

Bridging the Evidence Gap Across Specialties

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Introduction/Outline

- Case Presentation
- How do we judge evidence that create guidelines?
- What are the SCI guidelines and where do they come from?
- What are the standards and evidence from other specialties?
- How can we build bridges across specialties?
- Other Examples: ventilator management and wean, primary care in SCI













- Understand levels of scientific evidence
- Identify inherent difference in some medical specialties
- Appreciate variations in guidelines and begin to reconcile the differences











Disclosures

• None











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- Dr. Kim Anderson











- Damage to the nerves in the neck or spine
- Can effect *anything* at or below the neurologic level of injury
 - Motor
 - Sensory
 - Autonomic
 - Other

Spinal Cord Injury













<u>Tetraplegia:</u>

 cervical segments

Paraplegia:

 thoracic, lumbar, or sacral segments

Dermatome:

• The area of skin innervated by one sensory nerve root.

Myotome:

• The collection of muscles innervated by one motor nerve root.

Incomplete Injury:

 If there is preservation of motor and or sensory function in the lowest sacral segment.

Complete Injury:

• The absence of motor and/or sensory function in the lowest sacral segment.

Zone of Partial Preservation:

 Dermatomes and myotomes caudal to the neurological level that remain partially innervated (this term is only used in complete injuries).













Neurological Level of Injury:

The most caudal segment of the spinal cord with normal motor and sensory function on both sides.

Skeletal Level:

The radiographic level of greatest vertebral damage.













Epidemiology of Spinal Cord Injury

- Incidence: 54 cases per million
 - 17,810 new traumatic SCI per year
- Prevalence: 294,000 (250k-368k)
- Age: 43 year old
 - Up from 29 in 1970
- Gender: 78% males

	Average ` (in 20	Yearly Expenses)19 dollars)	Estimated Lifetime Costs by Age at Injury (discounted at 2%)		
Severity of Injury	First Year	Each Subsequent Year	25 years old	50 years old	
High Tetraplegia (C1–C4) AIS ABC	\$1,149,629	\$199,637	\$5,100,941	\$2,803,391	
Low Tetraplegia (C5–C8) AIS ABC	\$830,708	\$122,468	\$3,727,066	\$2,292,479	
Paraplegia AIS ABC	\$560,287	\$74,221	\$2,494,338	\$1,636,959	
Motor Functional at Any Level AIS D	\$375,196	\$45,572	\$1,704,144	\$1,202,832	

Data Source: Economic Impact of SCI published in the journal *Topics in Spinal Cord Injury Rehabilitation,* Volume 16, Number 4, in 2011. ASIA Impairment Scale (AIS) is used to grade the severity of a person's neurological impairment following spinal cord injury.











- 16931 Trauma in 5 NE Ohio hospitals

- 17810 Spinal Cord Injury in all of USA





Patients

Mechanism of Injury by Age Group

	Mechanism	<15	15-20	21-40	41-65	66-80	>80	Total
Fall	MVC	184	326	1389	996	323	135	3353
	Fall - 10ft or More	82	36	203	315	106	47	789
	Fall - Under 10ft	295	20	175	655	678	598	2421
GSW	Fall - Same Level	106	44	246	1008	1580	1822	4806
Assault	Fall - Not Further Specified	14	4	24	128	215	404	789
Other Blunt	Assault	55	85	357	235	3	8	70
Mechanism	Asphyxiation or Hanging	10		3	34			44
All Others	Motorcycle	20	6	208	206	29	0	469
All Others	MVC vs. Pedestrian	59	49	167	139	48	18	480
	Bicycle	88	30	62	125	29	0	334
	Other/ Off-Road Vehicle	29	34	78	51	1	4	206
	Horse and Rider	18		13	22	()	53
	Other Blunt	89	47	170	191	73	23	593
	Other Penetrating	18	21	77	77	16	0	209
	Stabbing	23 163		163		86		272
	Drowning	13					0	13
	GSW	20	195	522	143	10	0	890
	Biting	36	1	4	17	10	0	77
	Sport Injury	51	69	14	1	7	0	162
	Burn	4	5	27	32 1		7	121
University	Unknown		19		21	16	17	73
	Totals	1198	1031	3958	4461	3204	3079	16931

MECHANISM OF INJURY





Impact on research

SCI

- Almost rare
- Expensive
- Unemployed
- Diverse
 - Mechanism
 - Outcome
- Disproportionate underrepresented

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Heart Disease

- Common
- Inexpensive
- Employed

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• More uniform

• More representative

Impact on research

- Less grant funding
- Less motivation in free market
- Less motivation in public
- Harder to recruit, retain
- Hard to design/blind
- Fewer, Smaller, Poorer quality studies







SCI Model System (NIDILRR)

- 1970 to 2026
- Pooled
 - Data
 - Efforts
 - Knowledge
- Clinical Excellence















- Greg is a 20-year-old previously healthy male s/p MVA. He endorses loss of consciousness and paraplegia.
- Initial imaging shows a T4 burst fracture and exam suggests a T4 AIS B paraplegia. His blood pressure ranges 85-110/55-65
- Initial surgery is aborted due to hypotension













Case: What do you think?

- Unmute to answer or type in the chat
- What are the possible causes of his hypotension?
- How do we manage SCI related hypotension?
- When should we treat or not treat SCI related hypotension?













- Day 3, underwent surgical decompression and fusion
- SCI recommend maintain mean arterial blood pressure (MAP) > 85mmHg for 7 days after injury
- Spine surgeon recommends maintaining MAP > 80 mmHg for 48 hr post op
- Trauma surgeon treats symptomatically due to risk of vasopressors in asymptomatic 20yo















Evidence Based Medicine







John Chae



Sackett 1959; US Task Force 1996

Level of Scientific Evidence

Level	Description
1	Evidence based on randomized controlled clinical trials (or meta-analysis of such trials) of adequate size to ensure a low risk of incorporating false-positive or false-negative results.
II	Evidence based on randomized controlled trials that are too small to provide level I evidence. These may show either positive trends that are not statistically significant or no trends and are associated with a high risk of false-negative results.
111	Evidence based on nonrandomized, controlled, or cohort studies ; case series ; case- controlled studies; or cross-sectional studies.
IV	Evidence based on the opinion of respected authorities or expert committees as indicated in published consensus conferences or guidelines .
V	Evidence that expresses the opinion of those individuals who have written and reviewed this guideline, based on experience, knowledge of the relevant literature, and discussions with peers.
	peers.











Categories of the Strength of Evidence Associated with the Recommendations

Category	Description
А	The guideline recommendation is supported by one or more Level I studies.
В	The guideline recommendation is supported by one or more Level II studies.
С	The guideline recommendation is supported by only Level III, IV or V studies.











John Chae



Levels of Panel Agreement with the Recommendations

Description	
1.0 to 2.33	Patient
2.33 to 3.67	Clinical Values Experience
3.67 to 5.0	Research
	Description 1.0 to 2.33 2.33 to 3.67 3.67 to 5.0

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Evidence





- Consortium for Spinal Cord Injury (PVA) USA
- Spinal Cord Injury Research Evidence (SCIRE) Canada
- American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) - USA
- National Institute of Health and Care Excellence (NICE) – UK
- Others: Joint Trauma System (JTS CPG) Military



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SCRE

Spinal Cord Injury Research Evidence



NICE

American Association of Neurological Surgeons







Consortium for Spinal Cord Injury (PVA) -2008

• 16. Prevent and treat hypotension.

- (Scientific evidence–II/IV; Grade of recommendation–B; Strength of panel opinion–4)
- The <u>appropriate resuscitation end point and optimal mean arterial blood pressure</u> for maintenance of spinal cord perfusion are <u>not known</u>. Uncontrolled studies that used fluids and vasopressors to achieve a mean arterial pressure of 85 mmHg for a minimum of 7 days in patients with acute SCI have reported favorable outcomes (Levi et al., 1993; Vale et al., 1997).
- Hypotension may exacerbate central nervous system injury. Avoiding hypotension in brain-injured patients is paramount in early treatment because diminished cerebral perfusion pressure may contribute to secondary neuronal injury (R. M. Chesnut, 1993). Although separate clinical <u>data do not exist for patients with spinal cord injuries</u>, hypotension should be recognized, the cause of the hypotension sought, and fluid resuscitation initiated with the goal of treating hypotension (systolic blood pressure < 90). Further study is needed to define ideal mean arterial pressure (MAP) and the potential role for elevation of MAP with fluids or pharmacologic treatment (Vale et al., 1997).











Levi et al., 1993: Hemodynamic parameters in patients with acute cervical cord trauma: description, intervention, and prediction of outcome

- Invasive monitoring: arterial line and Swan-Ganz catheter
- Fluid and Pressors: dopamine and/or dobutamine
- Goal MAP > 90 mm Hg for 7 days: results 94.4 +/- 9.4
- 50 SCI patients: 6 week follow up
- Conclusion: aggressive monitoring and hemodynamic intervention is feasible and safe













Vale et al., 1997: 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

- Prospectively, uncontrolled
- Invasive monitoring, Fluid and Pressors: dopamine and/or dobutamine
 - All received NASCIS II Protocol
 - Complete tetraplegia admission MAP 66>mmHg, all others > 80mmHg
- Goal: MAP > 85mmHg for 7 days
- 77 patients with C/T-spine SCI

Initial Exam	Improved AIS Grade	Improved Ambulation	Improved Bladder function
Complete tetraplegia	60%	30%	20%
Complete paraplegia	33%	10%	10%
Incomplete Tetraplegia		92%	88%
Incomplete Paraplegia		88%	63%

Southwest General





Chesnut, 1993: Early and late systemic hypotension as a frequent and fundamental source of cerebral ischemia following severe brain injury in the Traumatic Coma Data Bank

- Severe head injury (GCS < = 8), prospective database, n=1210
- Hypotension (SBP < 90 mmHg), early (resuscitation), late (ICU)
 - Early hypotension associated with a doubling of mortality (55% vs. 27%)
 ➢ If shock was present on admission, the mortality was 65%
 - Late hypotension (without early hypotension): 66% died or were vegetative
 - No hypotension: 17% died or were vegetative
- Logistic regression modelling suggested that early and late shock were the most powerful independent predictors of mortality
 - Independent of age, admission GCS motor score, presence of hypoxia, or associated severe extracranial trauma



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Congress of Neurosurgeons - 2013

- ICU monitoring allows the early detection of hemodynamic instability, cardiac disturbances, pulmonary dysfunction, and hypoxemia
 - Management in an ICU or other monitored setting appears to have an impact on neurological outcome after acute cervical SCI
- Correction of hypotension in spinal cord injury (systolic blood pressure < 90 mmHg) when possible and as soon as possible is recommended.
- Maintenance of mean arterial blood pressure between 85 90 mmHg for the first 7 days following an acute spinal cord injury is recommended.



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- Hemodynamic support during the acute phase post SCI has been associated with improved neurological outcomes but no cause-and-effect relationship has been established.
- Management of hemodynamic changes during the acute phase of SCI has focused on the effectiveness of early aggressive support on neurological outcomes. In general, hemodynamic management involves a multipronged approach which includes administering fluids, vasopressors, decompressive surgery, and pulmonary catheters. Two studies have shown that this type of aggressive treatment may be effective for improving neurological outcomes post SCI (Vale et al., 1997; Levi et al., 1993).
- Level IV











Joint Trauma System (JTS CPG) 2020

- Avoid hypoxemia (SaO2 <92%) and hypotension (SBP<90) for all spinal cord injuries. (Level III)
- Maintain MAP >85 for all spinal cord injuries, with an *emphasis on avoiding hypotension*. (Level III)
 - Patients who sustain neurologic compromise should have an invasive arterial line for continuous blood pressure monitoring with a goal MAP of 85-90 mmHg for up to seven days following the injury. The evidence supporting this goal is mixed, at best, however it is the opinion of the authors that there is a net benefit to maintaining this goal. Regardless, hypotension (SBP < 90 mmHg) and hypoxemia (SaO2 <92%), must be avoided.
 - Vasopressor therapy (in the euvolemic patient) and/or supplemental oxygen are recommended, when necessary, to achieve these goals. Prior to the use of vasopressors, ensure that hypovolemia is addressed through adequate resuscitation and evaluation and control of any bleeding.
 Vasopressor use in the hypovolemic patient may contribute to additional ischemic loss in other injured tissues.











Orlando Regional Medical Center

- <u>https://www.surgicalcriticalcare.net/guidelines.php</u>
- Level 3 ➤ Mean arterial pressure (MAP) augmentation with norepinephrine (if needed) is recommended for at least the first 72 hours following injury to a maximum of 7 days.
 - Goal MAP ≥ 85 mmHg for blunt / incomplete penetrating injury
 - Goal MAP \geq 65 mmHg for complete penetrating injury
 - Do NOT use for patients with irreversible SCI

• 70/55 = MAP 65









ORMC Citations

- Readdy WJ, Saigal R, Whetsone WD, et.al. Failure of mean arterial pressure goals to improve outcomes following penetrating spinal cord injury. Neurosurgery. 2016; 79:708-14.
- Catapano JS, Hawryluk GWJ, Whetstone W, et.al. Higher mean arterial pressure values correlate with neurological improvement in patients with initially complete spine cord injuries. World Neurosurg. 2016; 96:72-9.
- Saadeh YS, Smith BW, Joseph JR, et.al. The impact of blood pressure management after spinal cord injury: a systematic review of the literature. Neurosurg Focus. 2017; 43:E20.
- Readdy WJ, Whestone WD, Ferguson AR, et.al. Complications and outcomes of vasopressor usage in acute traumatic central cord syndrome. J Neurosurg Spine. 2015; 23:574-80.



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Readdy et.al. 2016 Failure of mean arterial pressure goals to improve outcomes following penetrating spinal cord injury.

- 14 patients with complete penetrating SCIs compared to nonpenetrating
 - 7.1% experienced improved AIS Grade
 - 71.43% experienced cardiogenic complications











Catapano, et al. 2016 Higher mean arterial pressure values correlate with neurological improvement in patients with initially complete spine cord injuries

- Retrospective MAP recording correlated with AIS recovery, n=62
- 33 complete SCI: 11 improved at least 1 AIS grade by discharge. Of those that improved:
 - Initial average MAP was significantly higher (96.6 ± 0.07 mmHg vs. 94.4 ± 0.06mm Hg, respectively; P < 0.001)
 - Proportion of MAP values <85 mm Hg was significantly lower (13.5% vs. 25.6%, respectively; P < 0.001).
- A positive correlation was observed between MAP values and neurologic recovery in AIS A, B, and C patients but not AIS D patients



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Saadeh et.al. 2017 The impact of blood

pressure management after spinal cord injury: a systematic review of the literature.

- 11 studies: 9 retrospective, 2 uncontrolled prospective
 - MAP goal > 85-90 mmHg
 - Duration goal 1-7 days
 - More complications with dopamine than phenylephrine or norepinephrine
- No high-quality data
 - Based on the 2 prospective studies, MAP goals of 85–90 mm Hg for a duration of 5–7 days should be considered.
 - Norepinephrine for cervical and upper thoracic injuries and phenylephrine or norepinephrine for mid- to lower thoracic injuries should be considered.









Authors & Year	Data Collection	Study Type	Comparison Group	Neurological Outcome Measure	No. of Pts	MAP Goal (mm Hg)	MAP Goal Duration	Length of Follow-Up
Catapano et al., 2016	Retrospective	Case series	No	AIS grade	62	NS	NS	Until discharge
Cohn et al., 2010	Retrospective	Case series	No	AIS grade, ASIA motor score	17	NS	NS	Until discharge
Dakson et al., 2017	Retrospective	Comparative	Yes	AIS grade, ASIA motor score	94*	>85	5 days	After neurorehabili- tation
Hawryluk et al., 2015	Retrospective	Case series	No	AIS grade	74	>85	5 days	Until discharge
Inoue et al., 2014	Retrospective	Case series	No	AIS grade	131	>85	7 days	Until discharge
Kepler et al., 2015	Retrospective	Case series	No	ASIA motor score	92	>85	≥5 days	Until hospital Day 5
Levi et al., 1993	Prospective	Case series	No	Frankel grade	50	>90	7 days	6 wks
Martin et al., 2015	Retrospective	Case series	No	ASIA motor score	105	NS	NS	Until discharge
Readdy et al., 2015	Retrospective	Case series	No	AIS grade	34	>85	>24 hrs	Until discharge
Vale et al., 1997	Prospective	Case series	No	AIS grade, ASIA motor score	77	>85	7 days	12 mos
Wolf et al., 1991	Retrospective	Case series	No	Modified Frankel score, Yale Scale score	52	>85	5 days	12 mos

TABLE 1. Pertinent characteristics of the 11 articles included in this systematic review of BP management after spinal cord injury

NS = not specified; Pts = patients.

* Serial MAP data collected for 50 of these patients.











Cost of vasopressors and ICU

- Vasopressor complications (uptodate.com)
 - Hypoperfusion: extremities (acute limb ischemia/necrosis), kidneys (renal insufficiency and oliguria), mesenteric organs (gastritis, shock liver, intestinal ischemia, or translocation of gut flora with resultant bacteremia)
 - Dysrhythmias: powerful chronotropic effects (beta-1 adrenergic)
 - sinus tachycardia (most common), atrial fibrillation, re-entrant atrioventricular node tachycardia, or ventricular tachyarrhythmias
 - Myocardial ischemia including occult ischemia: chronotropic and inotropic effects
 - Local effects: extravasation results in skin necrosis necessitating central access
 - Hyperglycemia: inhibition of insulin secretion
 - Drug-drug interactions
- Price of ICU without mechanical ventilation:
 - Dasta et al. 2005 Daily cost of an intensive care unit day: the contribution of mechanical ventilation. Crit Care Med.
 - day 1 \$6,667; day 2 \$3,496; after day 3 \$3,184











How do you proceed?

- How do you come to agreement across disciplines?
- Is the data apples to oranges?
- Can you justify possible benefit given known risk (and costs)?
- Is no protocol the best solution?











How do I get home?

• Traffic

Weather

• Sports





Mean Arterial Blood Pressure Treatment for Acute Spinal Cord Injury (MAPS)

- Pilot: randomized acute SCI to a spinal cord perfusion pressure (SCPP = MAP - intrathecal pressure (ITP)) target of ≥ 75 mmHg or to a control group (hypotension avoidance, MAP ≥ 65 mmHg).
 - motor score showed no difference at one-year post-SCI
- Noninferiority study
 - Hypotension avoidance (MAP >= 65 mmHg) for 7 days
 - Induced hypertension (MAP >= 85 mmHg) for 7 days
- Completed 9/2019











MAPS trial

Dr. Wilson:

Thanks for the inquiry.

Unfortunately, our trial of maintenance of normotension (MAP ~ 65 mmHg) vs. induced hypertension (MAP ~ 85 mmHg) for 5 days following acute SCI has ceased recruitment secondary to a lack of recruitment and funding support. As such, I am unfortunately not able to provide any further insight into what I believe is an important and clinically relevant question in the care of the acute SCI patient population.

Kind regards,











Saadeh Conclusion

- Although there has been significant interest in the topic of promoting hypertension in SCI patients in the acute post injury phase for the past <u>several</u> <u>decades</u>, there is **limited and low-quality evidence** regarding the risks and benefits of this practice. The basis of MAP goals and duration are most commonly attributed to <u>2 articles from the 1990s</u>, which were both prospective studies reporting the goal of elevation of MAP for a specified duration of time postinjury. Based on a <u>sound theoretical basis</u>, other retrospective reviews and case series, and anecdotal reports, the practice of promoting elevated MAP goals is widely practiced and is formally recommended by the AANS/CNS Joint Committee guidelines.
- There are risks, however, associated with establishing elevated MAP in the period after SCI, which include complications due to vasopressor use, invasive monitoring, decreased patient mobilization, and prolonged hospitalization. Some of these risks, in particular vasopressor use, have been quantified and demonstrated to cause potentially major complications. Presently, the risk-benefit profile for vasopressor use is unclear, given the lack of definitive high-level evidence of BP augmentation in improving neurological recovery after SCI.



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Saadeh Conclusion

- With regard to the <u>optimal MAP</u>, there have been **no comparison studies** to date, randomized or nonrandomized, comparing differences in outcome with different MAP goals. The formal recommendation of MAP of 85–90 mm Hg appears to be derived from studies of Levi and Vale and their colleagues, in which MAP goals of 90 and 85 mmHg were <u>chosen</u>, respectively, <u>without a clear explanation</u>. There is the possibility that lower MAP goals may achieve similar results with less risk.
- Given that BP augmentation is currently the <u>standard of care</u> after SCI based on current recommendations, future studies in this patient population involving control groups will have to carefully consider the potential **ethical questions** of providing nonstandard-of-care treatment to a control group. This question is currently under investigation via the MAPS trial: Mean Arterial Pressure in Spinal Cord Injury (MAPS): Determination of Noninferiority of a Mean Arterial Pressure Goal of 65 mm Hg Compared with a Mean Arterial Pressure Goal of 85 mm Hg in Acute Human Traumatic Spinal Cord Injury (clinicaltrials.gov no. NCT02232165).
- The <u>duration</u> of maintaining elevated MAP is currently recommended at 7 days, although no studies have compared different durations. A number of retrospective review papers have reported pursuing elevated MAP goals for a total of 5 days and did not indicate adverse outcomes related to this duration.











Consensus understanding of early blood pressure management in acute spinal cord injury

- Avoid hypotension (MAP < 70mmHg or SBP < 90mmHg) for 7 days post SCI
- Consider more aggressive MAP goals in delayed decompression
- Consider patient specific goals in central cord and penetrating trauma











Improving Relationships

- Neuromuscular Service Line Leadership
- Cross department interactions
 - Meetings: Trauma PI and Multidisciplinary Rounds
 - Education: Spine/Ortho Rounds, Resident and Fellow Didactics
 - Research: Clinical Research Meetings, Model System Team
- Personal Relationships
 - Find champions in other departments









- Goal: standardize our approach to
- Stakeholders: Pulm, Respiratory, Trauma, Nursing, SCI
- Barriers: lack of early vent wean data in SCI, competing theories for vents in different populations, practices based on tradition, experience, practicality
- Outcome: Unified, RT lead approach at SCI rehab, hope to unify all vent management, Removed inefficient protocols











SCI Medical Home

- Goal: coordinate, competent, accessible preventative health care
- Stakeholders: FM/IM, Therapy, Research, SCI community, SCI providers, nursing/administration
- Barriers: reeducating providers and patients, coordination effort, space and cost, redundant effort
- Outcome: SCI Medical Home Clinic with PT, OT, SCI, PCP, Nursing and Research. Hope to continue to expand and streamline











SCI Urodynamics Clinic

- Goal: available, accessible urodynamic studies for SCI
- Stakeholders: Urology, Research, Nursing, SCI, administration
- Barriers: inaccessible equipment, lack of urology bandwidth or buy-in, resistance to shared research/clinical space and equipment, need support staff
- Outcome: SCI Urodynamic Lab (clinical/research collaboration)











What's Next for Metro SCI Interdisciplinary Efforts?

- SCI Wound Prevention Protocols
- SCI Women's Health Clinic
- SCI Sexuality and Fertility Clinic
- Model System Gabapentin Study











Feasibility of Early Gabapentin as an Intervention for Neuroprotection

- Preclinical and retrospective data suggest early gabapentin has a persistent, positive effect on motor and autonomic neurologic recovery.
- Several feasibility questions
- Randomized, controlled gabapentin vs placebo within 120 hours
 - Screening / Consent / Randomize / Baseline data











2021-2026 SCIMS Project















Questions?

• Thank you!!







