Spinal Cord (2011) 49, 17–29

www.nature.com/sc

REVIEW

The acute respiratory management of cervical spinal cord injury in the first 6 weeks after injury: a systematic review

S Berney[1], P Bragge[2], C Granger[1], H Opdam[3] and L Denehy[4]

[1]Physiotherapy Department, Austin Hospital, Melbourne, Victoria, Australia; [2]National Trauma Research Institute, Monash University, Melbourne, Victoria, Australia; [3]Department of Intensive Care, Austin Hospital, Melbourne, Victoria, Australia and [4]School of Health Sciences, The University of Melbourne, Parkville, Victoria, Australia

Study design: Systematic review.
Objectives: Identify, evaluate, and synthesize evidence regarding the effectiveness of various treatment strategies for the respiratory management of acute tetraplegia.
Setting: Melbourne, Australia.
Methods: A search of multiple electronic databases (Medline, Cinahl, EMBASE, Cochrane Library, Web of Science, http://www.guideline.gov and http://www.icord.org/scire) was undertaken accompanied by the reference lists of all relevant articles identified. Methodological quality was assessed using the Newcastle–Ottawa Scale and the PEDro Scale. Descriptive analysis was performed.
Results: Twenty-one studies including 1263 patients were identified. The majority of the studies were case series ($n=13$). A variety of interventions were used for the management of respiratory complications. Mortality (ARR = 0.4, 95% confidence interval (CI) 0.18, 0.61), the incidence of respiratory complications (ARR = 0.36, 95% CI (0.08, 0.58)), and requirement for a tracheostomy (ARR = 0.18, 95% CI (−0.05, 0.4)) were significantly reduced by using a respiratory protocol. A clinical pathway reduced duration of mechanical ventilation by 6 days 95% CI (−0.56, 12.56), intensive care unit length of stay by 6.8 days 95% CI (0.17–13.77) and costs. Intubation, mechanical ventilation, and tracheostomy are the mainstay of respiratory management for complete injuries above the level of C5.
Conclusion: This review showed a clinical pathway with a structured respiratory protocol that includes a combination of treatment techniques provided regularly is effective in reducing respiratory complications and cost. The overall study quality was moderate and further studies using specific interventions that target respiratory complications are associated with specific regions of the cervical spine using more methodologically rigorous designs are required.
Spinal Cord (2011) **49**, 17–29; doi:10.1038/sc.2010.39; published online 20 April 2010

Keywords: respiratory management; pulmonary complications; tetraplegia; intensive care

Introduction

Spinal cord injury (SCI) resulting in tetraplegia has a profound effect on respiratory function.[1] Pulmonary complications are the leading cause of morbidity and death both in the short- and longer-term after injury.[2–4] In the acute hospitalization phase respiratory complications are highly prevalent with 84% of patients with C1–4 and 60% of those with C5–C8 injuries experiencing respiratory compromise.[3] The number of respiratory complications during this acute phase contributes significantly to both hospital length of stay and costs.[4]

In addition to muscle paralysis, a period of spinal shock occurs immediately after a traumatic cervical SCI, resulting in flaccid paralysis of muscles below the level of the cord injury[5,6] that can last from a period of 4 weeks[7] up to several months.[6] The severity of spinal shock is related to the severity of the injury and is correlated with the incidence of respiratory complications.[6,8] The impact of spinal shock on respiratory function can be so severe as to require a transient need for an artificial airway and mechanical ventilatory assistance.[2] As spinal shock resolves the flaccid paralysis of muscles is replaced by spasticity and the chest wall becomes rigid resulting in an improvement in respiratory function particularly during inspiration.[5,9] As a result respiratory complications in the acute phase follow a predictable time course developing within the first 5 days and lasting up to 5 weeks post injury as spinal shock resolves.[3] Aggressive respiratory management has been advocated for the prevention and treatment of pulmonary complications and has been associated with improved outcomes.[2,10,11]

The frequency of respiratory complications is correlated with injury level and severity, associated injuries, and the age

Correspondence: S Berney, C/O Physiotherapy Level 3 HSB, Austin Hospital, 145 Studley Road, PO Box 5555 Heidelberg, Melbourne, Victoria 3084, Australia.
E-mail: sue.berney@austin.org.au
Received 3 February 2010; accepted 12 March 2010; published online 20 April 2010

and pre-existing co-morbidities of the patient.[8] The nature of the pulmonary complication can also vary with the level of the injury; with high injuries (C1–C4) being more likely to develop pneumonia and lower cervical injuries atelectasis.[3] Respiratory management encompasses a variety of strategies including airway management, weaning protocols, respiratory care protocols, and physiotherapy intervention.[6,12] Guidelines for respiratory management after SCI were published in 2005,[13] however, these recommendations were not specific to the acute care setting and relied on evidence that did not pertain to the acute SCI population. The aims of this systematic review are to identify, evaluate, and synthesize evidence regarding the effectiveness of various treatment strategies for the respiratory management of acute tetraplegia.

Materials and methods

Data sources and searches

Electronic literature searching was conducted in Medline (1950–2008), Cinahl (1982–2008), EMBASE (1980–2008), the Cochrane Library (2008), Web of Science (1900–1914–2008), http://www.guideline.gov and http://www.icord.org/scire/chapters.php on 20 October 2008 using the following terms: respiration disorders, mechanical ventilators/artificial respiration, respiratory insufficiency, tetraplegia/quadriplegia, spinal cord injuries, intubation/intratracheal, tracheotomy, tracheostomy, respiratory dysfunction, and respiratory management. Terms were mapped to the appropriate Medical Subject Heading (MeSH) and to the EMTREE subject headings in EMBASE and 'exploded'. The search was limited to articles published in English. In addition to this electronic search the reference list of retrieved articles as well as personal files that included invited reviews and clinical guidelines were hand searched to identify further relevant citations.

Study selection

Inclusion and exclusion criteria are detailed in Table 1. We included study designs without a comparison group because of the paucity of comparative studies on this topic. Case studies and conference abstracts were excluded as they provided insufficient information to evaluate methodological quality.

Titles retrieved from searching and their reference lists were screened against the inclusion and exclusion criteria to identify potentially relevant papers; these papers were then reviewed in abstract form and potentially relevant abstracts were selected for full text analysis, from which the final selection was made. Each of the steps was performed independently by two authors (SB and LD) and full text review by two authors (SB and CG). If any discrepancy occurred during the review of the selected articles a third author (PB) adjudicated. Agreement between the reviewers was estimated using the Kappa statistic.

Study design and quality

Studies were evaluated using two methods. Study design was classified according to the National Health and Medical Research Council (NHMRC) Hierarchy of Evidence[14] (Table 1). Using this method, study design is rated from I–IV with I being the strongest providing evidence from a systematic review of randomized controlled trials (RCTs) and IV being the weakest design providing evidence from a case series. Using a standardized data collection form, the methodological quality of RCTs was scored using the PEDro Scale. This scale is a validated quality assessment tool for RCTs.[15] The scale is scored out of 10 and specifically examines the internal validity and adequacy of statistical information presented. The methodological quality of relevant non-randomized and observational studies was assessed using the Newcastle–Ottawa Scale (NOS).[16] The NOS is a validated instrument specifically designed to assess the quality of observational studies in a systematic review and has been previously used in intensive care unit (ICU) populations.[17] The NOS evaluates three domains of methodology that include nine scored criteria: the selection of study groups (score range 0–4), the comparability of groups (score range 0–2), and the degree of certainty of the outcomes (score range 0–3) (Table 2).

Table 1 Inclusion and exclusion criteria

Inclusion criteria	*Exclusion criteria*
Adults >18 years who suffered traumatic injuries of the cervical spine resulting in quadriplegia regardless of injury level or severity	Articles concerned with the surgical management of the cervical spine and the administration of methylprednisolone within the first 48 h post injury were not included as they have been reviewed elsewhere
Acute respiratory management, defined as any treatment intervention or strategy designed to address respiratory complications arising from or associated with spinal cord injury in the first 6 weeks post injury. This time period was selected as the reversible adverse effects of spinal shock on the respiratory system should still be apparent necessitating a period of intense respiratory management (Lemmons;[8] Mansel[6])	Less than 50% of subjects in a study met the inclusion criteria with regards to neurological level or time after injury
Outcome measures included any of the following: changes in physiological parameters such as lung volumes and gas exchange; the incidence of respiratory complications; airway management; the use and duration of mechanical ventilation; and intensive care unit and hospital length of stay and costs	
Published in English	
Quantitative study designs that included randomized controlled trials, comparative studies, and case series	

Table 2 Scoring criteria used for synthesizing results of studies in the review

	Newcastle–Ottawa Scale	*PEDro Scale*
Strong evidence—consistent findings among multiple high-quality studies	6/9	6–10/10
Moderate evidence—consistent findings among multiple lower quality studies and/or one high-quality study	4–5/9	4–5/10
Limited evidence—one lower quality study	<4	<4
Conflicting evidence—inconsistent findings among multiple studies		
No evidence—no evidence among studies		

Newcastle–Ottawa Scale used for non-randomized controlled trials and PEDro Scale used for randomized controlled trial.

Table 3 Information and outcome measures extracted from studies

Patient information	*Outcome measures*
Patient demographic characteristics	Change in physiological variables such as gas exchange or lung volumes
Injury level	Intensive care unit and hospital length of stay
Injury severity	The incidence of respiratory complications
Type of respiratory management	Chest radiograph changes
Dose of respiratory management (when available)	The use and duration of mechanical ventilation
	Airway management
	Costs

Data extraction and synthesis

The following information was extracted from relevant studies when available (Table 3). Mean differences and 95% confidence intervals (CIs) and odds ratios or relative risk and 95% CIs were calculated if they were not provided. Owing to the heterogeneity of interventions and outcome measures, outcomes were not pooled.

Results of the included studies were narratively synthesized. An established protocol was used to aid interpretation of the results of the review for the NOS[18] consistent with previous systematic reviews[19] and for the PEDro Scale[20] (Table 2).

Results

Study selection

The initial search retrieved 336 citations. The subsequent review of titles, abstracts, and full length articles yielded 21 reports. All findings refer, unless otherwise stated, to the remaining 21 papers (Figure 1).

Study design and quality

The 21 included papers comprised 1 RCT, 3 cohort studies, 3 case–control studies, and 14 retrospective case series reports. The methodological quality of the studies was moderate overall with one RCT achieving a PEDro score of three and eight studies achieving an NOS >six and with mean score of five (Table 4). In general, as most studies were retrospective case series there was no score attributable for comparability; however, population selection, outcome assessment, and follow-up were satisfactory (Table 5).

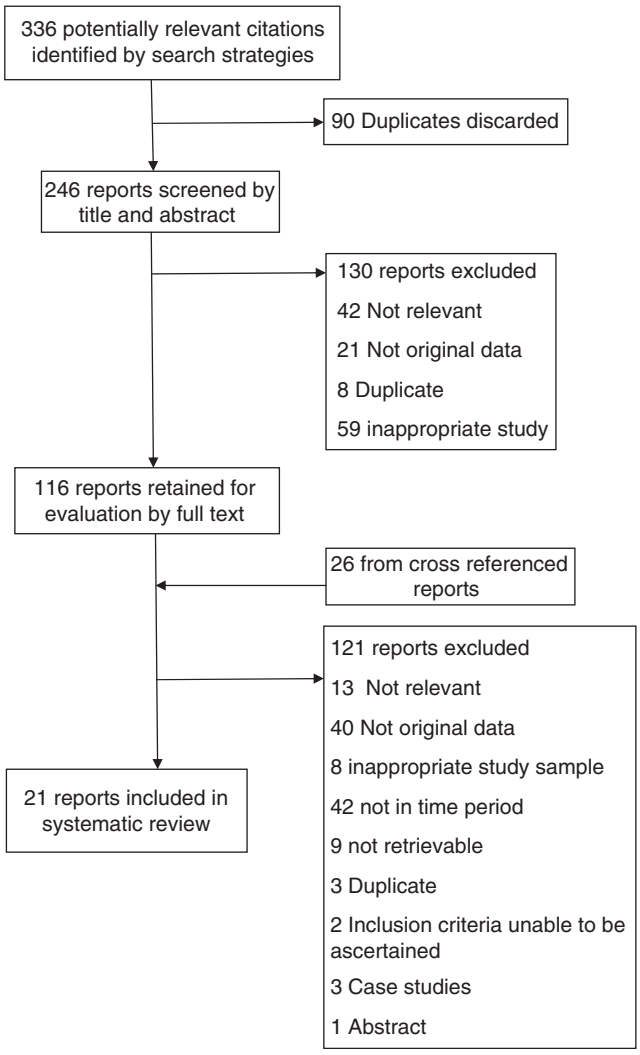

Figure 1 Flow of studies through the review.

Data extraction and synthesis

The mean sample size of the included studies was 68.52 (range 3–186) and a total of 1415 patients were included across all studies. Subjects were predominantly male with a complete injury between C4 and C6. Although all studies were single centre they reflected an international experience with 52% of studies from North America, 33% from Europe, and 14% from Australia. Specialist SCI centres were involved in 85% of the studies. Kappa statistics for inter-reviewer selection of potentially relevant titles and abstracts and full text articles were 0.87 and 0.77, respectively, showing substantial agreement.

Table 4 Study quality for randomized controlled trial

Study	*Random allocation*	*Concealed allocation*	*Groups similar at baseline*	*Participant blinding*	*Therapist blinding*	*Assessor blinding*	*<15% dropouts*	*Intention-to-treat analysis*	*Between-group difference reported*	*Point estimate and variability reported*	*Total (0–10)*	*NHMRC grade of evidence*
Pllastrini	Yes	No	Yes	No	No	No	No	No	No	Yes	3	II

Study quality and design for non randomized controlled trials

Newcastle–Ottawa Scale	*Selection*	*Comparability*	*Outcome*	*Total/9*	*Design*	*NHMRC grade of evidence*
Gregoretti *et al.*[22]	4	2	3	9	Case–control	III-2
Berney *et al.*[39]	4	2	3	9	Case–control	III-2
Vitaz *et al.*[33]	4	1	3	8	Retro cohort	III-3
Braun *et al.*[21]	2	2	2	6	Case–control	III-2
Berney *et al.*[35]	3	0	3	6	Case series	IV
Harrop *et al.*[36]	3	0	3	6	Case series	IV
Hassid *et al.*[30]	3	0	3	6	Case series	IV
Tromans *et al.*[31]	3	0	3	6	Case series	IV
Velmahos *et al.*[32]	3	0	3	6	Case series	IV
McMichan *et al.*[10]	3	0	2	5	Retro cohort	III-3
Lerman and Weiss[25]	2	0	3	5	Case series	IV
Como *et al.*[37]	2	0	3	5	Case series	IV
Romero *et al.*[38]	2	0	3	5	Case Series	IV
Bellamy *et al.*[34]	2	0	2	4	Cohort	III-2
Hornstein and Ledsome[24]	2	0	2	4	Case series	IV
Stiller *et al.*[27]	2	0	2	4	Case series	IV
Green *et al.*[28]	2	0	2	4	Case series	IV
Gardner *et al.*[40]	2	0	1	3	Case series	IV
Gupta *et al.*[23]	1	0	0	1	Case series	IV
Hachen *et al.*[29]	0	0	1	1	Case series	IV

Abbreviation: NHMRC, National Health and Medical Research Council.

Respiratory management interventions and protocols

A variety of treatment techniques, management strategies, and protocols including a clinical pathway were used for the treatment and management of respiratory complications in the studies (Table 6). Protocols included a combination of modalities at varied intensity. The clinical pathway was restricted to a description of timing of processes of care.

Results: physiological outcomes

Seven studies evaluated physiological outcomes.[21–27] There was moderate evidence to support the use of an assist cough to improve cough efficacy by significantly increasing peak expiratory flow[21] and that the use of trans-tracheal open ventilation (mechanical ventilation through minitracheostomy)[22] was effective in maintaining gas exchange and respiratory mechanics for an initial 24 h period. There was also moderate evidence for the provision of respiratory muscle resistance training to improve maximum inspiratory pressure[24,25] and vital capacity.[25] Two studies reported the effects of intermittent positive pressure breathing on lung volume.[25,27] The intervention was used differently in each study, one as part of a treatment package[25] and the other as a sole treatment.[27] The studies, both of low quality, reported a significant improvement in vital capacity. However, when intermittent positive pressure breathing was used as a sole intervention the improvement in lung volume was small and of limited clinical significance. There was limited evidence because of poor study quality to support the use of insufflation/exsufflation[26] and minitracheostomy.[23]

Incidence of respiratory complications

Seven papers reported the effect of various interventions on the incidence of respiratory complications.[10,28–33] Respiratory complications were defined as pneumonia, atelectasis, or respiratory insufficiency—a diagnosis that included respiratory failure, pneumonia, respiratory infection, and oxygen desaturation. Five of the studies were retrospective case series[10,28–32] and the remaining two studies were cohort designs that used a retrospective control group.[10,33] There was moderate evidence that a comprehensive clinical pathway[33] and a respiratory protocol[10] reduced respiratory complications. Similar to Lerman and Weiss, McMichan *et al*. used a package of respiratory interventions that showed a significant reduction in the incidence of atelectasis compared with a retrospective control group (ARR = 0.36, 95% CI (0.08, 0.58)) with a number needed to treat of three. In addition, there was a decreased requirement for tracheostomy (ARR = 0.18, 95% CI (−0.05,0.4)) with a number needed to treat of six. There was moderate evidence, albeit from a small case series, that showed non-invasive ventilation (NIV) was useful for the treatment of respiratory failure and may avoid the need for intubation.[31] Given the quality of the study and design,[28] there is little credible evidence to support the routine use of kinetic therapy (continuous bed

Table 5 Study characteristics for randomized control trials/case control and cohort studies

Citation	*Subjects*		*Injury level range/mode*		*ASIA*		*Setting*	*Outcome measure*
	Intervention *N* = *C/I* *Gender M/F* *Mean age (years)*	*Control* *N* = *C/I* *Gender M/F* *Mean age (years)*	*Intervention*	*Control*	*Intervention*	*Control*	*Site* *Specialist centre*	
Bellamy *et al.*[34]	54 30/24I 44/10 Age NS	8 CSCI NS Gender NS Age NS	C3–C7 Mode NS	NS	A I: NS	No deficit	SCI specialist ICU	Airway management
Vitaz *et al.*[33]	36 C: NS Gender NS 33 ± 15	22 C: NS Gender NS 34 ± 10	C1–T5 Mode C6/7	C1–T5 Mode = C5/6	AMS = 22 ± 22	AMS = 19 ± 24	ICU	Rate of pneumonia, ventilator days, ICU and hospital length of stay, cost comparison
McMichan *et al.*[10]	22 C: NS 18/4 24 ± 3	22 C: NS 20/2 29 ± 3	C4–C8 Mode NS	C3–C8 Mode NS	NS	NS	ICU	Incidence of mortality, atelectasis, need for mechanical ventilation, and tracheostomy
Gregoretti *et al.*[22]	10 C: NS 10/0 34	10 C: NS 10/0 34	C4–6 Mode = C5	C4–6 Mode = C5	A	A	ICU	Gas exchange, respiratory mechanics, respiratory rate
Braun *et al.*[21]	13 C: 13 11/2 30.9 ± 17.3	13 C: 13 11/2 30.9 ± 17.3	C4–T6 Mode level NS	C4–T6 Mode level NS	A	A	Acute ward	FVC, PEFR
Pillastrini *et al.*[26]	5 C: 5 4/1 31.5 ± 16.1	4 C: 4 3/1 52.2 ± 17.6	C1–C7 Mode NS	C1–C7 Mode NS	A	A	Acute ward	FEV1, FVC, PEF
Berney *et al.*[39]	7 C: 7 7/0 26.14	7 C: 7 4/3 29.43	C5–C6 Mode C5	C5–C7 Mode C5 and C7	A	A	SCI specialist ICU	ICU LOS, MV duration, cost

Case series characteristics

Citation	*Subjects* *N* = *C/I* *Gender M/F* *Mean age (years)*	*Injury level range mode*	*ASIA*	*Setting Site Specialist Centre*	*Outcome measure/description*
Romero *et al.*[38]	152 119/33 122/30 40.86 ± 1.86	C3–T12 C3–5	A–D	SCI specialist ICU	Pneumonia, duration of mechanical ventilation and ICU length of stay and mortality compared for tracheostomy inserted before and after 7 days
Hornstein and Ledsome[24]	20 16/4 18/2 25.5	C4–C7 C5	A/incomplete status NS	SCI specialist acute ward	Pimax
Berney *et al.*[35]	71 45/26 46/25 40.28 ± 19.22	C1–C8 C5	A–D	SCI specialist ICU	Tracheostomy timing after stabilization, infection rate for anterior and posterior approaches, and tracheostomy
Stiller *et al.*[27]	5 NS 3/2 34	C5–C7 C5	NS	SCI specialist ICU	TV, VC
Lerman and Weiss[25]	3 2/1 2/1 31	C3/4	A/B	SCI specialist ICU	VC, MIF, successful weaning
Gardner *et al.*[40]	44 NS 37/7 38.61	C2–L1 C4	NS	SCI specialist ICU	Mortality, method of ventilation

Table 5 Continued

Citation	*Subjects N = C/I Gender M/F Mean age (years)*	*Injury level range mode*	*ASIA*	*Setting Site Specialist Centre*	*Outcome measure/description*
Hachen[29]	188 117/71 NS NS	C4–T1 C6 (Mode C: C7 Mode I: C6)	A/ incomplete status NS	SCI specialist ICU	Mortality, airway management, respiratory complication rate
Harrop *et al.*[36]	156 156/0 NS 38	C2–C8 C4	A	SCI specialist ICU	Airway management
Velmahos *et al.*[32]	68 41/27 64/4 34 ± 16.5	NS 32/68 injuries above C5	A/ incomplete status NS	SCI specialist ICU	Airway management, risk factor model to predict patients who require intubation, incidence of respiratory compromise
Gupta *et al.*[23]	4 4/0 4/0 36.25	C5–C6 C5	A	SCI specialist ICU	Clinical use of a mini-tracheostomy
Como *et al.*[37]	119 45/74 93/26 45	C1–C8 NS	A/ incomplete status NS	SCI specialist ICU	Airway management, mortality, mechanical ventilation usage
Green *et al.*[28]	162 NS 143/19 NS	NS	NS	SCI specialist ICU	Mortality, respiratory complications
Hassid *et al.*[30]	186 108/78 NS 35.92	C5–T1 mode level not able to be determined	A/B	SCI specialist ICU	Airway management, respiratory complications, ventilation hours, ICU LOS, mortality
Tromans *et al.*[31]	28 (32 treatment occasions) 24/8 21/7 40	C2–T7 C4	A/B/C	SCI specialist ICU	Prophylactic: prevention of intubation and mechanical ventilation Weaning: weaning outcome

Abbreviations: AMS, ASIA motor score; ASIA, American spinal injury association classification; C, complete cervical spinal cord injury; CC, control cohort/cases; CG, control group; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; I, incomplete cervical spinal cord injury; IC, intervention cohort/cases; ICU, intensive care unit; IG, intervention group; LOS, length of stay; MV, mechanical ventilation; NS, not stated; PEF, peak expiratory flow; PEFR, peak expiratory flow rate; SCI, spinal cord injury. Mean age is at time of injury.

turning). The remaining three case series[29,30,32] reported the incidence of respiratory complications associated with their approach to airway management. Overall, the incidence of pneumonia from these three reports was between 40 and 55% with complete injuries having a higher incidence (60–70%) than incomplete injuries (20–30%).

Airway management

Seven studies reported outcomes concerning airway management.[29,30,32,34–37] Six studies were case series[29,30,32,35–37] and one study was a cohort design.[34] There were three issues addressed in the topic of airway management: (1) indications for intubation; (2) indications for tracheostomy; and (3) optimal timing of tracheostomy insertion after cervical stabilization surgery.

Intubation

One case series[32] compared the characteristics of patients who were intubated with those who were not. They identified three independent risk factors for intubation: injury severity score, SCI above the level of C5, and a complete injury. Overall, 74% of the patients required intubation. Three other case series of varying quality reported similar rates of intubation[29,30,37] although two of these studies included only patients with an injury of C5 and below.[29,30] All studies reported a higher rate of intubation for complete injuries that varied from 74%[29,32] to above 90%.[30,37]

Tracheostomy

There were two factors that accounted for the incidence of tracheostomy: whether the injury was complete and the injury level being above or below C5. One case series[36] reported the risk factors that predicted tracheostomy in patients with complete injures were age, pre-existing medical condition, pre-morbid lung disease, and injury level. The overall incidence of tracheostomy in these cases was 69%. This was similar for other groups for complete injury[30,34,37]

Table 6 Results for case series

Citation	*Treatment described*	*Results*					
		Airway management *Overall* *C* *I*	*Respiratory complications*	*Physiological*	*LOS (days)*	*MV incidence/ time (days)*	*Other*
Romero *et al.*[38]	Airway management—tracheostomy inserted before or after day 7		*Pneumonia*: *O* = 138/152 (91%) <7 days 62/71 (87.3%) >7 days 76/81 (92.7%)		<7 days 36.52 ± 1.6 days >7 days 54.58 ± 3 days *P* < 0.001	<7 days 26.07 ± 1.69 days >7 days 48.75 ± 3.45 days *P* < 0.005	*Mortality*: *O* = 6/152 (4%) <7 days 1/71 (1.4%) >7 days 5/81 (6%)
Hassid *et al.*[30]	Airway management of patients between C5 and T1 with no TBI	In = 127/186 (68%) *T* = 88/186 (47%) *C* In = 97/108 (90%) In to *T* = 73/97 (75%) *T* = 73/108 (68%) *I* In = 30/78 (38%) In to *T* = 15/30 (50%) *T* = 15/78 (19%)	*Pneumonia*: *O* = 92/186 *C* 73/108 (68%) 67/108 In+6/11 non-In *I* 19/78 (24%) 13/30 *I*+6/48 non-*I*				*Mortality*: *O* = 27/186 *C* 26/108 (24%) 16/97 In+10/11 non-*I* *I* 1/78 (In)
Velmahos *et al.*[32]	Airway management	In = 50/68 *C* = 37/50 *(28/50 above C5)* Risk factors for In identified ISS > 16 (OR = 12.96, 95% CI: 2.51, 65.98, *P* = 0.00) SCI above C5 (OR 8.71, 95% CI 1.46–51.87, *P* = 0.02) *C* (OR 7.96, 95% CI: 1.61, 37.13, *P* = 0.01)	*Pneumonia*: 27/68 (40%) In = 25/50 (50%)				*Mortality*: *O* = 11/68 (16%) In = 11/50 (22%)
Como *et al.*[37]	Airway management	In = 67/119 (56%) *T* = 31/119 (31%) *C* In = 41/45 (91%) In to*T* = 32/41 (78%) *T* = 32/45 (71%) All C C5 and above (31) required intubation and tracheostomy. C6 and below In = 11 *T* = 6 *I* In = 26/74 (35%) In to *T* = 5/26 (19%) *T* = 5/74 (7%) Days (mean) to *T* = 10				*MVDC*: *O* = 20/119 *C* 19/45 17/19 above C5 *I* 1/74	
Harrop *et al.*[36]	Airway management	*T* = 107/156 (69%) Factors identified to predispose to *T* Age (*P* = 0.05) pre-existing medical conditions (*P* < 0.05); pre-morbid lung disease (*P* < 0.05); injury level (*P* < 0.0001); 88/107 between C4 and C7					
Hachen[29]	Airway management	In = 63/108 (58%) *T* = 30/188 (16%) *T* complications = 8/30 (27%) *C*	*Respiratory insufficiency*: *O* = 101/188 (54%) *C* 82/117 (70%) *I*				

Table 6 Continued

Citation	*Treatment described*	*Results*					
		Airway management *Overall* *C* *I*	*Respiratory complications*	*Physiological*	*LOS (days)*	*MV incidence/ time (days)*	*Other*
		In = 50/117 In to *T* 26/50 (52%) *T* = 26/117 (22%) *I* In = 13/71 (18%) *T* = 4/71 (6%)	19/71 (27%)				
Berney *et al.*[35]	Timing of tracheostomy after stabilization surgery and comparison of infection rates between anterior and posterior approach	*T* timing (days) anterior 3.8 ± 2.6 posterior 3.1 ± 2.7 anterior and posterior 4.9 ± 2.3 days No significant difference between timing					*Stabilization approach*: Anterior = 32 Posterior = 15 Anterior and posterior = 24 *Incision infection risk*: Posterior fusion associated with higher risk of incision infection (OR 18.97, 95% CI 2.31–155.54)
Green *et al.*[28]	Kinetic therapy 2 weeks post acute injury		*Pneumonitis/atelectasis*: 9/162 (6%)				*Mortality*: 11/162 (7%)
Tromans *et al.*[31]	BIPAP for prevention of ventilatory failure and BIPAP to assist weaning from full ventilation		*Treatment of ventilatory failure/avoiding intubation*: 10/17 (59%)			*Successful weaning*: From full MV 13/15 (87%)	
Gupta *et al.*[23]	Minitracheostomy use to (1) treat retained secretions and prevent bronchcoscopy and intubation (2) weaning from tracheostomy	Successful decannulation		Clinical improvement in PaO_2/FiO_2 MD 95% CI = 103 (−97.34, 303.34)			CXR CXR clearing
Lerman and Weiss[25]	Respiratory protocol: respiratory muscle training, IPPB, chest percussion and vibration, postural drainage, assisted cough, suctioning	All patients were successfully weaned		Increase VC MD 95% CI = 410 (362.90, 1182.90) ml and increase MIF, MD 95% CI = −10.33 (−32.68, 12.02)			
Stiller *et al.*[27]	IPPB 2 hourly four reps of six breaths with 30–60 s of relaxed breathing			IPPB volume increased ($P < 0.001$) Post IPPB Vt not different VC increased 43 ml ($P < 0.02$)			
Gardner *et al.*[40]	Provision of mechanical ventilation for high quadriplegia						*Mortality*: 14/44 (32%) died on first admission
Hornstein and Ledsome[24]	Ventilatory muscle training protocol			Increase Pimax MD 95% CI = −13.55 (−28.87, 1.77)			

Table 6 Continued

Results for case control or cohort study

Citation	*Intervention*	*Control/cohort*	*Results*					
			Airway management Overall CI	*Respiratory complications*	*Physiological*	*LOS (days)*	*MV (incidence/time)*	*Other*
Gregoretti *et al.*[22]	Transtracheal open ventilation	Conventional mechanical ventilation			PaO_2/FiO_2, $PaCO_2$, RR not different after 1 and 24 h, pressure time product (PTP) of oesophageal pressure less after 24 h $P<0.05$ MD 95% CI $P/F=10$ (−47.31, 67.31) $PaCO_2=-2.2$ (−7.18, 2.78) $RR=-3$ (−6.82, 0.82) PTP = −63 (−29.39, −96.61)			
Braun *et al.*[21]	Assisted FVC and cough	Unassisted FVC and cough			Peak flow rate increased 13.8% with assistance $P<0.01$, no significant improvement in volume			
McMichan *et al.*[10]	Intensive respiratory care protocol: positioning, deep breathing, incentive spirometry, chest percussion, assisted cough	Historical standard care	Decrease tracheostomy use 2/22 and 6/22 for control ARR = 0.18, 95% CI (−0.05, 0.4) RRR = 0.67, 95% CI (−0.19, 1.47) NNT = 6	*Atelectasis*: reduction in atelectasis 4/22 intervention and 12/22 in control. ARR = 0.36, 95% CI (0.08, 0.58) RRR = 0.67, 95% CI (0.15, 1.06) NNT = 3			Decrease need for MV 3/22 and 9/22 in controls. ARR = 0.27, 95% CI (0.01, 0.49) RRR = 0.67, 95% CI (0.02, 1.21) NNT = 4	*Morality*: Reduction on mortality 0/22 mortality in intervention 9/22 in control ARR = 0.4, 95% CI (0.18, 0.61) RRR = 1, 95% CI (0.44, 1.50) NNT = 2
Vitaz *et al.*[33]	Clinical pathway—4 hourly chest physiotherapy; fixation within 2 days with tracheostomy if required at day 4	Historical standard care		Decreased episodes of pneumonia/ patient $P=0.05$		*ICU LOS*: Decreased mean difference 95% CI (days) 6.8 (−0.17, 13.77 *Hospital LOS*: Mean difference 95% CI (days) decreased 11.5 (3.49, 19.51)	MV days decrease mean difference 95% CI (days) 6 (−0.56, 12.56)	*Costs*: $20 000 per patient saved
Berney *et al.*[39]	Intensive physiotherapy to prevent tracheostomy	Patients who received tracheostomy				*ICU LOS*: Mean difference 95% CI decrease 8.71 (1.75, 15.67)	MV days Decrease $P=0.006$ Mean difference 95% CI decrease 8 days (4.66, 11.34)	*Cost*: Saving of $1270 per patient per day
Bellamy *et al.*[34]	Airway management	Cervical spine fracture with no neurology	OT = 31/54 (57%) CCSCI 23/30 (77%) ICSCI = 8/24 (33%) T performed within 3 days No neurology group 0 T = 0					*Mortality*: *O* = 15/54 (28%) CCSCI12/30 (40%) ICSCI 5/24 (21%)

Table 6 Continued

Results from randomized controlled trials/randomized trials

Author date	*n*	*Setting*	*Intervention*	*Control/comparison*	*Result*
Pillastrini *et al.*[26]	9	Acute	Manual respiratory kinesitherapy+ mechanical insufflations/exsufflation inhale pressure 15 cmH_2O, exhale pressure 45 cmH_2O	Manual respiratory kinesitherapy for 10 treatments: postural drainage, PEP assisted cough, AMBU bag, endoscopic bronchoaspiration	Increase FVC, FEV1 ($P=0.0001$), increased PEF ($P=0.0093$) MD and 95% CI in FVC 0.09 l (−0.23, 0.41) MD and 95% CI for FEV1 0.07 l (−0.14, 0.28)

Abbreviations: ARR, absolute risk reduction; BiPAP, bi-level airway pressure; C, complete spinal cord injury; CCSCI, complete cervical spinal cord injury; 95% CI, 95% confidence interval; CXR, chest radiograph; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; I, incomplete spinal cord injury; ICSCI, incomplete cervical spinal cord injury; ICU, intensive care unit; In, intubated; IPPB, intermittent positive pressure breathing; ISS, injury severity score; LOS, length of stay; MD, mean difference; MIF, maximal inspiratory force; MV, mechanical ventilation; MVDC, mechanical ventilation at discharge; NNT, number needed to treat; PEF, peak expiratory flow; PEP, positive expiratory pressure; RR, respiratory rate; RRR, relative risk reduction; SCI, spinal cord injury; T, tracheostomy; TBI, traumatic brain injury; VC, vital capacity; Vt, tidal volume.

except for one low quality[29] study that reported a much lower incidence of tracheostomy insertion (22%). The incidence of tracheostomy insertion in incomplete injuries was low (6–33%).[29,30,34,37] For complete injuries above the C5 level the incidence of tracheostomy was between 81[36] and 83%[37] compared with 49[36]–60%[37] for complete injuries C5 and below.

Tracheostomy timing

Three studies reported on the timing of tracheostomy insertion after injury,[34,37,38] which varied from 3 days[34] to 10 days[37] and one study[35] reported timing post cervical spine anterior surgical stabilization. This case series of 78 patients[35] also examined the relationship between timing of tracheostomy insertion and the risk of cross infection at the anterior stabilization incision site, which is an important clinical consideration . These authors reported that tracheostomy insertion as early as day 4 post anterior cervical stabilization did not appear to pose a risk of cross infection. Another case series[38] showed that tracheostomy inserted before day 7 reduced the duration of mechanical ventilation and ICU length of stay.

ICU and hospital length of stay and costs

Two good quality studies and one case series[38]used ICU and or hospital length of stay as an outcome.[33,39] Berney *et al.* using a case–control design showed in comparable groups of selected patients that intensive physiotherapy can prevent the need for tracheostomy and reduce length of stay in ICU (mean difference = 8.71 days, 95% CI 3.49, 19.51) therefore reducing costs. Romero *et al.* reported that tracheostomy insertion before day 7 reduced both duration of mechanical ventilation (mean difference = 22.68 days, 95% CI 21.79, 23.57) and ICU length of stay (mean difference18.06 days, 95% CI 17.29, 18.83). Vitaz *et al.* reported a reduction in ICU length of stay (mean difference = 6.8 days, 95% CI −01.7, 13.77) and hospital length of stay (mean difference = 11.5 days, 95% CI 3.49, 19.51) saving a mean of $20 000 USD per patient using a clinical pathway to direct all aspects of acute care.

Mechanical ventilation and weaning

The incidence or the duration of mechanical ventilation was described in six studies. There was moderate evidence that intensive respiratory protocols alter the need for mechanical ventilation. McMichan *et al.* showed a reduced need for mechanical ventilation (ARR = 0.27, 95% CI 0.01, 0.49) with a number needed to treat of four and an author of this review (SB), showed a reduction in the duration of mechanical ventilation (mean difference = 8 days 95% CI 4.66, 11.34).[39] Vitaz *et al.* similarly showed that a protocolized care pathway compared with historical standard care can reduce the duration of mechanical ventilation (mean difference 6 days 95% CI −0.56, 12.56). Overall, there was limited evidence to support the use of NIV to reduce the duration of mechanical ventilation.[31] One case series[38] reported that tracheostomy timing either before or after day 7 was independently associated with duration of mechanical ventilation.

Mortality

Six studies reported mortality rates associated with treatment.[10,28,30,32,34,40] A respiratory care protocol[10] showed a reduction in mortality compared with a historical control group who appeared to receive no specific respiratory treatment (ARR = 0.4, 95% CI 0.18, 0.61) with a number needed to treat of two. There is no high quality evidence to support the use of kinetic therapy to reduce mortality. Three studies[30,32,34] reported mortality rates between 16[32] and 28%.[34]

Discussion

There were three main outcomes of this review. First, respiratory complications are prevalent, however treatment protocols that include a combination of techniques, applied frequently, appear to be the most effective in preventing respiratory complications, reducing mortality, ICU length of

stay, and the duration of mechanical ventilation and improving the physiological status of the patient.[10,25,39] These treatment techniques include positioning, assist coughing/suctioning, and lung volume restoration therapy. Second, managing the processes of care with a clinical pathway is cost effective and appear also to be effective in reducing the incidence and severity of respiratory complications, the duration of mechanical ventilation, and ICU length of stay.[33] Third, intubation, mechanical ventilation, and tracheostomy remain the mainstay of respiratory management especially for injures American spinal injury association classification (ASIA) A injures above the C5 level.

Most studies in this review were either case series or cohorts studies with historical controls and all were from single centres. The results are therefore prone to bias and the only RCT rated poorly with little consideration of statistical power, blinding, or comparability between groups. In many studies there was inadequate classification of incomplete SCI, which may reflect the difficulties associated with neurological assessment in the early phase of injury because of instability of baseline neurological examination.[41] This in part can be influenced by the effects of cord swelling or bleeding that can result in patients losing a neurological level within the first few days.[37] It has been suggested if possible that patients not be recruited to trials until 48 h post injury so a more reliable base line neurological level can be established.[41] However, management for the prevention of respiratory complications must begin immediately[2] making research in this phase of SCI more complex.

This review has found that evidence addressing the acute respiratory management of SCI comprises predominantly low quality trials. In part, this is an illustration of the difficulties associated with trial design in the early phases of SCI. Performing the gold standard RCT in this population is problematic because of heterogeneity of injury, the lack of a consistent approach to management,[42] relatively small patient numbers,[43] and instability of baseline neurological assessment.[41] To overcome some of these issues, several studies in this review included only complete injuries. However, efficacy of interventions in this subgroup may not be able to be generalized to incomplete injuries. Large-scale multi-centre RCTs are possible in SCI;[44] however, they are major organizational undertakings that require stringent inclusion criteria to account for other trauma and co-morbidity and on-going close monitoring of sites and treatment protocols during the trial.[41] Alternative designs and strategies such as cluster randomization and adaptive randomization may enable phase III controlled trials to be performed.[41] Despite the difficulties that injury heterogeneity, generalizability, and design pose, respiratory complications are predictable both in their nature and time course. Future research could investigate the efficacy of specific interventions and protocols that address the known risk factors and time course such as specific protocols for upper cervical lesions for the prevention of pneumonia.

Transtracheal open ventilation is a novel treatment approach to both mechanical ventilation and airway management and conveys the potential benefits of communication and oral intake to the patients. It warrants further longer-term comparison with conventional mechanical ventilation and tracheostomy measuring outcomes such as respiratory complications, wound infection, duration of mechanical ventilation, and ICU length of stay.

Airway management was a strong theme of the reports included in this review. There was little conjecture about the airway management of complete cervical injuries above the level of C4 and most reports concentrated on lower complete and incomplete injuries. Future multi-centre studies examining the factors that predict the need for tracheostomy in lower cervical or incomplete injuries that consider the role of NIV are required. In the future a guideline for airway management in this population that included recommendations for timing of tracheostomy insertion would be of value particularly for patients who are managed outside a specialized spinal unit.

The role of NIV in the ICU continues to grow as evidence accumulates regarding the prevention of post-extubation respiratory failure and the successful treatment of respiratory failure.[45] The role of NIV in the respiratory management of acute SCI at the level of C4 and below warrants further investigation. These roles of NIV in the treatment of respiratory failure and weaning would appear plausible given the indications for NIV in other adult ICU populations.[45,46] However, the use of NIV as a substitute for conventional mechanical ventilation would be unlikely to receive widespread support in the ICU community and at best would be case dependent. Given the results of this review, future research using NIV should be examined in combination with other therapies such as an intensive respiratory care protocol and outcomes should include ICU and hospital length of stay and the use and duration of intubation, tracheostomy, and mechanical ventilation.

This review had several limitations. By restricting management to the first 6 weeks after injury, papers may have been omitted that discussed pertinent issues to the acute phase such as weaning and the role of early respiratory muscle training. However, the focus of this review was the acute period of reversible respiratory failure that occurs as a result of the SCI and the ensuing spinal shock. Prolonged weaning is usually associated with high cervical injuries and is not a respiratory complication but a consequence of injury severity. Long-term weaning strategies alone could be a subject of a future systematic review. Several papers were included that were greater than 20-years–old, which limited their generalizability to current practice. This was particularly evident in results pertaining to overall[28,34] and hospital mortality[10] where advances in medical practice in early resuscitation, ICU, and post-ICU care have resulted in improved rates of survival.[47] It was decided to include these papers as these data are referred to in recent narrative reviews and form the basis of current treatment recommendations.[48,49]

In conclusion, this systematic review has revealed that a clinical pathway with a structured respiratory protocol that includes a combination of treatment techniques provided regularly is effective in reducing respiratory complications and the cost of acute care. Future consideration of collaboration and trial design with particular emphasis on inclusion

criteria especially neurological severity and injury is necessary so trials of sufficient quality and power are performed that address effective ways of improving overall pulmonary function and performance and the prevention of respiratory complications.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We thank Ms Anne McLean for her assistance and also the Victorian Neurotrauma Initiative for the fellowship for Susan Berney.

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