiologic data. *J Neurotrauma* 2015;32:1958-1967.

Appendix I. Literature Searches

Search Strategies

PubMed

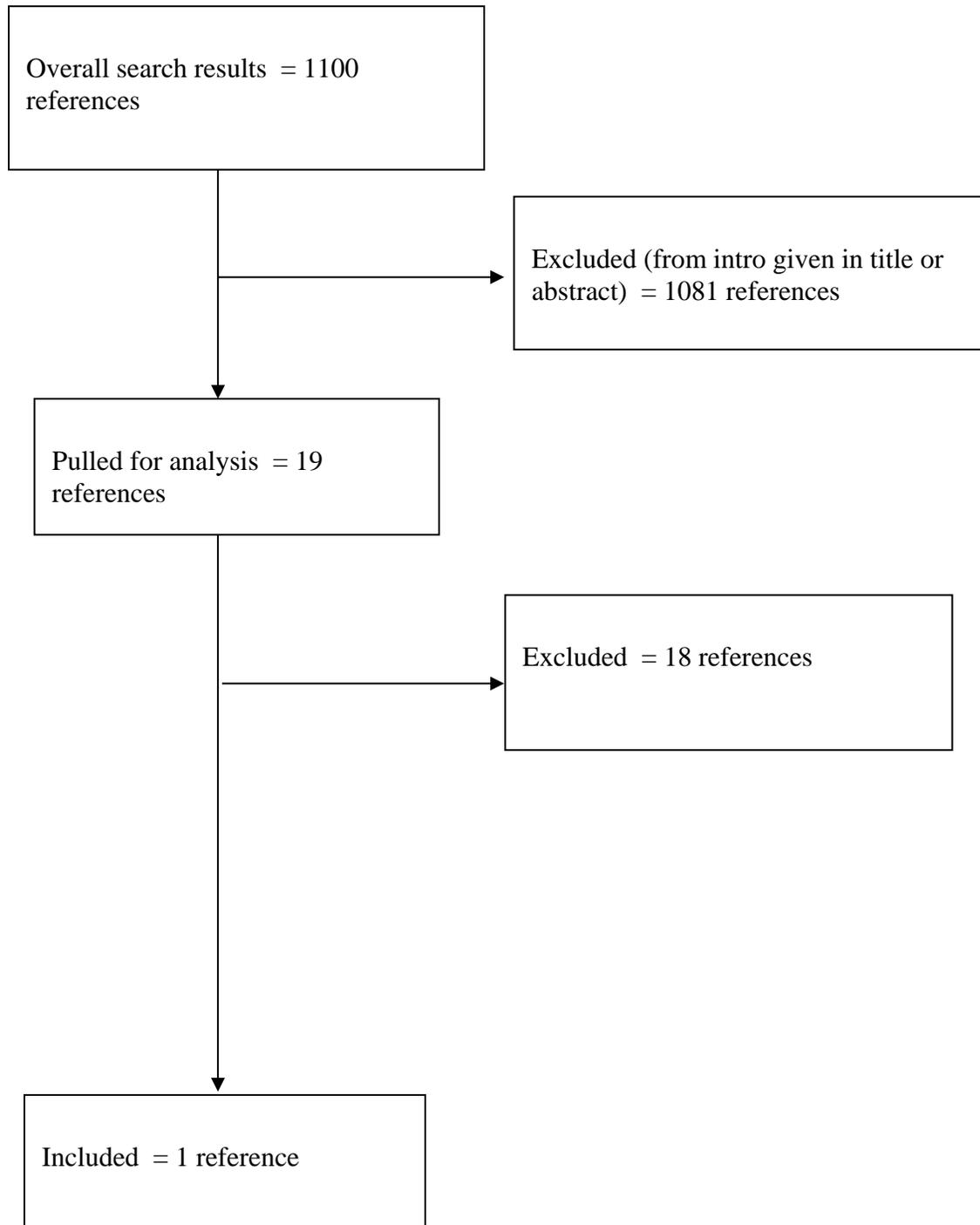
1. Lumbar vertebrae [MeSH] OR Thoracic vertebrae [MeSH]
2. Thoracolumbar [TIAB] OR thoraco-lumbar [TIAB] OR thoraco lumbar [TIAB] OR burst [Title]
3. Spinal Injuries [MeSH] OR Spinal Cord Injuries [MeSH]
4. (Vertebra*[tiab] OR spine[tiab] OR spinal[tiab] OR "spinal cord" [tiab]) AND (Injur*[tiab] OR trauma*[tiab] OR fractur*[tiab] OR dislocation*[tiab])
5. #1 OR #2 OR #3 OR #4
6. Arterial Pressure [Mesh] OR (Blood Pressure [MeSH:noexp] AND 1963:2012 [MHDA])
7. arterial blood pressure OR arterial pressure* OR mean arterial pressure* OR MAP OR MABP [TIAB]
8. #6 OR #7
9. #5 AND #8
10. (animal [MeSH] NOT human [MeSH]) OR cadaver [MeSH] OR cadaver* [Titl] OR comment [PT] OR letter [PT] OR editorial [PT] OR addresses [PT] OR news [PT] OR "newspaper article" [PT] OR Case Reports [PT]
11. #9 NOT #10
12. osteoporosis [MH] OR osteoporotic fractures [MH] OR osteopor* [TITLE] OR spinal neoplasms [MH] OR tumor* [TITLE] OR tumour* OR malignan* [TITLE]
13. #11 NOT #12
14. #13 AND English [Lang]
15. #14 AND ("1946/01/01"[PDAT] : "2015/03/31"[PDAT])

Cochrane Library

1. Lumbar vertebrae: MeSH descriptor, explode all trees
2. Thoracic vertebrae: MeSH descriptor, explode all trees
3. #1 OR #2
4. Spinal Injuries: MeSH descriptor
5. Spinal Cord Injuries: MeSH descriptor
6. #4 OR #5
7. #3 AND #6
8. (Thoracolumbar OR thoraco-lumbar OR thoraco lumbar OR burst) NEAR/4 (Injur* OR trauma* OR fractur* OR dislocation*):ti,ab,kw
9. Lumbar vertebrae/injuries: MeSH descriptor, explode all trees
10. Thoracic vertebrae/injuries: MeSH descriptor, explode all trees
11. #9 OR #10
12. #7 OR #8 OR #11
13. mh osteoporosis or mh osteoporotic fractures or mh spinal neoplasms
14. osteopor* or tumor* or malignan*:ti
15. #13 OR #14
16. #12 NOT #15

Appendix II. Article Inclusions and Exclusions

Included and Excluded Articles Flowchart



Appendix III. Rating Evidence Quality

Levels of Evidence for Primary Research Question^a

Types of studies				
	Therapeutic studies – Investigating the results of treatment	Prognostic studies – Investigating the effect of a patient characteristic on the outcome of disease	Diagnostic studies – Investigating a diagnostic test	Economic and decision analyses – Developing an economic or decision model
Level I	<ul style="list-style-type: none"> • High-quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals • Systematic review^b of level I RCTs (and study results were homogenous^c) 	<ul style="list-style-type: none"> • High-quality prospective study^d (all patients were enrolled at the same point in their disease with ≥80% follow-up of enrolled patients) • Systematic review^b of level I studies 	<ul style="list-style-type: none"> • Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference “gold” standard) • Systematic review^b of level I studies 	<ul style="list-style-type: none"> • Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses • Systematic review^b of level I studies
Level II	<ul style="list-style-type: none"> • Lesser quality RCT (e.g., ≤80% follow-up, no blinding, or improper randomization) • Prospective^d comparative study^e • Systematic review^b of level II studies or level I studies with inconsistent results 	<ul style="list-style-type: none"> • Retrospective^f study • Untreated controls from an RCT • Lesser quality prospective study (e.g., patients enrolled at different points in their disease or ≤80% follow-up) • Systematic review^b of level II studies 	<ul style="list-style-type: none"> • Development of diagnostic criteria on consecutive patients (with universally applied reference “gold” standard) • Systematic review^b of level II studies 	<ul style="list-style-type: none"> • Sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses • Systematic review^b of level II studies

Level III	<ul style="list-style-type: none"> • Case control study^g • Retrospective comparative study^e • Systematic review^b of level III studies 	<ul style="list-style-type: none"> • Case control study^g 	<ul style="list-style-type: none"> • Study of non consecutive patients; without consistently applied reference “gold” standard • Systematic review^b of level III studies 	<ul style="list-style-type: none"> • Analyses based on limited alternatives and costs; and poor estimates • Systematic review^b of level III studies
Level IV	Case series ^h	Case series	<ul style="list-style-type: none"> • Case-control study • Poor reference standard 	<ul style="list-style-type: none"> • Analyses with no sensitivity analyses

RCT, Randomized controlled trial.

^aA complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.

^bA combination of results from ≥ 2 previous studies.

^cStudies provided consistent results.

^dStudy was started before the first patient enrolled.

^ePatients treated one way (e.g., instrumented arthrodesis) compared with a group of patients treated in another way (e.g., unsinstrumented arthrodesis) at the same institution.

^fThe study was started after the first patient enrolled.

^gPatients identified for the study based on their outcome, called “cases” (e.g., pseudoarthrosis) are compared to those who did not have outcome, called “controls” (e.g., successful fusion).

^hPatients treated one way with no comparison group of patients treated in another way.

Appendix IV. Linking Levels of Evidence to Grades of Recommendation

Grade of recommendation	Standard language	Levels of evidence	
A	Recommended	Two or more consistent level I studies	
B	Suggested	One level I study with additional supporting level II or III studies	Two or more consistent level II or III studies
C	Is an option	One level I, II, or III study with supporting level IV studies	Two or more consistent level IV studies
Insufficient (insufficient or conflicting evidence)	Insufficient evidence to make recommendation for or against	A single level I, II, III, or IV study without other supporting evidence	>1 study with inconsistent findings ^a

^aNote that in the presence of multiple consistent studies, and a single outlying, inconsistent study, the Grade of Recommendation will be based on the level of the consistent studies.

Appendix V. Criteria Grading the Evidence

The task force used the criteria provided below to identify the strengths and weaknesses of the studies included in this guideline. Studies containing deficiencies were downgraded one level (no further downgrading allowed, unless so severe that study had to be excluded). Studies with no deficiencies based on study design and contained clinical information that dramatically altered current medical perceptions of topic were upgraded.

1. Baseline study design (i.e., therapeutic, diagnostic, prognostic) determined to assign initial level of evidence.
2. Therapeutic studies reviewed for following deficiencies:
 - Failure to provide a power calculation for an RCT;
 - High degree of variance or heterogeneity in patient populations with respect to presenting diagnosis/demographics or treatments applied;
 - <80% of patient follow-up;
 - Failure to utilize validated outcomes instrument;
 - No statistical analysis of results;
 - Cross over rate between treatment groups of >20%;
 - Inadequate reporting of baseline demographic data;
 - Small patient cohorts (relative to observed effects);
 - Failure to describe method of randomization;
 - Failure to provide flowchart following patients through course of study (RCT);
 - Failure to account for patients lost to follow-up;
 - Lack of independent post-treatment assessment (e.g., clinical, fusion status, etc.);
 - Utilization of inferior control group:

- Historical controls;
 - Simultaneous application of intervention and control within same patient.
- Failure to standardize surgical/intervention technique;
 - Inadequate radiographic technique to determine fusion status (e.g., static radiographs for instrumented fusion).
3. Methodology of diagnostic studies reviewed for following deficiencies:
- Failure to determine specificity and sensitivity;
 - Failure to determine inter- and intraobserver reliability;
 - Failure to provide correlation coefficient in the form of kappa values.
4. Methodology of prognostic studies reviewed for following deficiencies:
- High degree of variance or heterogeneity in patient populations with respect to presenting diagnosis/demographics or treatments applied;
 - Failure to appropriately define and assess independent and dependent variables (e.g., failure to use validated outcome measures when available).

Appendix VI. Evidence Tables

Author, Year	Level of Evidence	Task Force Conclusions Relative to Question and Rationale for Evidence Grading
Vale et al, 1997	III	This paper provides evidence that the enhanced neurologic outcome that was observed in patients after spinal cord injury in this study was in addition to, and/or distinct from, any potential benefit provided by surgery