REVIEW ARTICLE
BASIC SCIENCES/OTHERS
http://dx.doi.org/10.1590/S1808-185120222103265129

EFFECT OF TIME UNTIL DECOMPRESSION ON NEUROLOGIC RECOVERY AFTER SPINAL CORD INJURY

EFEITO DO TEMPO ATÉ DESCOMPRESSÃO NA RECUPERAÇÃO NEUROLÓGICA APÓS TRAUMATISMO RAQUIMEDULAR

EFECTO DEL TIEMPO DE DESCOMPRESIÓN EN LA RECUPERACIÓN NEUROLÓGICA DESPUÉS DE LESIÓN MEDULAR

EDUARDO AUGUSTO IUNES[1,2], FRANZ JOOJI ONISHI[1,2], HERTON RODRIGO TAVARES COSTA[2,3], THIAGO LEONARDI AZUAGA[2]

1. Universidade Federal de São Paulo, Discipline of Neurosurgery, São Paulo, SP, Brazil.
2 Sociedade Brasileira de Coluna - São Paulo Regional, São Paulo, SP, Brazil.
3. Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Department of Orthopedics and Anesthesiology, Ribeirão Preto, SP, Brazil.

ABSTRACT

Spinal cord injuries can have serious consequences for the individual, such as loss of motor function, sensory impairment, and alteration of physiological systems functions. Treatments for spinal cord injuries involve the use of drugs and surgical approaches. In the surgical field, there is a question about the ideal time after the trauma to perform the surgical procedure. The studies divide the time until surgery after the injury into two categories: "early" and "late". To review the scientific literature on this topic, and to assess the relative effectiveness of early versus late decompressive surgery, we considered early intervention up to 24 hours and late intervention from 24 hours after the injury. For this, we performed a literature review and selected retrospective, prospective observational studies, clinical studies, and reviews with meta-analysis that compared the recovery time of patients with spinal cord injury after surgeries performed within 24 hours (early) and after 24 hours (late). The results showed potential for neurological improvement with early or even ultra-early surgical decompression (up to 12 hours) in patients with traumatic cervical spinal cord injury. On the other hand, reports about the advantage of early decompression when there is a thoracic injury are scarce. In addition to the time to decompression, the concomitant use of some drugs seems to play an important role in patients' recovery. ***Level of Evidence II; Literature review.***

Keywords: Spinal Cord Injuries; Decompression, Surgical; Systematic Review.

RESUMO

Lesões na medula espinhal podem gerar sérias consequências para o indivíduo, como perda de função motora, prejuízo sensorial e alteração de funções de sistemas fisiológicos. Os tratamentos para lesões na medula espinhal envolvem o uso de fármacos e abordagens cirúrgicas. No âmbito cirúrgico, há o questionamento sobre qual o tempo ideal após o traumatismo para realizar o procedimento cirúrgico. Os trabalhos dividem em duas categorias o tempo até a realização da cirurgia após a lesão: "precoce" e "tardio". Com a finalidade de revisar a literatura científica sobre esse tema, a fim de avaliar a eficácia relativa da cirurgia descompressiva precoce versus tardia, consideramos a intervenção precoce até 24 horas e a tardia a partir de 24 horas da injúria. Para isto realizamos uma revisão da literatura e selecionamos estudos observacionais retrospectivos, prospectivos, estudos clínicos e revisões com meta-análise que comparavam o tempo de recuperação de pacientes com lesão medular após cirurgias realizadas em até 24 horas (precoce) e após 24 horas (tardio). Os resultados demonstraram potencial de melhora neurológica com a descompressão cirúrgica precoce ou até ultraprecoce (até 12 horas) em pacientes com lesão medular traumática cervical. Por outro lado, relatos acerca da vantagem da descompressão precoce quando há uma lesão torácica são escassos. Além do tempo até a descompressão, o uso concomitante de alguns fármacos parece ter um importante papel na recuperação dos pacientes. ***Nível de evidência II; Revisão de literatura.***

Descritores: *Traumatismos da Medula Espinal; Descompressão Cirúrgica; Revisão Sistemática.*

RESUMEN

Las lesiones de la médula espinal pueden tener consecuencias graves para el individuo, como pérdida de función motora, deterioro sensorial y alteración de funciones de los sistemas fisiológicos. Los tratamientos para las lesiones de médula espinal involucran uso de medicinas y enfoques quirúrgicos. En el campo quirúrgico, existe la duda sobre el momento exacto después del traumatismo para realizar lo procedimiento quirúrgico. Los estudios dividen el tiempo hasta la cirugía después de la lesión en dos categorías: "temprano" y "tardío". Con el fin de revisar la literatura científica sobre este tema, y con el fin de evaluar la efectividad relativa de la descompresión quirúrgica temprana frente a la tardía, se consideró la intervención temprana hasta las 24 horas y la intervención tardía a partir de las 24 horas después de la lesión. Para ello, efectuamos una revisión bibliográfica y seleccionamos estudios retrospectivos, prospectivos observacionales, estudios clínicos y revisiones con metaanálisis que compararon el tiempo de recuperación de pacientes con lesión medular con cirugías realizadas en 24 horas (temprano) y a las 24 horas (tardía). Los resultados presentaron potencial para la mejora neurológica con descompresión quirúrgica

Study conducted by the Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, SP, Brazil.
Correspondence: Eduardo Iunes. Rua Napoleão de Barros, 715, Vila Clementino, São Paulo, SP, Brazil. CEP 04024-002. eduardo@dreduardoiunes.com.br

Received on 06/27/2022 accepted on 07/19/2022
Reviewed by: Dr. Alexandre Fogaça Cristante

temprana o incluso ultra temprana (hasta 12 horas) en pacientes con lesión traumática de la médula espinal cervical. Por otro lado, son escasos reportes sobre la ventaja de descompresión temprana cuando existe una lesión torácica. Además del tiempo de descompresión, el uso concomitante de algunos fármacos parece jugar un papel importante en la recuperación de los pacientes. ***Nivel de Evidencia II; Revisión de literatura.***

Descriptores: *Traumatismos de la Médula Espinal; Descompresión Quirúrgica; Revisión Sistemática.*

INTRODUCTION

Traumatic spinal cord injuries (TLME) can have serious consequences for the individual, such as loss of motor function, sensory impairment, and alteration of physiological systems functions, profoundly affecting the lives of patients and their families with physical, psychological, and economic damages to society.[1-3] Its prevalence has been increasing yearly, with approximately 750 cases of TSCI/million inhabitants worldwide and 16 to 40 cases/million inhabitants per year in Brazil, with 80% of the victims being men and the majority between 10 and 10 years old. 30 years old.[4, 5]

LTME can be temporary or permanent and presents as a result of physical impacts, and its pathophysiology can be divided into two phases, primary and secondary.[6, 7] Direct spinal cord injury, or primary injury, results from rapid compression of the spinal cord, causing damage to axons, blood vessels, and cell membranes, or fracture of the vertebrae. The secondary injury results from a sequence of events that cause the death of neurons and glial cells by ischemia and inflammation. The secondary mechanism is initiated by the primary lesion. It includes a cascade of biochemical and cellular processes, such as vascular changes, electrolyte imbalance, free radical formation, edema, inflammatory reaction, and apoptosis, among other processes.[8] Preventing the activation of secondary mechanisms is an opportunity to mitigate neurological effects from LTME; thus, anti-inflammatory drugs and surgical decompression have been investigated as an effective treatment strategy.[3]

One of the first studies to establish the possible relationship between decompression surgery and neurological improvement in patients with LTME observed that patients had a neurological improvement soon after surgery, suggesting a cause and effect relationship between surgery and the observed improvement.[9] Corroborating these findings, another study observed an improvement in neurological outcomes compared to patients undergoing other treatment protocols and that patients undergoing immediate decompression surgery required a shorter hospital stay.[10]

Since then, beneficial effects have been associated with decompression surgery, especially early (< 24 h after injury) compared to late (> 24 h after injury), but the real influence of decompression time on the neurological improvement of patients with LTME is still challenging. There are differences in the time of early decompression, indicated by some groups as 72 hours after the injury and by others, 24 hours after the injury. There are many variables involved in the interpretation of the results, such as the mechanism of trauma, decompression route (posterior *vs.* anterior), specific surgical technique, levels of decompression, types of evidence (observational and interventional studies), and, mainly, the lack of complete information on the patients arriving admission at the emergency services.

To review the main scientific publications on this topic, but mainly to discuss the quality of the available scientific evidence and the clinical experience of early decompression surgery *vs.* late, we considered conducting a literature review of studies comparing surgical decompression time to clinical neurological outcomes after acute LTME.

METHOD

To search for the articles used in this literature review, the following electronic databases were used: Latin American Literature in Health Sciences (LILACS), accessed through the Virtual Health Library (BVS Bireme), Virtual Health Library (Scielo), and MEDLINE, accessed through the PubMed search platform. Searches were performed using a combination of the following descriptors: "spinal cord injury", "cervical", "early decompression", "late decompression", "therapeutics", "surgery" and "timing".

Full articles from peer-reviewed journals were included, including observational (case series, cross-sectional studies, cohort studies, real-world studies) and interventional, prospective comparative, and retrospective studies, and literature reviews and meta-analyses, in Portuguese or English, which compared the recovery time of patients with spinal cord injury (cervical, thoracic or lumbar portion) who received early (within 24 hours) or late (after 24 hours) surgical decompression. To obtain greater homogeneity among the articles evaluated, we selected studies with a minimum follow-up of 6 months that compared neurological outcomes before and after recovery evaluated by the AIS (*American Spinal Injury Association (ASIA) Impairment Scale*), which is a neurological examination standardized to assess sensory and motor levels affected by spinal cord injury that classifies patients A to E, with grade A being the most severe (no motor or sensory functions) and grade E representing normal motor or sensory functions.

RESULTS

To compare early (within 24 hours) or late (after 24 hours) surgical decompression, we selected nine articles, two retrospective observational studies, two prospective observational studies, two randomized and multicenter clinical studies, and three systematic reviews to compose our evaluation (Table 1).

Confirmatory evidence on the benefits of early spinal cord decompression

Of the nine articles evaluated, two observational studies, one randomized clinical trial, and two systematic reviews demonstrated significant improvement in neurological performance in the early group. The randomized clinical trial by Cengiz et al. compared decompression surgery performed within 8 hours after the occurrence of the spinal cord injury (early surgery) with surgery performed 3 to 15 days after the injury occurred (delayed surgery). The neurological assessment after surgery showed a neurological improvement in 10/12 patients operated on early, 4 of whom were classified as E on the AIS scale; that is, they had normal motor and sensory functions after surgery. Among the patients operated on late, 4/15 had neurological improvement, none classified as grade E.[16]

The neurological benefits of early decompression after LTME were also demonstrated by a large prospective cohort of the STASCIS (*Surgical Timing in Acute Spinal Cord Injury Study*) study by Fehlings et al., who followed 313 adults undergoing early (< 24 h post-injury) or late (≥ 24 h post-injury) decompression surgery. The 222/313 patients, 131 who underwent early surgery and 82 who underwent late surgery, with follow-up available six months after the injury, were evaluated using the AIS scale. The results obtained showed that 19.8% (25/131) of patients undergoing early surgery showed an improvement of ≥ 2 degrees on the scale compared to 8.8% (7/82) in the group undergoing late decompression. Of the 313 individuals included in the study, 194 (62%) received corticosteroids at hospital admission, according to the assistant surgeon's personal choice, with a higher proportion of administration in the early group than in the late group.[13]

Also, using the AIS scale to assess neurological improvement, another study evaluated 98 individuals with SCI who underwent early (≤ 24 h after trauma) or late (> 24 h after trauma) decompression surgery. The results showed that, six months after surgery, 23.3% of the patients undergoing early surgery showed an improvement of ≥ 2 degrees in the AIS. In contrast, only 8.7% of the group undergoing late surgery showed similar performance.[14]

Table 1. List of selected studies.

Study (author, year)	Kind of study	Number of early individuals/ late	Injury region-intervention	pharmacological intervention	FU (months)	Neurological Outcome
Aarabi, 2020(11)	EOR	47*/15	C	Methylpred.	6	There was no difference sig.
Sewell, 2018(12)	EOR	40/55	C	Not specified	6	There was no difference sig.
Fehlings, 2012(13)	EOP	182/131	C	Methylpred.	6	Improvement sig. in the early group
Umerani, 2014(14)	EOP	34/64	C	Not specified	6	Improvement sig. in the early group
Rahimi-Movaghar, 2014(15)	ECR	16/19	T and TL	Methylpred.	12	There was no significant difference
Cengiz, 2008(16)	ECR	12/15	TL	Methylpred.	12	Improvement sig. in the early group
Badhiwala, 2021(17)	RS	528/1020	C, T and TL	Methylpred.	12	Improvement sig. in the early group
Ter Wengel, 2019(18)	RS	1720/1989	T and TL	not standardized	6	There was no difference sig.
Qiu, 2021(2)	RS	1988/1989	C, T and TL	Not standardized	12	Improvement sig. in the early group

*32 ultra-early and 25 early. Subtitle: EOR – Retrospective observational study; EOP – Prospective observational study; RCT – Randomized clinical trial; RS – Systematic review; FU – *Follow-up* ; Methylpred. – Methylprednisolone; C – Cervical; T - Thoracic; TL – Thoracolumbar; Sig. – significant.

An important limitation of the studies presented is the lack of homogeneity among patients, lack of information on the severity of the lesion at baseline, and small sample size. The average age of participants in the early group was lower than that of participants in the late group study by Fehlings et al. This limitation was probably because most surgeons opted for earlier surgical interventions in younger patients.[13] In the randomized study by Cengiz et al., although the age range was the same in both groups (23-68 years), the median age in the early group was lower (38 years) compared to the late group (42 years). However, a statistical analysis of this difference was not presented.[16]

Recently, Badhiwala et al. compiled data from 1548 participants with acute spinal cord injury who underwent decompression between 1991 and 2017. Data were pulled from databases and included solid studies such as *North American Clinical Trials Network* (NACTN) SCI Registry, STASCIS, The Sygen trial, and the National Acute Spinal Cord Injury Study (NASCIS III). From this compilation of studies, it was possible to show that early surgical decompression (<24 hours) is associated with better sensory and neurological recovery, with an improvement in the AIS scale of 1, 2, or 3 degrees in one year compared to patients who had late surgery ($p = 0.0019$). Another important finding of this review was a decline in motor function in the first 36 hours after the injury. In general, through the review of these studies, it was possible to obtain strong evidence that patients with acute spinal cord injury should undergo the decompression procedure within the first 24 hours after the injury. However, this scenario may not be possible in cases of unstable patients due to multiple traumas or medical comorbidities.[17]

In another systematic review and meta-analysis, 16 studies involving the recovery of 3977 patients with spinal cord injury were reviewed. Significant improvements in motor scores, light touch scores, and sensitivity were observed in the early group (< 24 hours) compared with patients in the late group (> 24 hours). The authors also evaluated the neurological evolution of patients up to 12 months after surgery. They observed that in 788 patients, improvement ≥ 2 degrees AIS was more observed in patients undergoing early surgery, while improvement of ≥ 1 degree was similar between groups compared. The authors emphasize that there was no difference in mortality between the early and late groups. An important limitation of this study is the assessment of patients about global physical status. Patients with spinal cord damage often accompany other types of injury to other systems, and the severity of other injuries can influence patients' recovery.[2]

Controversial evidence on the benefits of early spinal decompression

While most studies demonstrate neurological improvement associated with early decompression after injury, such an effect was not observed in some studies.[11,12,15,18]

In a randomized clinical study with 35 patients, the recovery of patients with injuries in the thoracic and thoracolumbar regions was analyzed. An interesting factor about the work is that all patients were under the intervention and treatment decisions of the same doctor, thus decreasing a possible recovery variable. Although statistical differences between early and late have not been proven, in this study, it is possible to observe an improvement of two AIS degrees in 3 patients in the early group (16 participants) and only one in the late group (19 participants). Due to the small number of study participants, the work is limited in terms of statistical analysis. Thus, the authors concluded that there was no difference in recovery between the two groups studied.[15]

In some patients, it is possible to observe thoracic injury concomitant with the neck; in this sense, Sewell et al. reviewed to investigate the benefits of early decompression and stabilization of patients with this clinical condition. The group reported that early decompression surgery (< 24 hours) was associated with shorter ICU stay and a lower complication rate for patients with concomitant cervical and thoracic trauma. Still, no significant difference in neurological improvement was observed between the two groups (early 47.5% *vs.* late 42%, $p = 0.3$). However, it is worth mentioning that the neurological recovery was more noticeable in younger patients with a lower degree of base injury.[12]

A retrospective study by Aarabi et al. evaluated the effect of long--term decompression time on neurologic outcomes in 72 patients with traumatic cervical spinal cord injury. Patients were operated on at three different times: ultra-early up to 12 hours, early between 12-24 hours, and late from 24-138.5 hours. AIS score at admission and preoperative intramedullary lesion length were the strongest predictors of neurologic outcome. While in the ultra-early and early groups, 84.3 and 72% of the patients were classified as grade A and B on the AIS scale before surgery, this proportion was 33% in the late group. The Aarabi group observed an improvement of ≥ 1 degree on the AIS scale in 65.6%, 60%, and 80% undergoing ultra-early, early, and late decompression, respectively. However, multiple regression analysis revealed that the extent of the intramedullary injury was the only significant variable predicting AIS grade conversion. Thus, the authors concluded that the long-term neurological outcome was not determined by the time of surgery but by the extent of the intramedullary injury. Importantly, the mean lesion length in the ultra-early group (43.4 mm) was greater than in the early (37.5 mm) and late (30.6 mm) groups.[11]

The gap in robust data on the beneficial effect when the intervention occurs within 24 hours can also be explained as many systematic review studies do not specify the area of spinal injury. In this scenario, Ter Wengel et al. conducted a systematic review in which they investigated the neurological improvement after early and late surgery in patients with lesions in the thoracic and thoracolumbar

region (T11-L2). The systematic search retrieved 14 study publications reporting outcome measures after surgery in 1075 patients. However, the authors did not observe a significant beneficial effect of 24-hour surgical decompression in patients with traumatic thoracic and thoracolumbar spinal cord injury. The rate of improvement of ≥ 1 grade or ≥ 2 grades on the AIS scale in the early surgery group was 66.8% and 42.0%, respectively, while in the late surgery group, the improvement rate was 48.9 % and 27.3%, respectively. However, the quantitative analysis performed in this meta-analysis did not confirm a significantly beneficial effect when patients underwent early surgery.[18]

Pharmacological intervention

Overall, no correlation was observed between the administration of pharmacological intervention on the neurological benefit of patients undergoing early or late decompression. In one study, methylprednisolone was given to 22 of 62 patients based on the year the surgery was performed. Until 2009 this was a research center protocol. As of 2010, the use of steroids was discontinued for patients with spinal cord trauma as there was no correlation between the use of methylprednisolone and clinical improvement.[11]

In studies by Fehlings et al., a better neurological prognosis in patients who suffered cervical injuries. However, the authors performed a statistical adjustment to eliminate bias for medication and pre-surgical neurologic status, which was significantly different across groups. Yet, the odds of an improvement of ≥2 degrees in ASIA were 2.8 times higher for individuals undergoing early surgery.[13]

Both randomized clinical trials used the same pharmacological intervention protocol recommended by the NASCIS II study. In one study, significant improvement was observed in the early group;[16] in the other, no difference was observed between the groups.[15] Although pharmacological intervention can be a confounding factor for evaluating a surgical intervention, the standardization of the pharmaceutical protocol in both studies reduces the confounding bias.

In the systematic review carried out by Qui et al., when evaluating the subgroup of patients who received methylprednisolone with those who did not receive the drug, it was possible to observe a difference in the patients in the early group who received the drug before surgery, so that the authors suggest that some factors may influence the effect of glucocorticoid, such as the time window in which it is used, and administration of the drug within 8 hours after injury was positive for the recovery of patients. Another factor that may be related to the drug's effect is the level of spinal cord injury, with incomplete injury being the most promising for using methylprednisolone.[2]

Confirmatory evidence on the benefits of ultra-early spinal decompression (<12h)

Some observational studies have supported the idea of interventions even earlier than 24 hours for surgical intervention after injury. Cengiz et al. showed the benefit of the surgery in up to 8 hours. However, the comparison was performed with patients undergoing surgery three days after the injury occurred. In the study by Aarabi et al., no neurological benefit was observed in patients undergoing decompression within 12 h of injury, compared with 12 to 24 h or > 24 h.[11]

Although they were not included in our review to compare early (within 24 hours) or late (after 24 hours) surgical decompression, these studies show the effects of ultra-early surgery within 5 to 12 hours (Table 2). Three studies showed benefits of 8 hours[19,20] and 12 hours[21] of decompression after LTME, while the study by Mattiassich et al. demonstrated no neurological benefit in patients undergoing decompression within 5 hours of injury.[22]

Grassner et al. reported that patients with SCI who underwent ultra-early surgical decompression (< 8 h after injury) had better functional and neurological outcomes compared to individuals who underwent late surgery (> 8 h after injury). The authors concluded through the review that ultra-early decompression is an independent predictor of improved bladder function and mobility after one year. The neurological improvement assessed by the AIS scale was generally greater in patients in the ultra-early group. In addition, in this study, it was possible to observe a significant functional improvement in patients who received corticosteroids, suggesting that the use of drugs can also play an important role in the recovery of patients.[19]

Mattiassich et al. analyzed a limited surgery time window of 5 h compared with 5-24 h post-injury. An improvement of 1 degree on the AIS scale was observed in 31% and 42% of patients in the 24h and five h groups, respectively. Improvement by 2 degrees on the same scale was observed in 31% and 6% of patients in the 24h and five h groups, respectively. An improvement of three degrees on the scale was observed in 6% and 3% of patients in the 24 h and five h groups, respectively. The results generally show that spinal cord decompression within 24 h of spinal cord injury is associated with better neurologic outcomes. No additional neurologic benefit was seen in patients undergoing decompression within five h of injury. The authors point to the need for more scientific evidence to determine whether very early surgery (5 h) is associated with reduced improvement levels, as suggested by the results.[22]

To investigate short-term neurological damage, the group Burke et al. researched the optimal time for surgery after cervical spinal cord injury through the analysis of the AIS scale. The authors collected data from 48 patients with cervical spinal cord injury based on the time from emergency department presentation to surgical decompression. Patients were grouped into ultra-early (decompression within 12 h of presentation), early (within 12-24 h), and late (> 24 h). The results showed that patients who were operated on within 12 hours of admission had an improvement in AIS grade up to discharge. Overall, the data from Burke's review suggest that surgical decompression after cervical cord injury that occurs within 12 hours may lead to faster neurological recovery compared to surgeries that occur after 12 hours.[21]

As with the previously reviewed retrospective studies, Jug et al. performed a prospective observational study investigating the effects of ultra-early decompression performed within 8 hours of spinal cord injury and a second group with decompressions performed from 8 to 24 hours. The authors observed that after six months of follow-up, there was an improvement of at least 2 degrees AIS in 45.5% of the patients in the ultra-early group and in 10% of the patients in the group that underwent decompression from 8 to 24 hours. Therefore, the authors suggest that patients who undergo decompression within 8 hours have superior neurological outcomes than patients who undergo decompression within 8 to 24 hours, with no increase in the rate of adverse effects.[20]

Table 2. List of studies evaluating the ultra-early time.

Study (author, year)	Kind of study	Number of ultra-early individuals/precocious	Injury region-intervention	pharmacological intervention	FU	Neurological Outcome
Grassner, 2016(19)	EOR	35/35	C	Methylpred.	12 months	Improvement sig. in the ultra-early group
Burke, 2019(21)	EOR	18/30*	C	Not specified	Until hospital discharge	Improvement sig. in the ultra-early group
Mattiassich, 2017(22)	EOR	33/16	C	Methylpred.	6 months - 3 years	There was no difference sig.
Jug, 2015(20)	EOP	26/22	C	Methylpred.	6 months	Improvement sig. in the ultra-early group

* 17 early and 13 late. Subtitle: EOR – retrospective observational study; EOP – prospective observational study; FU – *Follow-up* ; Methylpred. – Methylprednisolone; C – cervical; sig. – significant.

DISCUSSION

Acute spinal cord injuries can result in severe motor and sensory disturbances, autonomic functions, and psychosocial problems for the patient due to these factors.[1-3]

Despite recent efforts in data meta-analyses, the truth is that most of the available literature on the effects of early *versus* late spinal cord decompression time in patients after spinal cord injury consists of retrospective or prospective observational studies with important methodological limitations. These studies cover data collected from patients over the last three decades, with different diagnostic assessments, surgical techniques, and postoperative rehabilitation strategies, with small sample size, short follow-up period, and lacking information about the patient's baseline condition. And that does not assess complete scores, such as motor and sensory scores, as clinical outcomes.

The first point that makes it difficult to conclude the ideal time to carry out the operation is the lack of a definition and acceptance of the time limit of the term "early." When searching for articles on the subject in a database is observed that the "early" time varies in most cases from 24 to 72 hours after the injury. For this reason, possible variance in patient recovery may be lost when placed in the same analysis group for up to 24 hours with those up to 72 hours.

The second factor that makes data analysis difficult is the lack of information about the patient's condition during admission to emergency services. When evaluating the articles on the subject, most of the time, there is no data on the physical and clinical condition of the patient, degree of base injury and what other interventions he had to perform, time to perform exams, to complete the diagnosis and even the choice of procedures by the surgeon in charge, which leads to the third limiting factor in the interpretation and consideration of the results available in the literature: the lack of information on reasons for choosing and defining which type or route of decompression surgical approach was used—carried out.

To assess the relative effectiveness of early *versus* late decompressive surgery, we considered early intervention up to 24 hours after the injury and late intervention from 24 hours after the injury. However, to encompass diverse outcomes with different decompression times, we included an analysis of studies that assess surgery time within a narrower window, such as up to five, eight, or 12 hours post-injury. It is important to note that by stratifying the early time in smaller groups, it is possible to suggest that ultra-early decompression surgeries may bring more benefits to patients. Of the five articles cited in this review in which shorter times for medical intervention were included,[11,19-22] three showed positive data regarding procedures that were performed for less than 12 hours.[19-21]

Regarding late treatment, there is also no consensus on time, being established in a variation of 24 hours from the injury to more than two weeks for the decompression procedure to be performed.[16]

The literature seems to be quite consolidated on the importance of early or even ultra-early decompression in patients with traumatic cervical spinal cord injury. The studies presented here, both observational and retrospective,[19,21] as for prospective[13,14,20] and the meta-analyses[2,17] corroborate the hypothesis that early decompression improves patients' long-term neurological and functional responses. The reviewed papers followed the patients for at least six months.

In general, the studies that demonstrate the neurological benefit of early surgical intervention evaluated by the AIS scale show not only a general improvement on the AIS scale but also observe an improvement rate ≥ 2 degrees with early decompression, and result in a higher classification. E (normal motor or sensory functions). Consistent with these data, the STASCIS study, the largest prospective multicenter study comparing early *versus* late surgical decompression in the setting of acute traumatic spinal cord injury, indicates a recovery of 2 degrees AIS of patients with early decompression in at least six months of follow-up.[13]As reported by the Sygen trial, the largest therapeutic trial of traumatic spinal cord injury that described significant neurological recovery in patients who underwent the procedure within 24 hours with at least 2 degrees of improvement in AIS score at six months of follow-up. follow-up.[23]

On the other hand, reports about the advantage of early decompression when there is a chest injury are scarce. The systematic review by Ter Wengel et al. did not describe a significant beneficial effect of early surgical decompression of patients with traumatic thoracic and thoracolumbar spinal cord injuries. It is noteworthy that, although no difference was observed between early and late decompression in this study, it is possible to note a higher rate of improvement in the AIS scale for patients undergoing early surgery.[18] Likewise, both in the observational study by Swell et al., which included patients with cervical injuries and in the clinical trial conducted by Rahimi-Movaghar et al., which evaluated the recovery of patients with injuries in the thoracic and thoracolumbar region, it was possible to observe a trend of improvement in recovery with early surgery. However, the authors emphasize that the lack of statistical significance between the groups may be due to the small sample of patients included in the studies.[12,15] In addition, some factors, such as the AIS score at the time of admission and the length of the intramedullary lesion, were attributed to the neurological improvement of the patients in the study by Aarabi et al. However, most patients with greater neurological impairment and lesion extension were operated on in less than 24 h, which may have contributed to the similar neurological improvement observed between the groups.[11]

In addition to the time for decompression, the concomitant use of some drugs seems to play an important role in the recovery of patients with spinal cord injury,[13] especially when treatment is performed in conjunction with early intervention.[2] However, the lack of clarity regarding drug therapy does not allow us to assess whether there is a clear benefit of drug therapy for patients undergoing early *versus* late surgery. However, some studies also suggest that for long-term neurological improvement, the extent of the intramedullary injury in the preoperative image analysis is more important than the time after injury to perform decompression.[11]

An important limitation observed is that physicians/researchers use different clinical scales to verify the patient's improvement. Therefore, we only included studies that used the AIS scale for neurological assessment. In addition, another limiting factor may be related to possible individual complications of injured patients. It knows that any particular complications may affect the patient's recovery. In most cases, the urgency of surgery is also related to complications other than spinal cord injury, so it would be ideal to report what other injuries the patient had to assess each situation better.

CONCLUSION

The evaluation of spinal decompression time in neurological recovery after LTME is challenging because when interpreting the results, other variables must be considered in addition to the decompression time, such as, for example, the cause of the trauma, the route of decompression (posterior *versus* anterior), specific surgical technique used, and levels of injury/decompression. These limitations are due to variations in the admission of patients to emergency services, the time taken to perform tests to complete the diagnosis, and the choice of procedures by the surgeon in charge.

Most of the literature found supports the hypothesis that early surgical decompression is the strategy that results in better clinical outcomes. Although early decompression seems to be the most indicated option, it is still necessary to expand the understanding of specific clinical outcomes in homogeneous populations, considering gender and age, for example, and considering different surgical techniques. In addition, long-term patient follow-up studies may reveal the effects of decompression time after LTME on quality-of-life levels, which will correspond to a better clinical interpretation.

ACKNOWLEDGMENTS

The publication receives funding from the Brazilian Column Society (www.coluna.com.br)

All authors declare no potential conflict of interest related to this article.

CONTRIBUTIONS OF THE AUTHORS: Each author contributed individually and significantly to the development of this manuscript. EAI: conception of the work, acquisition, analysis, and interpretation of data, writing and critical review of its intellectual content, final approval of the manuscript; FJO: acquisition, analysis, and interpretation of data, critical review of its intellectual content, final approval of the manuscript; HRTC: analysis and interpretation of data, critical review of its intellectual content; TLA: conception of the work, critical review of its intellectual content, final approval of the manuscript.

REFERENCES

1. Fehlings MG, Tetreault LA, Wilson JR, Aarabi B, Anderson P, Arnold PM, et al. A Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury and Central Cord Syndrome: Recommendations on the Timing (</=24 Hours Versus >24 Hours) of Decompressive Surgery. Global Spine J. 2017;7(Suppl 3):195S-202S.
2. Qiu Y, Chen Y, Xie Y, Xie H, Dong J. Comparative analysis of the efficacy of early and late surgical intervention for acute spinal cord injury: A systematic review and meta-analysis based on 16 studies. Int J Surg. 2021;94:106098.
3. Venkatesh K, Ghosh SK, Mullick M, Manivasagam G, Sen D. Spinal cord injury: pathophysiology, treatment strategies, associated challenges, and future implications. Cell Tissue Res. 2019;377(2):125-51.
4. Rouanet C, Reges D, Rocha E, Gagliardi V, Silva GS. Traumatic spinal cord injury: current concepts and treatment update. Arq Neuropsiquiatr. 2017;75(6):387-93.
5. Wyndaele M, Wyndaele JJ. Incidence, prevalence and epidemiology of spinal cord injury: what learns a worldwide literature survey?. Spinal Cord. 2006;44(9):523-9.
6. Anjum A, Yazid MD, Fauzi Daud M, Idris J, Ng AMH, Selvi Naicker A, et al. Spinal Cord Injury: Pathophysiology, Multimolecular Interactions, and Underlying Recovery Mechanisms. Int J Mol Sci. 2020;21(20):7533.
7. Ahuja CS, Nori S, Tetreault L, Wilson J, Kwon B, Harrop J, et al. Traumatic Spinal Cord Injury--Repair and Regeneration. Neurosurgery. 2017;80(Suppl 3):S9-S22.
8. Tator CH, Fehlings MG. Review of the secondary injury theory of acute spinal cord trauma with emphasis on vascular mechanisms. J Neurosurg. 1991;75(1):15-26.
9. Benzel EC, Larson SJ. Functional recovery after decompressive operation for thoracic and lumbar spine fractures. Neurosurgery. 1986;19(5):772-8.
10. Papadopoulos SM, Selden NR, Quint DJ, Patel N, Gillespie B, Grube S. Immediate spinal cord decompression for cervical spinal cord injury: feasibility and outcome. J Trauma. 2002;52(2):323-32.
11. Aarabi B, Akhtar-Danesh N, Chryssikos T, Shanmuganathan K, Schwartzbauer GT, Simard JM, et al. Efficacy of Ultra-Early (< 12 h), Early (12-24 h), and Late (>24-138.5 h) Surgery with Magnetic Resonance Imaging-Confirmed Decompression in American Spinal Injury Association Impairment Scale Grades A, B, and C Cervical Spinal Cord Injury. J Neurotrauma. 2020;37(3):448-57.
12. Sewell MD, Vachhani K, Alrawi A, Williams R. Results of Early and Late Surgical Decompression and Stabilization for Acute Traumatic Cervical Spinal Cord Injury in Patients with Concomitant Chest Injuries. World Neurosurg. 2018;118:e161-e5. (sem número)
13. Fehlings MG, Vaccaro A, Wilson JR, Singh A, D WC, Harrop JS, et al. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). PLoS One. 2012;7(2):e32037.
14. Umerani MS, Abbas A, Sharif S. Clinical Outcome in Patients with Early versus Delayed Decompression in Cervical Spine Trauma. Asian Spine J. 2014;8(4):427-34.
15. Rahimi-Movaghar V, Niakan A, Haghnegahdar A, Shahlaee A, Saadat S, Barzideh E. Early versus late surgical decompression for traumatic thoracic/thoracolumbar (T1-L1) spinal cord injured patients. Primary results of a randomized controlled trial at one year follow-up. Neurosciences (Riyadh). 2014;19(3):183-91.
16. Cengiz SL, Kalkan E, Bayir A, Ilik K, Basefer A. Timing of thoracolomber spine stabilization in trauma patients; impact on neurological outcome and clinical course. A real prospective (rct) randomized controlled study. Arch Orthop Trauma Surg. 2008;128(9):959-66.
17. Badhiwala JH, Wilson JR, Witiw CD, Harrop JS, Vaccaro AR, Aarabi B, et al. The influence of timing of surgical decompression for acute spinal cord injury: a pooled analysis of individual patient data. Lancet Neurol. 2021;20(2):117-26.
18. Ter Wengel PV, Martin E, De Witt Hamer PC, Feller RE, Van Oortmerssen JAE, Van der Gaag NA, et al. Impact of Early (<24 h) Surgical Decompression on Neurological Recovery in Thoracic Spinal Cord Injury: A Meta-Analysis. J Neurotrauma. 2019;36(18):2609-17.
19. Grassner L, Wutte C, Klein B, Mach O, Riesner S, Panzer S, et al. Early Decompression (< 8 h) after Traumatic Cervical Spinal Cord Injury Improves Functional Outcome as Assessed by Spinal Cord Independence Measure after One Year. J Neurotrauma. 2016;33(18):1658-66.
20. Jug M, Kejzar N, Vesel M, Al Mawed S, Dobravec M, Herman S, et al. Neurological Recovery after Traumatic Cervical Spinal Cord Injury Is Superior if Surgical Decompression and Instrumented Fusion Are Performed within 8 Hours versus 8 to 24 Hours after Injury: A Single Center Experience. J Neurotrauma. 2015;32(18):1385-92.
21. Burke JF, Yue JK, Ngwenya LB, Winkler EA, Talbott JF, Pan JZ, et al. Ultra-Early (<12 Hours) Surgery Correlates With Higher Rate of American Spinal Injury Association Impairment Scale Conversion After Cervical Spinal Cord Injury. Neurosurgery. 2019;85(2):199-203.
22. Mattiassich G, Gollwitzer M, Gaderer F, Blocher M, Osti M, Lill M, et al. Functional Outcomes in Individuals Undergoing Very Early (< 5 h) and Early (5-24 h) Surgical Decompression in Traumatic Cervical Spinal Cord Injury: Analysis of Neurological Improvement from the Austrian Spinal Cord Injury Study. J Neurotrauma. 2017;34(24):3362-71.
23. Geisler FH, Coleman WP, Grieco G, Poonian D, Sygen Study G. The Sygen multicenter acute spinal cord injury study. Spine. 2001;26(Suppl 24):S87-98.