Management and Prognosis of Acute Traumatic Cervical Central Cord Syndrome – Systematic review and Spinal Cord Society – Spine Trauma Study Group Position Statement

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Concise title: Acute traumatic cervical central cord syndrome

Abstract

Purpose: Spinal Cord Society (SCS)and Spine Trauma Study Group(STSG) established a panel tasked with reviewing management and prognosis of acute traumatic cervical central cord syndrome (ATCCS) and recommend a consensus statement for its management.

Methods: A systematic review was performed according to the PRISMA 2009 guidelines. Delphi method was used to identify key research questions and achieve consensus. PubMed, SCOPUS and Google Scholar were searched for corresponding keywords. The initial search retrieved 770articles of which 37 articles dealing with management, timing of surgery, complications or prognosis of ATCCS were identified. Literature review and draft position statements were compiled and circulated to panel members. The draft was modified incorporating relevant suggestions to reach consensus.

Results: Out of 37 studies, 15 were regarding management strategy, 10 regarding timing of surgery and 12 regarding prognosis of ATCCS.

Conclusion: There is reasonable evidence that patients with ATCCS secondary to vertebral fracture, dislocation, traumatic disc herniation or instability have better outcomes with early surgery (<24 hrs.). In patients of ATCCS secondary to extension injury in stenotic cervical canal without fracture/ fracture-dislocation/traumatic disc herniation/instability, there is requirement of high quality prospective randomized controlled trials to resolve controversy regarding early surgery versus conservative management and delayed surgery if recovery plateaus or if there is a neurological deterioration. Until such time decision on surgery and its timing should be left to the judgment of physician, deliberating on pros and cons relevant to the particular patient and involving the well informed patient and relatives in decision making.

Key words: traumatic, cervical, central cord syndrome, management, timing, complications, prognosis

Introduction

Spinal Cord Injury (SCI) can be traumatic or non-traumatic. The damage inflicted to the spinal cord can be primary or secondary, with primary injury taking place at the time of initial insult and secondary injury occurring due to the biochemical cascade initiated due to the primary insult. These insults can lead to functional impairment of the spinal cord which could affect the function of the cord completely below the injury level (complete injuries) or with some preservation of cord function below the injury level(incomplete injuries) [1]. Incomplete SCI can manifest clinically in the form of a specific pattern of neurological involvement depending on the anatomical region of damage suffered by the spinal cord[2]. Central cord syndrome is one such incomplete cord syndrome characterized anatomically by the involvement of the centre of the spinal cord. The common causes of central cord syndromes are trauma, syringomyelia and intramedullary spinal cord tumors. Among these etiologies, acute trauma of the cervical

spine leading to central cord syndrome is the commonest[3]. This usually occurs after a hyper- extension injury in a stenotic cervical spine. However it can sometimes be seen associated with cervical fractures or fracture dislocation or disc herniation after an acute trauma[4–6]. Various treatment options exist in the management of such injuries, ranging from conservative[4, 5] to delayed surgery [7–9]to early surgery[10–12].

The Spinal Cord Society(SCS) and Spine Trauma Study Group(STSG) established a panel tasked with reviewing the management options, timing of surgery and prognosis of ATCCS and come to a consensus for management of ATCCS. This panel consisted of various national and international experts from orthopedics, spine and neurosciences. A coordinator for the panel was selected from Indian Spinal Injuries Centre, New Delhi. The task of the coordinator was to compile the existing literature on aetio-pathogenesis, management and prognosis of ATCCS and circulate the same along with a draft position statement to the panel members for their comments via e-mail. The draft was modified incorporating relevant suggestions and recirculated to reach a consensus. The final recommendations of the panel were then discussed in an open forum during the annual meeting of the Spinal Cord Society(ISSICON) held in New Delhi, India.

Methods

A systematic review was performed followingthe PRISMA 2009 guidelines[13]. Delphi method was used to identify and prioritise the key research questions to be addressed by the systematic review and to achieve a consensus on the response. Consensus was defined as an agreement of >75.0%. Consensus was reached among six Indian experts of Spinal Cord Society and eight international experts of Spine Trauma Study Group (STSG)in three study rounds and compiled as agreement scores[14]. The first study round was for the development of the position statement through a set of questions identified by the panel members. The panel members scored these questions on the basis of their importance. The analysis of these responses from panel members was done using median score [upper quartile and lower quartile] and the questions prioritised on highest median scores. These questions were forwarded to the subsequent rounds. In second and third rounds, panel members were provided analysis for each question from the previous round and requested to revise the score if they wished to move closer to the group consensus. Finally, in the third round the panel members received a list of research questions in priority order to identify research questions for this systematic review. In this round, a final decision was made on how many research questions had to be included based on the extent of the evidence and the resources available for the research.

A systematic review of literature was conducted by searching PUBMED, Scopus and Google Scholar from 1st January 1980 to 1st August 2017using the following search strategy:

“central cord syndrome” [All fields] and “trauma” [All fields] and “management” [MeSH terms]; “prognosis” [MeSHterms];“complications” [MeSH terms]

The authors of this study were blinded to the authors' and the journals' name while reviewing. Journal's scores (Impact Factor etc.) were not considered as exclusion criteria for this review.

Statistical Methods

Meta-analysis was conducted by Revman v5.3 (Review Manager) software. A random effects regression model was applied to calculate primary outcomes, including number of events (bivariate) and ASIA Score (continuous). Forest plot was plotted for each outcome with Cochran's Q test and Higgin's I^2 statistic examining the heterogeneity considering I^2>50% as significant heterogeneity between the studies. Odds Ratio (OR) or Mean Difference (MD) with corresponding 95% Confidence Interval (CI) was presented as per the nature of the outcome variable. The quality of evidence was assessed using GRADEpro software (GRADEpro 2014).

Results and Discussion

Initial search retrieved 770 articles of which 204 were pertaining to the concerned topic of interest. Abstracts of all the 204 articles were studied and full text articles were retrieved wherever necessary. Further appropriate cross references from full text articles were retrieved wherever necessary. A total of 37articles,which dealt with the management (conservative or surgical) or timing of surgery (early versus delayed) or prognosis of ATCCS, were identified from the retrieved articles (Figure 1) and included in the systematic review [4 – 12, 19, 21 – 30, 37 - 53] with 18,931 ATCCS patients from 1980 to 2017. These articles were then segregated based on the outcome of interest. The content was extracted from the relevant papers and presented/circulated for further discussions. Relevant references from retrieved publications were also included. Duplicate references were separated by manual search.

Table 1 shows the characteristics of included studies with geographic variations, study design, number of participants, level of evidence, outcome and results. All the included studies, except two RCTs, have a high risk of selection bias, performance bias or detection bias as they are either retrospective cohort studies or case series or case reports.

ATCCS: Historical Perspective

The clinical features suggestive of traumatic central cord syndrome were presented by Thorburn in his publication in 1887[15].Later in 1954, Schneider [4] first mentioned the involvement of central cervical spinal cord after an acute cervical spine injury and described it as traumatic central cord syndrome. This is generally caused due to an extreme hyperextension injury without vertebral damage and secondary to antero-posterior pinching or squeezing of the spinal cord. The anterior compression could either be due to arthritic spur or a calcified or non–calcified herniated disc and the posterior compression due to the buckling of ligamentum flavum. However this syndrome can sometimes be seen associated with a cervical fracture with or without dislocation and acute traumatic disc herniation [4–6].This syndrome is characterized by disproportionately greater motor involvement of the upper limbs than lower limbs with bladder involvement, and with a sensory loss that is variable below the level of lesion. The usual sequence of recovery starts with motor power of the lower limbs followed by bladder and then the upper limbs with

Figure 1: PRISMA study flow diagram

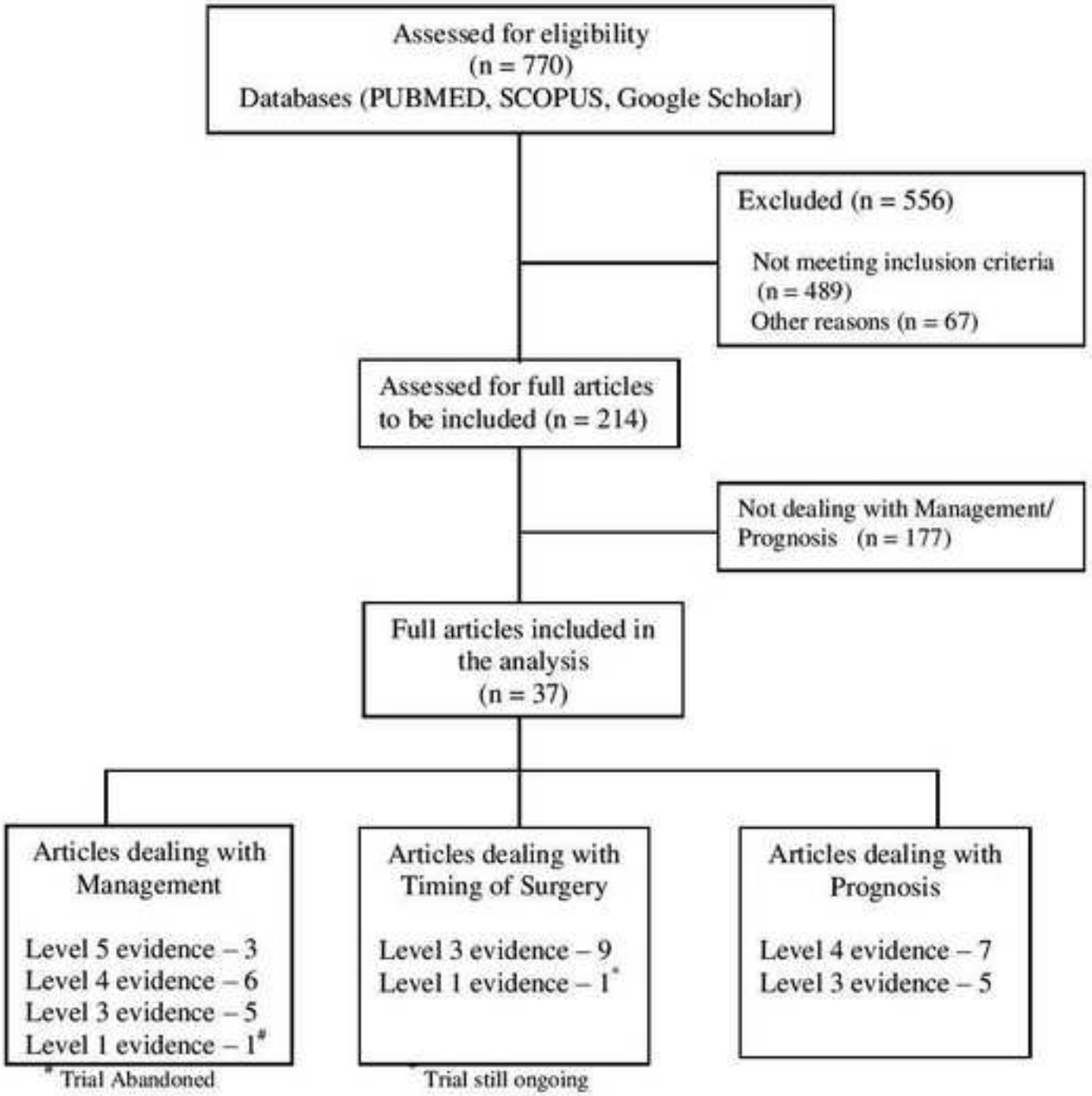


Table 1: Characteristics of the included studies

SN	Study/ Author	Study Design	Place	Sample Size	Level of Evidence	Outcome	Result	Ref
1	Schneider et al. 1954	Case Series	Michigan, USA	9	4	Neurological recovery	Delayed surgical management (after subsidence of cord edema) in cases of # dislocation reduced by traction.	[4]
2	Schneider et al. 1954	Case Series	Michigan, USA	12	4	Neurological recovery	Immediate surgery is indicated if there is a block in Queckensted t test. Others can be managed by cervical traction followed by fusion after cord edema subsides.	[5]
3	Dai et al. 2000	Retrospective cohort study	Shanghai, China	24	3	Neurological recovery	Surgical intervention, performed on all the patients. If the herniated disc is observed in the patients with acute central cord injuries and determined as the compression factor of the spinal cord, surgical intervention is preferable.	[6]
4	Bose et al. 1984	Retrospective cohort study	Philadelphia, USA	28	3	Neurological recovery	Patients managed surgically had better neurological scores at the time of discharge.	[7]
5	Chen et al. 1997	Retrospective cohort study	Taoyuan, Taiwan	114	3	Neurological recovery	Early surgical intervention is required in certain cases (ATCCS with ongoing compression and long segment stenosis) to hasten motor recovery and reduce the probability of chronic myelopathy.	[8]
6	Chen et al. 1998	Retrospective cohort study	Taoyuan, Taiwan	37	3	Neurological Improvement	In patients with stenotic cervical canal with incomplete spinal cord injury without fracture/instability/sequest rated disc, surgical decompression promotes neurological recovery as well as early mobilization and reduces the length of hospital stay.	[9]
7	Guest et al. 2002	Retrospective cohort study	Phoenix, Arizona	50	3	Neurological Improvement	Among both the groups, early surgery cohort had short ICU stay and short duration of	[10]

							hospital stay.	
8	Yamazaki et al. 2005	Retrospective cohort study	Tsukuba, Japan	47	3	Neurological recovery	Among conservative group, recovery rate is poor in patients with less pre-op JOA, less sagittal canal diameter and with T2W signal intensity changes on MRI. Among Surgical group, recovery rate was better in those operated early(<2wks).	[11]
9	Lenehan et al. 2010	Systematic review	Vancouver, Canada	73	3	Neurological Improvement	Patients with ATCCS due to stenotic canal without fracture or instability and with severe neurological deficit (AIS C)with ongoing spinal cord compression can be contemplated for early surgical intervention (<24 hrs). Those with less profound deficit (AIS D) can be managed Conservatively initially and surgery can be considered later depending on the scope and temporal profile of neurological improvement.	[12]
10	Bosch et al. 1971	Case Series	Los Angeles, USA	42	4	Neurological recovery	Prognosis of neurologic recovery in the early post injury time can be expected in approximately three fourths of the cases; however, a functional ambulation was maintained only in 59% of the cases and 56% had a functional hand usage.	[19]
11	Rand et al. 1960	Case report	California, USA	2	5	Neurological recovery	Conservative management has good prognosis	[21]
12	Shrosbree et al. 1977	Case Series	Cape, South Africa	99	4	Neurological Improvement	58%(43/74) were independently ambulant with minimal hand weakness whereas 42%(30/74) had poor hand function. 8% (4/74) were wheel chair bound at 3yrs follow up.	[22]
13	Brodkey et al. 1980	Case Series	Ohio, USA	7	4	Neurological Improvement	All improved neurologically after surgery	[26]

14	Maxted et al. 1982	Case report	Liverpool, England	3	5	Neurological recovery	All patients recovered and became ambulant, but had weak hand intrinsics	[23]
15	Morse et al. 1982	Case report	Philadelphia, USA	2	5	Neurological recovery	Both of them recovered motor grip in upper limbs	[24]
16	Ishida et al. 2002	Prospective Multicentric case series	Yamaguchi, Japan	22	4	Neurological Improvement	Nearly full neurological involvement in all	[25]
17	Song et al. 2005	Retrospective case series	Aichi-gun, Japan	22	4	Neurological Improvement	All patients improved clinically. 10 of the 22 patients became AIS D neurologically.	[27]
18	Uribe et al., 2005	Retrospective case series	Miami, USA	14	4	Neurological Improvement	At 3 month follow-up, 71% improved at least by 1 AIS grade.	[28]
19	Pollar d et al. 2003	Retrospective cohort study	Atlanta, USA	57	3	Neurological Improvement	Neurological improvement was observed in both groups with no statistical significance	[29]
20	Aito et al. 2007	Retrospective cohort study	Florence, Italy	82	3	Neurological Improvement	Neurological and functional improvements were recorded on discharge from rehabilitation. No specific details on hand function were compared between the two cohorts	[30]
21	Chen et al. 2009	Retrospective cohort study	Republic of China	49	3	Neurological Improvement	Significant neurological improvement was seen within first 6 months in all pts. No distinction was found in neurological recovery between early(<4d) and late (>4d) Operated cohorts	[37]
22	Stevens et al. 2010	Retrospective cohort study	NC, USA	126	3	Neurological Improvement	Surgery is a safe option in ATCCS but there exists no difference in neurological outcome between early and late operated cohorts.	[38]
23	Aarabi et al. 2011	Retrospective cohort study	Baltimore, Maryland	42	3	Neurological Improvement	Timing of surgery did not influence the neurological outcome at the final follow up.	[39]
24	Anderson et al. 2012	Retrospective	Philadelphia, USA	69	3	Neurological Improvement	There was not a significant difference in rate of improvement in AMS among	[40]

		cohort study					the groups treated early or late (timing of surgery).	
25	Kepler et al. 2015	Retrospective cohort study	Vancouver, Canada	68	3	Nurologica Improvement	No differences in change of AMS at 7 days or ICU stay or length of hospital stay is seen between the two groups	[41]
26	Samuel et al. 2005	Retrospective cohort study	New Haven, CT, Europe	1060	3	Neurological recovery	Delayed surgery for ATCCS is related to a reduced mortality, after regulating pre-existing comorbidity and injury severity. This finding is however in contradiction to The enhanced outcomes noticed with early surgical intervention for other incomplete SCI syndromes.	[44]
27	Bartels et al. 2013	Randomized Control Trials	Nijmegen, Netherlands	72	1	Neurological Improvement	Abandoned Trial – A goal of the study was to determine which treatment will result in the best quality of life for the patients. This study might have certainly contributed to more uniformity of treatment offered to patients with a special sort of spinal cord injury. This study has recently been discontinued due to insufficient number of patients meeting the inclusion criteria.	[42]
28	Chikuda et al. 2013	Randomized Control Trials	Tokyo, Japan	100	1	Neurological Improvement	Ongoing Trial – OSCIS study is designed to provide evidence of the potential benefit of early surgical decompression over a wait-and-see strategy. We believe that the results of this trial will have a substantial impact on the management of cervical SCI.	[43]
29	Brodell et al. 2015	Retrospective cohort study	New York, USA	16134	3	Neurological recovery	Elderly patient cohort with medical illnesses are found to be associated with a low surgical rate and a high mortality rate.	[45]
30	Lenehan et al. 2009	Retrospective cohort study	Dublin, Ireland	50	3	Neurological Improvement	The clinical outcomes are significantly worse in pts >70 yrs. of age than patients aged 70 years or older.	[46]
31	Penrod et al.	Retrospective	Philadelphia, USA	55	3	Neurological recovery	Favorable prognosis in young years of age (<50)	[47]

	1990	cohort study						
32	Dvorak et al. 2005	Case Series	Vancouver, Canada	70	4	Neurological Improvement	Significant predictive variables of functional outcome included the initial AMS, formal education, comorbidities, age and evolution of spasticity	[48]
33	Roth et al. 1990	Case Series	Chicago, USA	81	4	Neurological recovery	Favorable prognosis with young age, pre injury employment status, no lower limb weakness on admission and documented upper/lower extremities recovery during rehabilitation	[49]
34	Hohl et al. 2010	Case Series	Pittsburgh, USA	37	4	Neurological recovery	Favorable prognosis is seen in patients with high initial AMS and no evidence of abnormal signal intensity on MRI.	[50]
35	Merriam et al. 1986	Case Series	Australia	77	4	Neurological recovery	Favorable prognosis at admission was seen in cases with better hand function, hyperpathia, Lhermittes sign and intact peri anal sensation.	[51]
36	Miranda et al. 2008	Case Series	Valencia, Spain	15	4	Neurological Improvment	Length of spinal cord edema on MRI relates to the initial neurological deficit.	[52]
37	Schroeder et al. 2015	Retrospective cohort study	Philadelphia, USA	80	3	Neurological recovery	Though patients with ATCCS with fracture have an initial severe neurological deficit when compared to those without a fracture, neurological recovery with in 1st week is better in patients with fracture than those without fracture.	[53]

Table 2: Research Questions in PICO format

Question Type	Population	Intervention	Comparison	Outcome Measure
Therapy	Patients suffering from post-traumatic cervical central cord syndrome	1)Is surgical treatment more effective than	1)conservative management?	inimproving neurological outcome?
		2) Is early surgery better than	2)delayed surgery?	
		3) Is incidence of complications in the " early surgery" different from	3) complications of conservative treatment and delayed surgery if recovery plateaus or there is deterioration in neurology	In improving outcome ?

fine finger movements recovering at the last. The variable sensory loss doesn't follow a set pattern of recovery. The amount of overall recovery is based on the nature of damage to the central spinal cord. Poor recovery is seen with hematomyelia and good recovery with edema of the spinal cord due to concussion or contusion. The central hematomyelia if extensive could spread proximally leading to substantial morbidity and possibly mortality of the patient. Though Schneider'sfindings indicate involvement of central grey matter secondary to hemorrhage or contusion and cortico-spinal tract secondary to edema, some recent studies based on MRI concluded that the global weakness in ATCCS could be explained by involvement of cortico-spinal tracts only [16]. Schneider et al. also concluded that recovery occurs spontaneously in most of the acute injuries of cervical central cord and durotomy with or without myelotomy will be more detrimental in such a condition. They believe that decompressive laminectomy is futile in such cases because there is no subarachnoid block in the majority of their cases with no fracture or dislocationas observed by the Queckensted t-test. So as per the authors, conservative treatment is most satisfactory in patients with ATCCS[4, 5]. Schneider's proposed conservative management consisted of cervical traction in the neutral position until cord edema subsided. They also concluded that surgical fusion is indicated when ATCCS is associated with cervical fracture – dislocation. Schneider et al. [17] also identified an entity called chronic central cord syndrome in patients who sustained a whiplash or a hyperextension injury long before the onset of symptoms. This syndrome is characterized by progressive weakness of all 4 limbs with disproportionately more weakness in the upper limbs and sensory symptoms in the form of reduced pinprick and temperature sensation in the lower cervical and upper thoracic dermatomes. The authors observed that there is no spontaneous recovery in this entity as observed in ATCCS, so surgical intervention in the form of laminectomy with or without myelotomy is needed for neurological improvement. The same authors [18] also noted a different presentation of patients who have recovered after acute cervical central cord syndrome with conservative management. There are case reports of such patients who presented at a later date with anterior spinal cord compression due to hypertrophic spursand responded to surgical management involving laminectomy, resection of dentate ligaments as well as resection of hypertrophic spurs [18]. However few authors concluded that the presence of instability could be the cause for this delayed deterioration after initial recovery [19, 20].The incidence of chronic central cord syndrome after conservative management of ATCCS is around 24% as per one study[19].

Since the initial description of ATCCS by Schneider et al [4, 5],its management principles have been evolving with time astheanesthetic and surgical technologies evolved. For the purpose of a better analysis of the evolution of management of ATCCS, further review will be discussed in the following sections.

Research Question 1: Is surgical treatment more effective than conservative management in improving neurological outcome in patients suffering from ATCCS?

Literature review

9 case series/reports (Level 4/5 evidence), 5 retrospective cohort studies(Level 3 evidence) and no RCTs(Level 1 or 2 evidence) were found answering the research question 1.

- Case series or case reports

Of the 10 retrospective case series, conservative management alone was done in 5 studies [21–25] and surgical management alone was done in three studies [26–28]. In two studies both surgical and conservative management was done [4, 5].Among the studies in which the patients were managed conservatively, the studies of Rand et al.[21] and Shrosbree et al.[22] included patient cohort with ATCCS secondary to fracture/ fracture dislocation and ATCCS secondary to extension injury in cervical canal stenosis, while the studies of Maxted et al.[23], Morse et al.[24] and Ishida et al.[25]included patient cohorts with ATCCS secondary to extension injury in a stenotic canal with no evidence of instability, fracture dislocation or disc herniation. Most of these studies [21–23] concluded that the motor recovery of lower limbs and bladder had a good prognosis and the motor recovery in hand intrinsics had a poor prognosis. However in studies[24, 25] including a variant of ATCCS with preserved power in the lower limbs at the time of presentation, the recovery of hand function was excellent.

Among the studies that managed the patients surgically, the studies of Brodkey et al.[26]and Uribe et al.[28]included patient cohort with ATCCS secondary to extension injury in a stenotic canal, while the study of Song et al.[27]included patients with ATCCS secondary to traumatic disc herniation or extension injury in a stenotic canal. The indication of surgery in the study of Brodkey et al.[26]was a plateau of neurological recovery after conservative management and all the patients improved neurologically after surgery. The indication for surgery in the study of Song et al. was the presence of a neurological deficit with a surgically amenable lesion, i.e. presence of ongoing cord compression. Neurologically recovering cases were operated after a few days and those not recovering were operated earlier. All the patients improved clinically after surgery.

The studies of Schneider et al.[4, 5], managed the patients surgically and conservatively, included patient cohorts with ATCCS secondary to fracture or fracture dislocation or extension injury in a stenotic canal. The first case of ATCCS secondary to extension injury in stenotic canal was managed surgically and the patient deteriorated neurologically. The surgery was futile in the next case. Later, the rest of similar cases were managed conservatively and all of them improved neurologically but with a poor hand function. Delayed surgical management (i.e. after subsidence of cord edema) was done in cases with fracture dislocation reduced by traction preoperatively.

- Retrospective cohort studies

Five retrospective cohort studies were identified which compared conservative management with surgical management in ATCCS [7–9, 29, 30].Among these, four studies(Bose et al. 1984,Chen et al. 1997, Chen et al.1998 and Aito et al. 2007) compared non–homogenous cohorts [7–9, 30] while one study(Pollard et al,2003) [29]compared homogenous cohorts.

The study by Pollard et al. compared patient cohort with acute traumatic incomplete cervical spinal cord injury in stenotic canal without fracture /dislocation / traumatic disc herniation managed conservatively or surgically. The authors of this study found no statistically significant difference in the neurological improvement between these two groups and concluded that surgical decompression of stenotic canals without fracture or dislocation or traumatic disc herniation was not associated with improved neurological outcomes.

Aito et al.[30] compared patients with fracture or traumatic disc herniation managed surgically with patients without

fracture or traumatic disc herniation managed conservatively. They concluded that surgical intervention had not influenced short or long term neurological and functional outcomes. However the non-homogenous cohorts lead to a bias in their interpretation. The other non-homogenous cohort studies concluded that surgery can be safely done in patients with ATCCS with a plateau of neurological recovery after conservative management [7–9] or with instability[7, 8].The study by Chen et al.[8]concluded that early surgical intervention is required in cases of ATCCS with ongoing cord compression and long segment stenosis to obtain rapid motor recovery and to lower the chance of chronic myelopathy.

Meta-analysis

Meta-analysis was performed to compare conservative management and surgical management including separate analysis to see impact of a particular type of management in ATCCS patients through neurological improvement (ASIA score). Figure 2 (A) and Figure 2 (B) presents Forest plots for ASIA scores in ATCCS patients those got surgical management and ASIA scores in ATCCS patients those received only conservative management respectively. Figure 2(C) shows Forest plot including three studies [7, 18, 11] with 109 subjects (54 in surgical and 55 in conservative management). There was no significant difference in neurological improvement in ATCCS patient's between the surgical management and conservative management [MD = 2.35, 95%CI (-5.38 – 10.07); I^2= 98%, p-value = 0.550]. Whereas both type of management separately shows significant improvement i.e. surgical management [MD = 19.70, 95%CI (9.24 – 30.16); I^2= 99%, p-value < 0.001] and conservative management [MD=13.36, 95%CI (5.37 – 21.35); I^2=97%, p-value= 0.001].

Delphi Consensus

With the available evidence, patients with ATCCS secondary to an extension injury in a stenotic canal without fracture/dislocation/instability/disc herniation can be given the options to undergo either surgical management {especially in selected cases with substantial neurological deficit (AIS C) in the presence of ongoing cord compression} or an initial conservative management followed by surgery at a later date, if there is a neurological deterioration or a plateau of neurological recovery. There is a need for high quality prospective randomized control trials to resolve this controversy between surgical and conservative management. Until such time, the decision should be left to the judgment of the physician, deliberating on the pros and cons relevant to the particular patient and involving the well informed patient and relatives in the decision making.

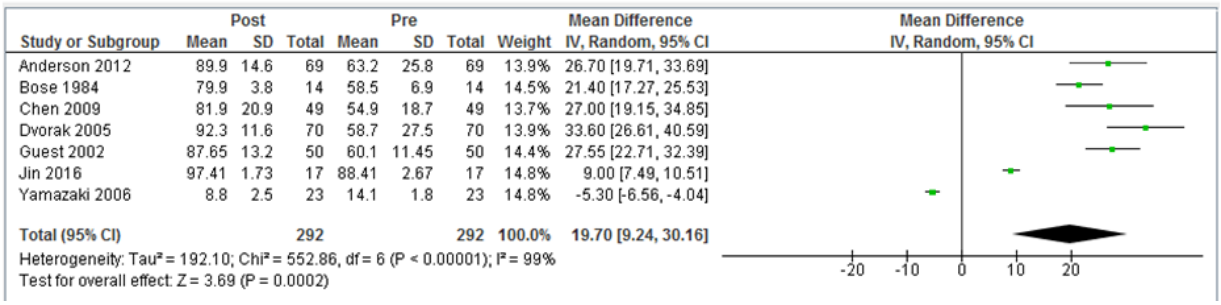
Research Question 2: **Is early surgery better than delayed surgery in improving neurological outcome in patients with ATCCS?**

Literature review:

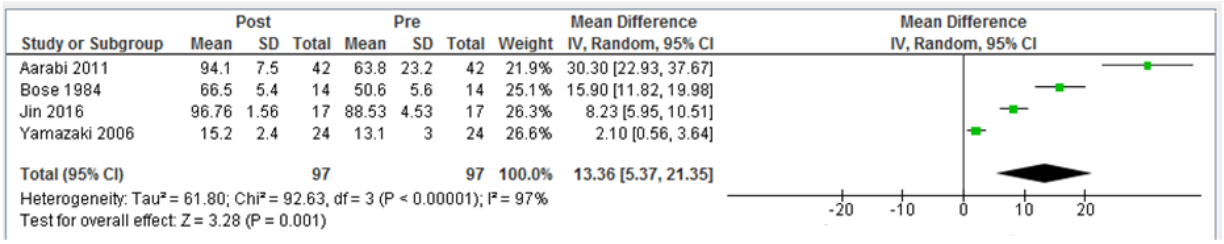
9 retrospective cohort studies and 1 RCT(ongoing) were found answering the research question 2.

Figure 2 : Forest Plots of ASIA scores

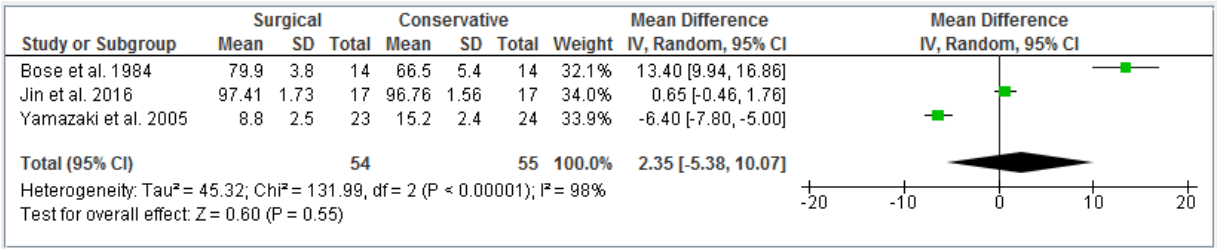
A) ASIA Score-Surgical group



B) ASIA Score- Conservative group



C) Surgical vs Conservative group



Many studies have been performed to assess the timing of surgery in SCI. Existing preclinical [31] and clinical studies [32–35] support an early surgery (within 24hrs) in traumatic spinal cord injury secondary to spinal fracture or related instability. Many experts however differ with regard of timing of surgical intervention in ATCCS secondary to extension injury without fracture/dislocation/ traumatic disc herniation [36].

Studies concluding that the timing of surgery did not affect neurological outcome of patients with ATCCS

Five retrospective cohort studies(level 3 evidence)[37–41] have compared patients of ATCCS undergoing early or late surgery and concluded that the timing of surgical intervention has no effect on the final neurological outcome. Among these the study of Chen et al.[37]considered patients with ATCCS operated within 4 days as the early cohort and those operated after 4 days as the late cohort. The studies of Aarabi et al. [39] and Anderson et al.[40]divided the patients of ATCCS in to 3 cohorts (<24 hours, 24-48 hrs,>48 hrs groups). The rest of the studies[38, 41] divided ATCCS patients in to 2 cohorts (early <24hrs and late >24 hrs groups). Similar cohorts were compared in the studies of Chen et al.[37], Aarabi et al.[39] and Anderson et al.[40].However the details of surgical cohorts are not clearly mentioned in the studies of Stevens et al. [38] and Kepler et al.[41].

Studies concluding that early surgery has better outcomes in patients with ATCCS

There is a lack of uniformity of the definition of early surgery among different studies.

Three retrospective cohort studies (Level 3 evidence)[10–12] compared cases of ATCCS operated early to those operated late and concluded that early surgery is associated with better outcomes in patients with ATCCS. Among these , the study of Yamazaki et al.[11]also analyzed conservatively managed patients with ATCCS. 47 patients with ATCCS secondary to traumatic disc herniation or extension injury in a stenotic cervical canal with persistent significant motor deficit were considered in this study. Of these, 24 patients were managed conservatively, 13 patients underwent early surgical intervention (< 2 wks) and 10patients underwent late surgical intervention (> 2weeks). They observed poor recovery in conservatively managed patients with low preoperative JOA(Japanese Orthopedic Association) scores, lower sagittal canal diameters and T2 weighted intensity changes on MRI. Among the surgical group, they found a better recovery rate in the early (<2 weeks) operated group.

The studies of Guest et al.[10] and Lenehan et al.[12]compared patients with ATCCS undergoing early (<24 hrs) or late (>24 hrs) surgery. The study of Guest et al.[10]included two cohorts of patients with ATCCS. The first group was patients with ATCCS secondary to fracture / fracture-dislocation or traumatic disc herniation. The second group was patients with ATCCS secondary to extension injury in a stenotic cervical canal with instability or those that reached a plateau of neurological recovery with conservative management. Both these groups were subdivided in to early and late surgery. Among both the groups, patients undergoing early surgery had a shorter ICU stay and shorter LOS (length of stay) in the hospital. A better motor recovery was also seen in patients undergoing early surgery in ATCCS due to fracture/ fracture-dislocation or traumatic disc herniation. However there was no dissimilarity in the motor recovery between early and late operated subgroups in patients with ATCCS secondary to extension injury in a stenotic cervical canal with instability or those that reached a plateau of neurological recovery with conservative management.

The study of Lenehan et al.[12] was an ambispective analysis of observational data as well as an expert consensus on management of patients with ATCCS secondary to an extension injury in a stenotic cervical canal without instability and traumatic disc herniation with AIS C or AIS D neurology. The authors of this study identified a statistically significant better improvement in the motor score of patients in the early operated subgroup (<24 hrs) as compared to that in late operated subgroup (>24 hrs) at 6month and 12 month follow-up. The authors of this study concluded that if patients had severe neurological deficit (AIS C) and ongoing neurological compression due to developmental canal stenosis without fracture or instability, early surgical decompression can be reasonably and safely considered. Those patients with less severe initial deficit (AIS D) can initially be managed conservatively and surgery can be opted at a later date if the neurological recovery plateaus.

Randomized controlled clinical trials

There are two randomized control trials pertaining to the management of incomplete SCI in patients with stenotic cervical canal without fracture or dislocation or instability or traumatic disc herniation. The COSMIC (Conservative or Surgical treatment for Incomplete Cord lesion) trial [42]compares early decompressive surgery(<24 hrs) and conservative treatment in such patients. However, this study has recently been discontinued due to insufficient number of patients meeting the inclusion criteria over one and half year duration and hence been omitted from this systemic review. The OSCIS trial[43]compares similar patients undergoing either early surgical intervention (within 24 hours after admission) or delayed surgical intervention i.e. after at least two weeks of conservative management. The OSCIS trial is still going on and the results of the study are not yet validated.

Meta-analysis

Meta-analysis was conducted to compare early (<24 hrs) vs. late (>24 hrs) surgery. Literature shows various definitions of early surgery such as < 24 hrs, <2 weeks etc. This meta-analysis (Figure 3) comprise of seven studies [10, 36 – 40, 44] reported early surgery as surgery within 24 hours including 1257 ATCCS patients. There was no significant association between early (<24 hrs) and late (>24 hrs) surgery [OR = 1.76, 95%CI (1.00 – 3.11); I^2= 29%, p-value = 0.05]. There is not enough evidence to conclude that early surgery is better than late.

Summary of findings (Table 3) shows low quality of evidence as most of the included studies were retrospective cohort studies. Risk of bias, inconsistency in results and indirectness have been reported. The probable explanations for a low quality of evidence are as under:

a. Studies have a high risk of bias for selection bias, performance bias and detection bias

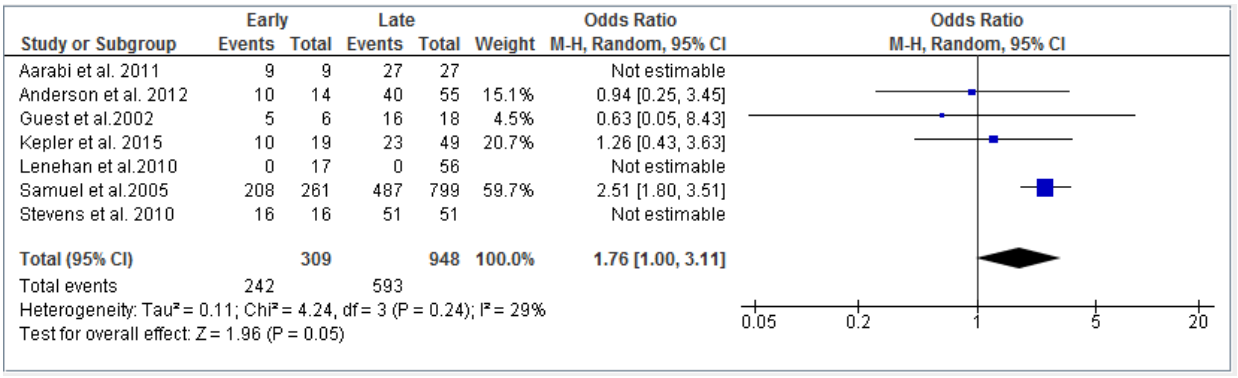
b. Studies have different results and also definition of early surgery is not consistent in literature

c. Results could be imprecise because there are relatively few patients. Also CI does not include meaningful benefit and harm, or a meaningful effect and no effect (consistent or inconsistent effects) **Delphi consensus**

Table 3 : Summary of Findings for Question: Early (<24 hrs) surgery compared to Late (>24 hrs) surgery for ATCCS patients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Early (<24 hrs) surgery**	**Late (>24 hrs) surgery**	**Relative (95% CI)**	**Absolute (95% CI)**		
Timing of surgery (assessed with: hours)												
7	observational studies	serious	serious	not serious	serious	all plausible residual confounding would suggest spurious effect, while no effect was observed	242/390 (62.1%)	593/948 (62.6%)	**OR 1.76** (1.00 to 3.11)	**121 more per 1,000** (from 0 fewer to 213 more)	⨁⨁◯◯ LOW	IMPORTANT

Figure 3 : Forest Plots of recovery rate in Early (<24 hrs) vs. Late (>24 hrs) surgery



The experts first came to a consensus on the definition of early (< 24 hrs) and late surgery (> 24 hrs). Patients with ATCCS secondary to an extension injury in a stenotic canal without fracture/dislocation/instability/disc herniation can be given the options to undergo either early surgery {especially in selected cases with substantial neurological deficit (AIS C) in the presence of ongoing cord compression} or an initial conservative management followed by surgery at a later date, if there is a neurological deterioration or a plateau of neurological recovery. There is a need for high quality prospective randomized control trials to resolve this controversy between early surgery versus delayed surgery if there is a neurological deterioration or a plateau of neurological recovery. Until such time, the decision on surgery and its timing should be left to the judgment of the physician, deliberating on the pros and cons relevant to the particular patient and involving the well informed patient and relatives in the decision making.

Research Question 3: Is there a difference in incidence of complications in the "early surgery" versus "conservative treatment and delayed surgery in patients with ATCCS ?

Literature Review:

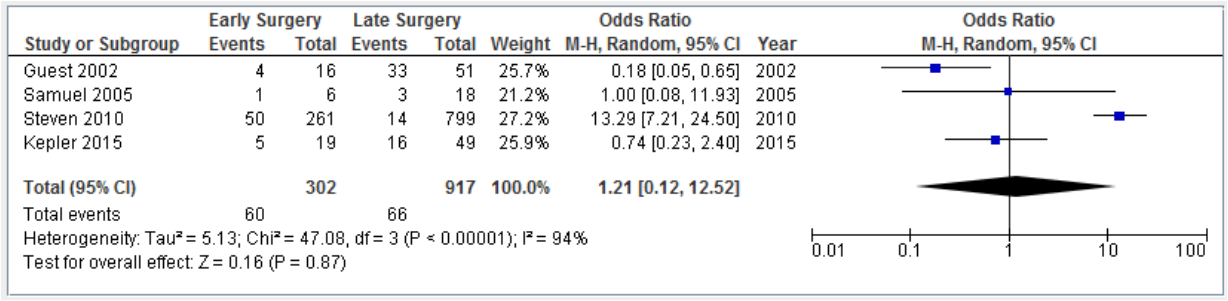
4 retrospective cohort studies (Level 3 evidence) and no RCTs (Level 1 evidence) were found answering the research question.

The study by Samuel et al.[44] analyzed 1060 patients with ATCCS managed surgically either within 24 hrs or after 24 hrs. The authors found that after regulating the preexisting comorbidities and injury severity, delayed surgical intervention was associated with reduced inpatient mortality. This finding is different from the better outcomes noted after early surgical intervention after SCI for other incomplete SCI syndromes. However as the authors had not provided the natural course of the ATCCS patients of their cohort, the conclusions of this study cannot be given due weightage. Also as mentioned before, there are studies that proved that surgery can be safely done in patients with ATCCS with a stenotic canal with a plateau of neurological recovery or neurological deterioration after conservative management[7–9].

Meta-analysis

Meta-analysis was performed to compare complications in early (<24 hrs) vs. late (>24 hrs) surgery. This meta-analysis (Figure 4) comprises of four studies [10, 36, 39, 40] which reported early surgery as surgery within 24 hours and late surgery as surgery done after 24 hours, including 1219 ATCCS patients. There was no significant association between early (<24 hrs) and late (>24 hrs) surgery for complications [OR = 1.21, 95%CI (0.12–12.52); I^2=94%, p-value = 0.87]. Hence there is no enough evidence to conclude that there is difference in complication rate in early surgery vs. late surgery.

Figure 4 : Forest Plots of Complications in Early (<24 hrs) vs. Late (>24 hrs) surgery



Delphi consensus

Surgery can be safely done in patients with ATCCS with a stenotic canal whether done early (< 24 hours) or delayed (> 24 hours) if there is a plateau of neurological recovery or neurological deterioration after conservative management. There is no difference in the incidence of complications between the two groups.

Miscellaneous: Prognostic factors in ATCCS

Some prognostic indicators in ATCCS mentioned in literature are age [45–49], comorbidities [48], initial neurology [22, 48–51],documented recovery during rehabilitation[49],canal diameter[11], MRI signal intensity and length of edema [52],ongoing cord compression [15,18,48] , presence of vertebral fracture [53], formal education and absence of spasticity[48]. However these are all Level 4 studies and appropriate quantitative data was not extractable for meta-analysis. Hence we could not present Forest plot for any of the prognostic factors except age.

For age as prognostic factor, literature shows various classifications such as <50 yrs, <70yrs etc. This meta-analysis (Figure 5) comprises of four studies [20, 43, 45, 50] which reported age as prognostic factor including 16294 ATCCS patients. Statistically significant difference of functional recovery was reported between age< 50 yrs and age >50yrs reported [OR = 2.74, 95%CI (1.17–6.40); I^2=64%, p-value = 0.02]. There is enough evidence to conclude that there is better or approximately 3 times more functional recovery in young age (<50 yrs) as compared to older age (>50 yrs).

SCS-STSG POSITION STATEMENT

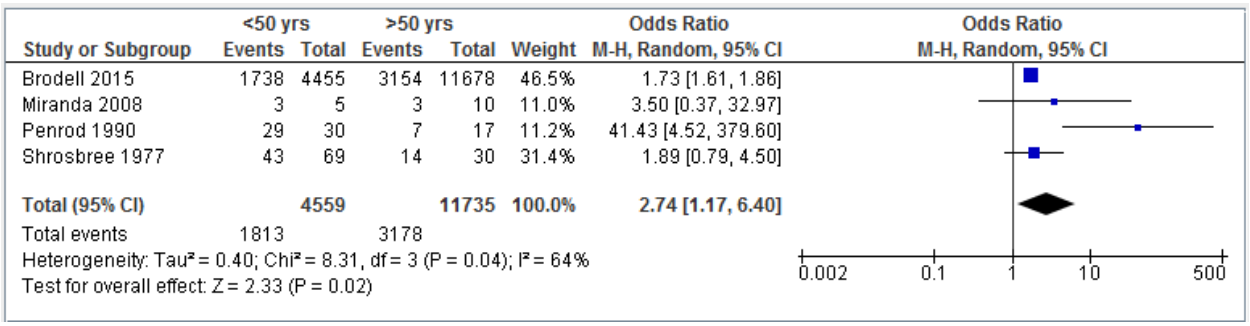
Based on the reviewed literature, the recommendations of the expert panel and discussions in an open forum during its annual meeting, Spinal Cord Society and Spine Trauma Study Group have issued a position statement as under (also available on www.scs-isic.com):

Management and Prognosis of Acute Traumatic Cervical Central Cord Syndrome

Acute traumatic cervical central cord syndrome is characterized by a disproportionately greater motor involvement of upper limbs than that of lower limbs with bladder involvement and a sensory loss that is variable below the injury level. This is usually caused by an extreme hyperextension injury of the cervical spinal cord secondary to antero-posterior pinching or squeezing without vertebral damage. The anterior compression could be either due to arthritic spur, a calcified/non –calcified herniated disc or ossified posterior longitudinal ligament. The posterior compression is due to the buckling of ligamentum flavum. However this syndrome can sometimes be seen associated with cervical fracture with or without dislocation and acute traumatic disc herniation.

The usual sequence of recovery starts with motor power of the lower limbs followed by bladder and then the upper limbs with fine finger movements recovering the last. The variable sensory loss doesn't follow a set pattern of recovery. The amount of overall recovery is based on the nature of damage to the central spinal cord. Good prognostic factors regarding recovery in ATCCS are young age (<50 yrs.) and less severe initial neurological deficit. Poor prognostic factors regarding recovery are narrow sagittal diameter of cervical canal, signal intensity changes on MRI (intramedullary edema /hemorrhage/hematoma) and ongoing compression of spinal cord.

Figure 5 : Forest Plots of Functional recovery in young (<50 yrs) vs. older (>50 yrs) age



There is reasonable evidence that patients with ATCCS secondary to vertebral fracture, dislocation, traumatic disc herniation or instability have better outcome with an early surgery(<24 hrs) [6, 32]. To date, ideal management of patients with ATCCS secondary to extension injury in a stenotic cervical canal without fracture, fracture-dislocation, instability or traumatic disc herniation is still a controversy[36].After the initial poor surgical experience of such cases by Schneider et al.[4], many surgeons [5, 21–23]managed cases of ATCCS secondary to extension injury in a stenotic canal conservatively, with good motor recovery in the lower limbs and bladder but with a poor hand function. However, some studies involving a variant of ATCCS with preferential upper limb involvement in patients with a stenotic canal[24, 25] showed good hand recovery with conservative management. Subsequently the option of decompressing the stenotic cervical canal if neurological recovery plateaued was explored by surgeons. Even though there is substantial(level 3) evidence of the benefit of surgery in ATCCS, the majority of studies[7–9, 30]compared non-identical cohorts, introducing a bias in their interpretation. However these studies proved that surgery can be safely done in patients with ATCCS with a stenotic canal with a plateau of neurological recovery or neurological deterioration after conservative management[7–9] or with instability[7, 8].Pollard et al.[29]compared identical cohorts (traumatic incomplete SCI in patients with a stenotic canal without fracture/dislocation/disc herniation) who underwent surgical or conservative management and identified no difference in neurological recovery between operative and non-operative cohorts.

Many retrospective cohort studies[37, 38, 40, 41] including patients with ATCCS secondary to fracture / fracture dislocation /disc herniation / extension injury in a stenotic canal concluded that there is no advantage with early surgery in ATCCS. However these studies included the entire etiological spectrum causing ATCCS and didnnot provide a meaningful interpretation of ATCCS in stenotic canals without fracture/dislocation/disc herniation/instability. Aarabi et al.[39] compared identical cohorts of patients (ATCCS secondary to spinal stenosis with AIS C or AIS D neurology without fracture dislocation / disc prolapse) who underwent early (<24 hrs), intermediate (24 – 48 hrs) or delayed surgery(> 48 hrs) and concluded that timing of surgery did not influence neurological outcome. However Lenehan et al.[12] compared patients with ATCCS in identical cohorts (extension injury in a stenotic canal without fracture / dislocation / traumatic disc herniation with AIS C or AIS D neurology) who underwent early surgery (<24 hrs) or late surgery (> 24 hrs) and identified a statistically significant improvement in the motor score of patients in the early operated subgroup (<24 hrs) in comparison with the subgroup operated late (>24 hrs) at 6month and 12 month follow-up.

With the available evidence, patients with ATCCS secondary to an extension injury in a stenotic canal without fracture/dislocation/instability/disc herniation can be given the options to undergo either early surgery {especially in selected cases with substantial neurological deficit (AIS C) in the presence of ongoing cord compression} or an initial conservative management followed by surgery at a later date, if there is a neurological deterioration or a plateau of neurological recovery. There is a need for high quality prospective randomized control trials to resolve this controversy between conservative management versus early surgery versus delayed surgery in patients of ATCCS secondary to extension injury in a stenotic cervical canal without fracture/ fracture- dislocation/traumatic disc herniation/instability. Until such time, the decision on surgery and its timing should be left to the judgment of

the physician, deliberating on the pros and cons relevant to the particular patient and involving the well informed patient and relatives in the decision making.

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