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Introduction

Spinal cord injury is a devastating event that most often results in a major disability for an individual and an enormous financial burden for the family. Temporary or permanent motor, sensory, and autonomic impairment may result, thus having a significant impact on one's quality of life. It is estimated that in the United States nearly 12,000 new cases of spinal cord injury (SCI) occur each year and more than 250,000 people are currently living with spinal cord injury (National Spinal Cord Injury Statistical Center [NSCISC], 2012).

Spinal cord injuries can occur at any age, however, the peak incidence occurs in young, adult males between the ages of 25 and 40. This is the time in which many people get married, begin raising a family, and are at the prime of their careers, thus making spinal cord injury even more devastating. It is estimated that more than 50 percent of people with SCI are working at the time of their injury. One year after injury, only ten percent of these people are able to work. The average yearly medical cost for a person with paraplegia is approximately \$500,000 for the first year and \$65,000 for each subsequent year. If a person has tetraplegia the average yearly medical cost is greatly increased to \$850,000 for the first year and more than \$100,000 for each subsequent year. The lifetime cost for SCI at any level often exceeds \$3 million dollars making SCI a costly problem for an individual and society (NSCISC, 2012).

Etiology

Spinal cord injuries can be caused by a number of different injuries to the spine. Motor vehicle accidents are the leading cause of SCI in the United States. In the elderly, the most common cause of SCI is due to a fall. Other causes of spinal cord injuries include violent trauma, (especially gunshot wounds and assault), sports related injuries, diving into shallow water, and industrial accidents (NSCISC, 2012).

Level of Injury

Spinal cord injury is classified according to the vertebral level at which the injury occurred and the severity of the injury to the spinal cord. The lowest level of the spinal cord that maintains motor and sensory function is referred to as the neurological level of injury (Mayo Clinic, 2011). An injury occurring in the cervical segments of the spinal cord will result in tetraplegia, however, an injury occurring in the thoracic, lumbar or sacral segments of the spinal cord will result in paraplegia (Mayo Clinic, 2011). The severity of the injury is classified as being either complete or incomplete. It is also given a grade according to the American Spinal Injury Association (ASIA) Impairment Scale. The ASIA Impairment Scale has five categories listed A-E, and each injury is classified after a neurological examination is performed. ASIA grade A is a complete injury in which there is no motor or sensory function maintained below the level of injury. ASIA grade B is an incomplete injury in which sensory, but not motor function is maintained below the level of injury. ASIA grade C is an incomplete injury in which motor function is maintained below the level of injury and more than half of the key muscles below the level of injury have a muscle grade of 0-2. ASIA grade D is an incomplete injury in which motor function is maintained below the level of injury and at least half of the key muscles below the neurologic level have a muscle grade of 3-5. Lastly, ASIA grade E means that the spinal cord is normal and there are no motor or sensory deficits (American Spinal Injury Association, 2012).

Mechanisms of Injury

The primary mechanisms involved in spinal cord injuries are usually associated with injury to the vertebral column. These mechanisms include concussion, contusion, fracture or

laceration (Hansebout & Kachur, 2011). In addition, various directional movements such as excessive flexion, extension, rotation, or compression often occur simultaneously and contribute to the spinal cord injury (Hansebout & Kachur, 2011). Therefore, a spinal cord injury is a reflection of both the force and direction of the traumatic event.

Pathophysiology (Primary vs. Secondary Injury)

When sustaining a spinal cord injury, there are two types of tissue damage that occur, which are referred to as primary and secondary injury. Primary injury is the initial insult to the spinal cord. It is caused by the mechanical damage to the spinal cord as a result of the force and direction of movements sustained during injury (Hansebout & Kachur, 2011). This type of damage to the spinal cord is immediate and is irreversible. Secondary injury, on the other hand, is caused by a cascade of events that is not completely understood. Within minutes to hours of the initial insult to the spinal cord, a cascade of events is triggered within the body that leads to further spinal cord damage. These events involve disturbances in homeostasis, electrolyte imbalances, vascular changes, edema, inflammation, ischemia, hypoxia, apoptosis and many other processes (Hansebout & Kachur, 2011). Damage from secondary injury extends into a much larger portion of the spinal cord than damage sustained during primary injury. In addition, secondary injury may be preventable if treatments are developed to minimize, slow, or prevent this cascade of events from further damaging the spinal cord. For this reason, SCI research is aimed at targeting secondary mechanisms of injury in hopes of preventing further spinal cord damage and improving neurological functioning after spinal cord injury (Hansebout & Kachur, 2011).

Recently, there has been a great deal of discussion regarding optimal timing of spinal surgery to decompress an injured spinal cord. The goal in spinal decompression surgery is to

relieve pressure from an injured spinal cord in hopes of preventing further damage to the spinal cord by secondary mechanisms of injury and to optimize neurological recovery. Arguments for early surgical intervention in patients with spinal cord compression are based on the knowledge that patients may benefit neurologically from early surgery because by decompressing the spinal cord secondary mechanisms of injury such as hypoxia, ischemia, edema, and inflammation may be reduced, thus leading to less spinal cord damage and better neurological function (Vaccaro et al., 1997). On the other hand, arguments against early surgical intervention are based on the theory that if a patient is not medically stabilized to the maximal level, the respiratory, circulatory, and neurological systems could further deteriorate during surgery, leading to further complications such as massive blood loss, respiratory failure and further spinal cord damage (Vaccaro et al., 1997).

Currently, treatment of acute SCI includes stabilization of the vertebral column, anatomical alignment, administration of medications, especially steroids, such as methylprednisolone, and surgical intervention (Hansebout & Kachur, 2011). In the 1990s, a randomized controlled trial known as the National Acute Spinal Cord Injury Study II or NASCIS II concluded that a neurological benefit was seen in patients with both complete and incomplete spinal cord injuries if methylprednisolone, a steroid, was administered within 8 hours of SCI (Bracken et al., 1990). This study suggests the possibility that a window of opportunity exists in which secondary injury mechanisms can be minimized by medical and surgical interventions to reduce further SCI and thus improve neurological outcome. It also raises the question of whether or not a specific window of time is needed for surgical decompression of the spinal cord in order to optimize neurological functioning following spinal cord injury. The issue of optimal timing of spinal cord decompression surgery has been greatly debated and thus this clinical review was

undertaken to evaluate the current clinical studies and determine whether or not the optimal timing of surgical decompression following acute SCI could be suggested.

Methods

This clinical review was accomplished by conducting a MEDLINE search of the literature to obtain articles pertaining to the timing of surgical decompression in acute cervical spinal cord injuries. The medical subject headings of spinal cord injury, SCI, quadriplegia and paraplegia were paired with the terms surgery, decompression, cervical, and timing. Studies from all countries were included, but the English language was required. The search was limited to clinical studies involving humans, cervical SCI, and adults. To help focus on the most recent and relevant evidence, only articles published in the last 15 years were considered for review. An exception was made to include the results of the National Acute Spinal Cord Injury Study or NASCIS 2 that was published in 1990 because this study was relevant to the clinical question of this review. Finally, the reference lists of articles selected for review was examined to ensure that relevant studies were not excluded.

Discussion

Mirza et al. Study (1989 – 1991)

A retrospective study conducted by Mirza et al. (1999) evaluated the optimal timing of surgical intervention for cervical spinal cord injuries. Forty-three patients from two separate institutions were part of the study. At one institution patients underwent surgical intervention within 72 hours of injury, and at the other institution patients underwent surgical intervention 72 hours after injury. Neurological status, length of stay in the hospital, and acute complication rates in regards to the timing of surgical intervention were all evaluated during the study. The results showed that the length of stay in the hospital was significantly different between the two groups. The length of stay in the hospital was shorter for the early group (21.9 days vs. 36.8 days). The number of complications was also significantly different between the two groups. The early group had less complications compared to the late group. In regards to neurological function, there was no significant difference in neurological improvement between the two groups (Mirza et al., 1999). It should be noted that this study like many other studies had a very small sample size with only 43 patients, which makes it difficult to determine if a neurological benefit to early surgery truly existed in this study. The two groups in this study were also from different institutions and other factors such as quality of care, provider training, equipment etc. between these two hospitals could have influenced the outcome.

Vaccaro et al. Study (1992 – 1995)

A three year, randomized, prospective study conducted from 1992 – 1995 by Vaccaro et al. (1997) evaluated length of hospital stay, length of inpatient rehab, and neurological outcome of patients with cervical SCI after they underwent either early (≤ 72 hours after SCI) or late (> 5 days after SCI) surgery at one hospital. A total of 123 patients were admitted to the hospital

during the study, but only 64 patients met the inclusion criteria. One of the major inclusion criteria of the study was that patients had to be admitted to the hospital within 48 hours of SCI to allow for scheduling of surgery within the 72 hour window. In this prospective study, 64 patients were randomly assigned to either the early or late surgery group. The early surgery group underwent surgery at a mean of 1.8 days and the late surgery group underwent surgery at a mean of 16.8 days. The results of this study showed that there was no benefit to early surgery with regards to length of hospital stay, length of inpatient rehab, and more importantly, neurological function (Vaccaro et al., 1997).

Like many other studies, the sample size of this study was small, which makes it difficult to determine if a neurological benefit to early surgery existed. Furthermore, the time frame of less than 72 hours used in this study may not have been adequate to determine a neurological benefit. The mean time that the early group underwent surgery was 1.8 days after injury. This period of time may have been too long to reduce secondary damage to the spinal cord and improve neurologically.

Tator et al. Study (1994-1995)

In a multicenter, retrospective study conducted by Tator et al. (1999), 585 patients' records were reviewed in 36 different centers throughout North America to determine the role and timing of surgery in acute SCI. The data covered a nine month period from 1994-1995. The timing in which surgery was performed varied widely in this study from less than 24 hours (23.5%), 25-48 hours (15.8%), 48-96 hours (19.0%), and more than 5 days (41.7%) post injury. This study showed that a small percentage of patients were able to undergo surgery within 24 hours of their injury and when comparing the data from all 36 centers, a consensus on the optimal timing of surgery for acute SCI could not be determined (Tator et al., 1999). The

different time frame under which surgery was performed was likely to be the reason why a consensus could not be determined.

Sapkas and Papadakis Study (1987-2000)

Sapkas and Papadakis (2007) performed a retrospective study to determine if early surgery defined as within 72 hours had an effect on the neurological outcome of patients with cervical SCI. The study was conducted with patients who sustained cervical SCI from 1987 to 2000. In this study, a total of 67 patients underwent either early or late surgery. Thirty-one patients underwent early surgery and 36 patients underwent late surgery. The study concluded that after surgery, only patients with incomplete SCI showed neurological improvement, but overall the timing of surgery did not affect the neurological outcome (Sapkas and Papadakis, 2007).

McKinley et al. Study (1995-2000)

McKinley et al. (2004) performed a retrospective study that consisted of 779 patients using a multicenter database. Neurological outcomes, complications and hospital length of stay were measured. Patients studied were admitted to a hospital within the first 24 hours after injury with acute, non-penetrating traumatic SCI from 1995 – 2000. Participants selected for the study were divided into three groups that either underwent early surgery (≤ 72 hours after injury) late surgery (> 72 hours) or no surgery. The study found that the group of patients undergoing late surgery had significantly increased length of stay in the hospital as well as more complications. This was not true of the early or no surgery group, however, no significant differences in neurological outcome occurred between the three groups (McKinley et al., 2004).

The study did not address the timing of medical complications, therefore, it could not differentiate between complications that may have occurred prior to surgery or as a result of the

surgery (McKinley et al., 2004). For this reason, the conclusions regarding length of stay and complications as a result of early or late surgery may be questionable; however, the conclusion that the neurological outcome was the same is still relevant.

Ng et al. Study (1996-1997)

Ng et al. (1999) performed a prospective pilot study from 1996 to 1997. Twenty-six patients from eight North American centers were examined to determine if it was feasible and safe to perform surgery to decompress the cervical spinal cord within eight hours. Neurological outcome was also looked at to determine if improvement was seen with early surgery defined as within eight hours. Twenty-six patients were included in the study however, only two patients were able to meet this eight hour surgery window. In total, 22 patients underwent surgery with an average time of 40.1 hours, with only seven of these patients receiving surgery within twelve hours. During this study, the average time it took to obtain necessary spinal cord images was measured. On average it took 3.7 hours from the time of injury to perform a CT myelogram and approximately eight hours to perform a MRI of the spinal cord (Ng et al., 1999). As a result, this study demonstrated that the ability to perform surgery within eight hours of injury for these eight centers was extremely difficult, even when all of these centers were specialized centers trained to handle SCI patients. The time required for first responders to arrive at the scene of an accident, stabilize the patient, transport the patient to the hospital and the time for hospitals to complete necessary imaging and surgical preparation usually exceeded the eight hour window from injury-to-surgery (Ng et al., 1999). It is also important to note that because this sample size was too small, the study was unable to conclude whether or not there was a benefit to early surgery (<8 hrs). However, the information gained in the study allowed them to identify the critical factors that delay early decompression surgery, the most important of which were delayed referral to

hospitals specialized in treating patients with SCI and delayed imaging studies such as CTs and MRIs (Ng et al, 1999). It is believed that these issues can be overcome and that protocol standards for decompression surgery within eight hours of injury can be established (Ng et al, 1999). Faster transfer of potential SCI patients to the hospitals can be achieved by educating first responders, emergency physicians and physician assistants. In addition, earlier access to MRI imaging could be accomplished by gaining the cooperation of the radiologists and emphasizing the importance of early decompression. Further educating spine surgeons and emergency medicine physicians on the importance of this 8 hour window would also help to overcome this barrier.

Papadopoulos et al. Study (1990-1997)

A prospective study performed by Papadopoulos et al. (2002) recorded data from patients suffering from cervical spinal cord injury who received their care at the University of Michigan from 1990 – 1997. This study was performed to assess the feasibility and outcome of early surgical decompression. The study emphasized the need for immediate surgical decompression and therefore, developed a protocol that if a patient arrived at the University of Michigan for acute care of SCI and was stable enough for surgery, every attempt was made to quickly image the spinal cord by using MRI. For the study, 91 patients were prospectively studied. Sixty-six patients were included in the protocol group. This group underwent immediate MRI of the spine to determine if spinal cord compression was present and if stable, the patient then underwent immediate spinal decompression surgery. Twenty-five patients were included in the reference group. This group consisted of patients that were not able to undergo an immediate MRI or required other emergency surgeries to sustain life. The mean time from spinal cord injury to obtaining an MRI for the study group was 4.1 hours. The average time from injury to arrival at

hospital was 3.8 hours. Most critical, the average time from injury to surgery was 9.6 hours for the study group. When neurological improvement was measured, 39 out of 66 patients in the study group showed improvement. The study patients on average spent 14 fewer days in the ICU and 29 fewer total days in the hospital than the reference group. Fifty-four percent of the study patients, compared with only 24% of reference patients, improved from their admitting ASIA grade (Papadopoulos et al., 2002). This study not only demonstrates that it is feasible to perform spinal cord decompression within twelve hours, but also showed that there is significant benefit to the patient. Since the mean time of surgery was less than 10 hours and a neurological improvement was noted, this suggests that there may be an even greater benefit to early surgery defined as less than eight hours.

Wilson et al. Study (2007-2009)

During a two year period from 2007-2009 a prospective study by Wilson et al. (2012) was conducted to determine if early surgery had a benefit on neurological outcome following SCI. A total of 84 patients were enrolled over a two year study period. Patients were divided into two groups. One group underwent early surgery (< 24 hours after injury) and another group underwent late (> 24 hours after injury) surgery. In this study, 35 patients (41.7%) underwent early surgery and 49 patients (58.3%) underwent late surgery. The mean time of surgery for the early group was 12.7 hours and the mean time for surgery for the late group was 155.0 hours. The average length of stay in the hospital was 24.8 days. There was no difference in the average length of stay between the early surgery group and the late group. After the two year study was analyzed, it was determined that there may be a significant neurological benefit to early surgery. In the early group, there were more patients with complete injuries as opposed to the late group

that had more patients with ASIA grade D scores. However, the early group showed a significant improvement in neurological functioning (Wilson et al., 2012).

Fehlings et al. Study (2002-2009)

Fehlings et al. (2012), Surgical Timing in Acute Spinal Cord Injury Study (STASCIS) was a prospective controlled study that was designed to determine the effectiveness of early (< 24 hours post injury) versus late (> 24 hours post injury) spinal cord decompression surgery on the neurological outcome of patients with cervical SCI. This study was conducted over a seven year period, from 2002-2009 at six North American centers that all specialized in treating patients with SCI. During the study period neurological outcome, complication rates and mortality were evaluated to compare early versus late decompression surgery. A total of 313 patients were enrolled in the study of which 182 patients underwent early surgery at a mean of 14.2 hours and 131 patients underwent late surgery at a mean of 48.3 hours. The study concluded that there was a neurological benefit to early surgery as defined as being less than 24 hours after injury. Out of 222 patients with post-surgery follow-up available, 19.8% of the patients undergoing early surgery showed neurological improvement compared to only 8.8% in the late surgery group. Additionally, 24.2% of the early group experienced complications compared to 30.5% of the later surgery patients (Fehlings et al., 2012).

Conclusion

After performing a review of the clinical studies regarding the optimal timing of decompression surgery for acute spinal cord injuries, it becomes apparent that there may be a benefit to early surgical decompression. However, based on a review of the current studies available, it becomes apparent that more work needs to be done before a recommendation for optimal timing can be determined.

There was a different conclusion in studies that attempted to answer the question of whether or not early surgery was beneficial. Overall, the studies that classified early surgery as <72 hours did not determine that there was a significant benefit to early surgery. However, those that classified early surgery as <24 hours, did conclude that early surgery was beneficial. Many of these studies indicated neurological improvement, reduced length of stay, and reduced complications were identified in patients who had surgery within 24 hours of injury.

Based on current clinical evidence, it would not be beneficial to conduct more studies on the benefit of decompression surgery < 24 hours until we can improve the time period from injury to surgery. The studies that attempted to narrow this time period to <8 hours, were inconclusive because too few patients were operated on within eight hours of injury. Instead of conducting more studies, a concerted effort should be made to educate all people who encounter a person who they suspect may have suffered a spinal cord injury on the importance of getting the patient to surgery quickly. Everyone from the first responder at the scene of an accident, to emergency room providers, and even radiologists, need to be educated if we are going to improve long-term effects of spinal cord injuries. Once we are able to get patients to surgery within eight hours, additional studies can be made to determine the optimal timing for surgical decompression of spinal cord injuries

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Abstract

Objective: To evaluate the clinical evidence and determine recommendations regarding the optimal timing of decompression surgery following acute cervical spinal cord injury. **Methods:** A MEDLINE search of the English literature was performed using the search terms spinal cord injury, SCI, quadriplegia and paraplegia, which were paired with the terms surgery, decompression, and timing. To focus on the most recent and relevant evidence, only articles published in the last 15 years were considered for review. **Results:** Recent studies classifying early decompression surgery as <72 hours showed minimal to no improvement in patient outcomes. However, studies where the decompression surgery occurred < 24 hours from injury resulted in significant improvement. **Conclusion:** There is a benefit to performing decompression surgery in <24 hours following acute cervical spinal cord injury. However, concerted efforts to operate within eight hours of injury are needed to further advance our understanding of the optimal timing for decompression surgery.