Blood Pressure Management after Acute Spinal Cord Injury

RECOMMENDATIONS
STANDARDS: There is insufficient evidence to support treatment standards.
GUIDELINES: There is insufficient evidence to support treatment guidelines.
OPTIONS:
- **Hypotension (systolic blood pressure <90 mm Hg) should be avoided if possible or corrected as soon as possible after acute spinal cord injury.**
- **Maintenance of mean arterial blood pressure at 85 to 90 mm Hg for the first 7 days after acute spinal cord injury to improve spinal cord perfusion is recommended.**

RATIONALE

Acute traumatic spinal cord injury is frequently associated with systemic hypotension. Hypotension may be attributable to associated traumatic injuries with hypovolemia, direct severe spinal cord trauma itself, or a combination. The occurrence of hypotension has been shown to be associated with worse outcomes after traumatic injury, including severe head injury (1, 2, 8, 16, 21, 25). Although a prospective controlled assessment of the effects of hypotension on acute spinal cord injury (ASCI) in humans has not been performed, laboratory evidence suggests that hypotension contributes to secondary injury after ASCI by further reducing spinal cord blood flow and perfusion (1, 3, 4, 8, 16, 18–22, 25). Hypotension in animal models of spinal cord injury (SCI) results in worse neurological outcome (13, 14, 23, 26, 28, 29). Several clinical series of human patients with ASCI managed in an aggressive fashion with attention to blood pressure, oxygenation, and hemodynamic performance report no deleterious effects of therapy and suggest improved neurological outcome (13, 14, 23, 26, 28, 29). Despite these observations, most patients with ASCI treated in contemporary practice are not routinely monitored or treated with blood pressure augmentation after injury. For these reasons, the issues of routine blood pressure support and threshold levels of mean arterial pressure maintenance after ASCI have been raised.

SEARCH CRITERIA

A computerized search of the National Library of Medicine database of the literature from 1966 to 2001 was undertaken. The following medical subject headings were used in combination with "spinal cord injury": medical management, nonoperative management, hypotension, and spinal cord blood flow. Approximately 3000 citations were acquired. Non-English language citations were deleted. Titles and abstracts of the remaining publications were reviewed, and relevant articles were selected to develop the guidelines. We focused on two specific topics concerning human patients with ASCI: hypotension (22 articles reviewed) and spinal cord blood flow (no articles identified). Additional references were culled from the reference lists of the remaining papers. Finally, members of the author group were asked to contribute articles known to them on the subject matter that were not found by other search means. Articles describing nonhuman laboratory investigations germane to the topic, related general review articles, and relevant studies of hypotension and human traumatic brain injury referenced in the Scientific Foundation are included among the 29 citations in the references. These efforts resulted in six articles describing clinical case series (Class III medical evidence), which form the foundation for this guideline. They are summarized in *Table 8.1.*

SCIENTIFIC FOUNDATION

Ischemia of the spinal cord is thought to be one of the most important contributors to neuronal injury and neurological deficit after ASCI. Both local and systemic vascular alterations can contribute to ischemia after ASCI by further reducing spinal cord blood flow that can exacerbate and extend the principal spinal cord insult (1, 6, 8, 16, 21, 25).

In the normal, noninjured spinal cord, arterial blood supply is diffuse, primarily delivered via a single anterior spinal artery and two posterior spinal arteries. A variable number of anterior and posterior radicular arteries provide segmental contributions over the length of the cord (24, 25). They feed anastomotic arterial channels over the pial surface that supply the outer half of the cord and penetrating central arteries from the anterior spinal artery, which supply the central portion of the cord. Terminal branches of the central arteries extend rostral and caudal to overlap with adjacent terminal arteries, but the terminal arterioles that originate from the terminal arteries do not interconnect within the cord. They in turn give rise to an extensive capillary network, which does interconnect within the deep gray and white matter of the cord. Capillaries are much more numerous and extensive in the

TABLE 8.1. Summary of Reports on Blood Pressure Management after Acute Spinal Cord Injury[a]

Series (Ref. No.)	Description of Study	Evidence Class	Conclusions
Vale et al., 1997 (26)	Prospective assessment of 77 ASCI patients treated in ICU, aggressive hemodynamic support, MAP >85. No control group.	III	Improved outcome with aggressive medical care, distinct from potential benefit from surgery at 1-yr follow-up.
Levi et al., 1993 (13)	50 patients treated in ICU, aggressive medical treatment, MAP >90.	III	Improved outcome with aggressive hemodynamic support at 6 wk postinjury.
Levi et al., 1991 (14)	103 ACSI patients, 50 incomplete (Group A), 53 complete (Group B), ICU care, hemodynamic support, MAP >85.	III	Improved neurological outcome, no significant difference between early and late surgery in either group.
Wolf et al., 1991 (28)	52 patients with locked facets reduced within 4 h, ICU care, MAP >85. 49 operated on, 23 day 1, 26 delayed.	III	Closed reduction 61%. 52% 1-yr follow-up. In general, improved neurological outcome with hemodynamic therapy.
Tator et al., 1984 (23)	144 ASCI patients managed per protocol of ICU care, hemodynamic support. Compared with earlier cohort.	III	Improved neurological outcome, less mortality with early transfer and ICU care.
Zach et al., 1976 (29)	Prospective assessment of 117 ACSI patients at Swiss center, ICU setting. Aggressive medical therapy and blood pressure support (Rheomacrodex[b] × 7 d; dexamethasone × 10 d). No comparison or control group.	III	Improved neurological outcome with aggressive medical treatment and blood pressure management. Better outcome for early referrals.

[a] ASCI, acute spinal cord injury; MAP, mean arterial pressure; ICU, intensive care unit.
[b] Rheomacrodex, dextran 40 (Medisan, Parsippany, NJ).

gray matter than in the white matter, reflecting the increased metabolic needs of cell bodies compared with axons (24, 25). Perfusion of the spinal cord under normal physiological circumstances is maintained over a wide range of systemic blood pressure by autoregulatory mechanisms that seem identical to those that regulate cerebral blood flow (1, 3–5, 7, 9, 10, 15, 16, 18, 20–22, 25).

Local vascular alterations after ASCI are multiple, and the precise mechanisms of injury-induced ischemia of the cord have yet to be elucidated. Most investigators cite direct vascular injury at the site of the primary trauma as the earliest component of the ischemic injury process (1, 6, 8, 19–21). The principal SCI not only leads to white and gray matter injury at the insult site but, because of sulcal vessels and collateral terminal arteries that pass through the primary injury site, creates white matter ischemia distal to the direct injury site (8, 21, 22, 25). In addition, the primary SCI creates intraluminal thrombosis and vasospasm and initiates a variety of secondary injury biochemical phenomena that further reduce blood flow, injure endothelium, increase edema and microvascular compression, and contribute to microvascular collapse (1, 8, 19, 21, 22, 27). Posttraumatic spinal cord ischemia has been shown to become progressively worse over the first several hours after injury in animals (1, 4, 6, 7, 16, 21). Laboratory models of SCI have convincingly demonstrated that autoregulation of spinal cord blood flow is lost after injury, exacerbating local spinal cord ischemia and rendering the spinal cord vulnerable to systemic hypotension (1, 3–5, 7, 8, 16, 18, 21, 27). This is analogous to what often occurs in regional cerebrovasculature after acute traumatic brain injury (1, 4, 5, 7–9, 15, 16, 19, 21, 25, 27).

Systemic hemodynamic alterations after ASCI have been well documented and include hypotension, cardiac dysrhythmias, reduced peripheral vascular resistance, and reduced cardiac output (1, 12–14, 17, 21, 26). Patients with the most severe injuries, particularly those with severe cervical SCIs, are at greatest risk for cardiac, hemodynamic, and respiratory disturbances in the first week after ASCI (11, 12, 17). These untoward occurrences, which may be episodic in nature, can result in hypotension and hypoxia. If, as many investigators suspect, ASCI with loss of spinal cord autoregulation is analogous to acute traumatic brain injury, hypotension and hypoxia can worsen the severity of the original insult and can be disastrous for potential neurological recovery (1, 8, 20, 21). Although the relationship between systemic hypotension and outcome after ASCI has not been directly studied in human patients, inference from studies of patients with traumatic brain injury seems appropriate (2, 8, 21). Prospectively col-

lected data from the Traumatic Coma Data Bank (Class II evidence) demonstrate that hypotension (systolic blood pressure <90 mm Hg) or hypoxia (paO$_2$ <60 mm Hg) was independently associated with significant increases of morbidity and mortality after severe traumatic brain injury (2). A single episode of hypotension was associated with a 150% increase in mortality. It is in this very setting that therapeutic intervention aimed at correcting hypotension and maintaining threshold levels of mean arterial pressure (MAP) to improve cerebral or spinal cord perfusion has its greatest potential. Several reports of case series suggest that treatment of hypotension and resuscitation to maintain MAP at high-normal levels, 85 to 90 mm Hg, may enhance neurological outcome after acute traumatic SCI (13, 14, 23, 26, 28, 29).

Zach et al. (29) used a prospective aggressive medical management paradigm in the treatment of 117 consecutive ASCI patients. All patients were treated in the intensive care unit (ICU) with central venous pressure monitoring and were treated with volume expansion (Rheomacrodex 40 [dextran 40; Medisan, Parsippany, NJ], 500 ml/d) for maintenance of systemic blood pressure for 7 days. Patients were stratified by injury level, degree of deficit (Frankel grade), and time of admission after injury. The authors reported that 62% of cervical level SCI patients they managed in this way improved at last follow-up, including 8 of 18 Frankel Grade A patients, with 2 patients improving by two grades, and 1 patient improving by three grades. No patient with a cervical injury worsened; 38% were unchanged from admission. Of patients who arrived within 12 hours of injury, 67% improved compared with their admission neurological examination. Of patients admitted between 12 and 48 hours after injury, only 59% improved. When admission occurred 48 hours after injury, improvement was seen in only 50% of patients. The authors concluded that early transfer and immediate medical specific treatment of the spinal injury with attention to maintenance of acceptable blood pressure seemed to improve neurological recovery (29).

Tator et al. (23) in 1984 described their experience with 144 patients with ASCI managed between 1974 and 1979 at a dedicated SCI unit in Toronto, Ontario, Canada. The authors compared their results with a cohort of 358 SCI patients managed between 1948 and 1973, before the development of the acute care SCI facility. All 144 patients managed from 1974 to 1979 were treated in an ICU setting with strict attention to the treatment of hypotension and respiratory failure. Hypotension was "treated vigorously" with crystalloid and transfusion of whole blood or plasma for volume expansion. Patients with respiratory dysfunction were treated with ventilatory support as indicated. Tator et al. reported that mean time from injury to admission and treatment was 4.9 hours, compared with more than 12 hours from 1948 to 1973. Neurological improvement was observed in 41 (43%) of 95 patients managed under the aggressive ICU medical paradigm. Fifty-two patients (55%) demonstrated no improvement. Only two patients (2%) deteriorated. The authors reported lower mortality, reduced morbidity, shorter length of stay, and lower cost of treatment with their contemporary comprehensive management paradigm compared with the

1948 to 1973 experience. They cited improved respiratory management in their ICU as one of the principal factors responsible for reduced mortality and credited the avoidance of hypotension, sepsis, and urological complications for reduced morbidity after injury. These improved management results were realized despite the fact that 28% of the ASCI patients they treated had additional injuries that increased their risk of morbidity and mortality.

Wolf et al. (28), in 1991, reported their experience with 52 patients with acute cervical bilateral facet dislocation injuries managed with an aggressive treatment paradigm that included ICU care, aggressive resuscitation, invasive monitoring, and hemodynamic manipulation to maintain mean blood pressure above 85 mm Hg for 5 days. Thirty-four patients had complete neurological injuries, 13 patients had incomplete injuries, and 5 patients were intact. The authors attempted closed reduction within 4 hours of patient arrival to their center and performed early open reduction on patients who could not be reduced by closed means. The authors described neurological improvement at discharge in 21% of complete SCI patients and in 62% of patients with incomplete cervical SCIs at admission. No intact patient deteriorated. The authors concluded that their protocol of aggressive, early medical and surgical management of patients with ASCI improved outcome after injury. Treatment in the ICU setting, hemodynamic monitoring with maintenance of MAP above 85 mm Hg, and early decompression of the spinal cord by open or closed means seemed to reduce secondary complications after ASCI in their study.

Levi et al. (13) treated 50 acute cervical SCI patients in the ICU setting according to an aggressive management protocol that included invasive hemodynamic monitoring and volume and pressor support to maintain a hemodynamic profile with adequate cardiac output and mean blood pressure above 90 mm Hg. Their 1993 report described 31 patients with Frankel Grade A injuries at admission, 8 patients with Frankel Grade B injuries, and 11 patients with Frankel Grades C and D. Eight patients had shock at the time of admission (systolic blood pressure <90 mm Hg), and 82% of patients had volume-resistant hypotension requiring pressors within the first 7 days of treatment. Volume-resistant hypotension was 5.5 times more common among patients with complete motor injuries. Forty percent of patients managed by protocol improved, including several with complete injuries; 42% remained unchanged; and 18% (9 patients) died. There was minimal morbidity associated with invasive hemodynamic monitoring. The authors concluded that hemodynamic monitoring in the ICU allows early identification and prompt treatment of cardiac dysfunction and hemodynamic instability and can reduce the potential morbidity and mortality after ASCI.

Vale et al. (26), in 1997, reported their experience with a nonrandomized, prospective pilot study in the assessment of aggressive medical resuscitation and blood pressure management in 77 consecutive ASCI patients. All patients were managed in the ICU with invasive monitoring (Swan Ganz catheters and arterial lines) and blood pressure augmentation to maintain MAP above 85 mm Hg for 7 days after injury. The

authors reported 10 patients with complete cervical SCIs, 25 patients with incomplete cervical injuries, 21 patients with complete thoracic SCIs, and 8 patients with incomplete thoracic level SCIs. The average admission MAP for complete cervical SCI patients was 66 mm Hg. Nine of 10 complete cervical SCI patients required pressors after volume replacement to maintain MAP at 85 mm Hg. Fifty-two percent of incomplete cervical SCI patients required pressors to maintain MAP at 85 mm Hg. Only 9 of 29 patients with thoracic level SCIs required the use of pressors. The authors reported minimal morbidity with the use of invasive monitoring or with pharmacological therapy to augment MAP. At 1-year follow-up (mean, 17 mo), 3 of 10 complete cervical SCI patients regained ambulatory capacity and 2 patients regained bladder function. Incomplete cervical SCI patients fared better. Twenty-three of these patients regained ambulatory function at 12 months follow-up, only four of whom had initial examination scores consistent with walking. Twenty-two (88%) of 25 patients regained bladder control. Thirty-one of 35 cervical SCI patients and 27 of 29 thoracic level SCI patients were treated surgically. The authors statistically compared selection for and timing of surgery with admission neurological function and compared surgical treatment, early and late, with neurological outcome and found no statistical correlation. They concluded that the enhanced neurological outcome identified in their series after ASCI was optimized by early and aggressive volume resuscitation and blood pressure augmentation and was in addition to and/or distinct from any potential benefit provided by surgery.

The collective experience described in these case series (Class III evidence) strongly suggests that maintenance of MAP at 85 to 90 mm Hg improves spinal cord perfusion or affects neurological outcome (13, 14, 23, 26, 28, 29). Prompt treatment of hypotension and resuscitation to MAP levels of 85 to 90 mm Hg is safe and suggests that elevation of MAP to threshold levels may be beneficial to patients with ASCIs. The 7-day duration of treatment and the threshold levels of MAP maintenance seem to have been chosen arbitrarily by the individual clinical investigators (13, 26, 28). They are thought to be analogous to initial duration and threshold MAP level recommendations for management of patients after acute traumatic brain injury. None of the authors provides a specific recipe or an algorithm to guide blood pressure augmentation. All of the articles describe acutely injured patients who have arterial lines and central venous or Swan Ganz catheters in place to monitor pressures and volume status (13, 14, 23, 26, 28, 29). Initially, crystalloid is given intravenously in response to MAP levels below 85 mm Hg. Colloid is administered if the hematocrit is low (blood) or as a volume expander (albumin). If the patient's volume status is optimal but the MAP remains below threshold, the authors describe the use of pressors, typically (although not exclusively) a β-agonist (dopamine), before the addition of an α-agonist (Neo-Synephrine [Sanofi Winthrop Pharmaceuticals, New York, NY]), to elevate the MAP. These agents are titrated to the appropriate dose level to achieve the threshold MAP using volume, pressure, and cardiac performance data provided by the invasive monitoring devices.

SUMMARY

Hypotension is common after acute traumatic SCI in humans. Hypotension contributes to spinal cord ischemia after injury in animal models and can worsen the initial insult and reduce the potential for neurological recovery. Although unproven by Class I medical evidence studies, it is likely that this occurs in human SCI patients as well. Because the correction of hypotension and maintenance of homeostasis is a basic principle of ethical medical practice in the treatment of patients with traumatic neurological injuries, depriving ASCI patients of this treatment would be untenable. For this reason, Class I evidence about the effects of hypotension on outcome after acute human SCI will never be obtained. However, correction of hypotension has been shown to reduce morbidity and mortality after acute human traumatic brain injury and is a guideline level recommendation for the management of traumatic brain injury. Although a similar treatment guideline cannot be supported by the existing SCI literature, correction of hypotension in the setting of acute human SCI is offered as a strong treatment option. Class III evidence from the literature suggests that maintenance of MAP at 85 to 90 mm Hg after ASCI for 7 days is safe and may improve spinal cord perfusion and, ultimately, neurological outcome.

KEY ISSUES FOR FUTURE RESEARCH

The issue of whether blood pressure augmentation affects outcome after human SCI is important and deserves further study. If augmentation of MAP is determined to be of potential benefit, the threshold levels of MAP most appropriate and the length of augmentation therapy need definition. These issues are best analyzed in a multi-institutional prospective cohort study or a properly designed multi-institutional retrospective case-control study.

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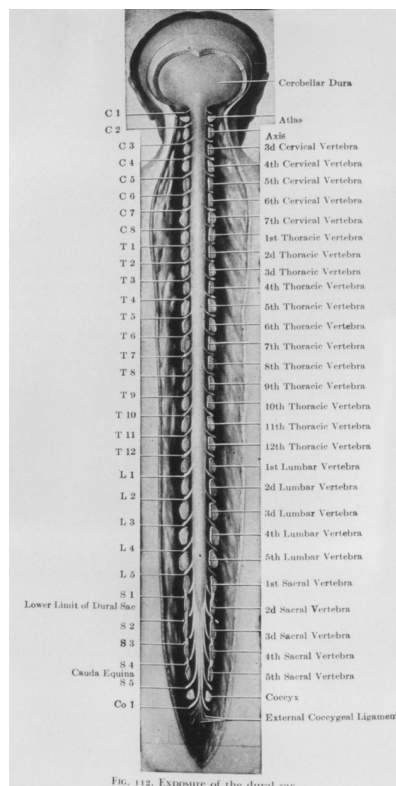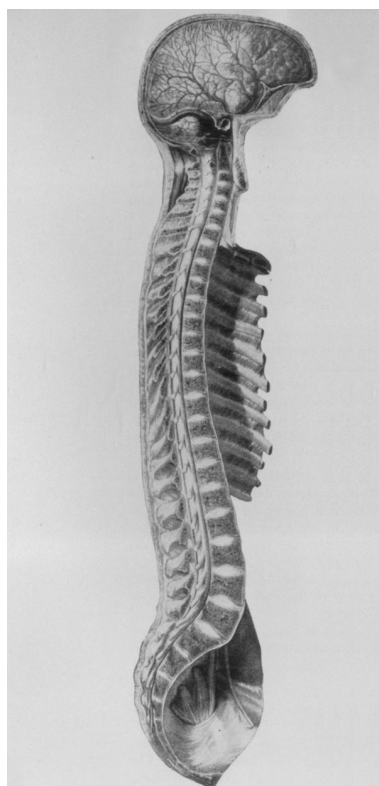

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