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Systematic Review / Meta-Analysis

A critical appraisal of clinical practice guidelines for management of four common complications after spinal cord injury

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Abstract

BACKGROUND CONTEXT: Complications such as pressure sores, pulmonary infection, urinary tract infection (UTI), and venous thromboembolism (VTE) are common after spinal cord injury (SCI). These have serious consequences for patients' physical, social, and vocational well-being. Several authoritative organizations have developed guidelines for managing these complications after SCI.

PURPOSE: We aim to systematically review and appraise guidelines on the management of four common complications (pressure sores, pulmonary infection, UTI, and VTE) after SCI as well as to summarize relevant recommendations and assess the quality of their supporting evidence.

DESIGN: Systematic review.

METHODS: We searched Medline, Embase, Cochrane, and Web of Science, as well as guideline-specific databases (eg, National Guideline Clearinghouse) and Google Scholar, from January 2000 to January 2022. We included the most updated guidelines developed by specific authoritative organizations. We evaluated the included guidelines using the Appraisal of Guidelines for Research and Evaluation 2nd edition instrument, which measures six domains (eg, applicability). Recommendations extracted from guidelines were categorized as for, against, or neither for nor against. An evidence assessment was adopted to classify the quality of supporting evidence as poor, fair, or good.

RESULTS: Eleven guidelines from 2005 to 2020 were included, all of which, among the six domains, scored lowest in the domain of applicability. For pressure sores, guidelines recommended for skin inspection, repositioning, and the use of pressure reduction equipment as preventive measures and dressings, debridement, and surgery as treatment measures. For pulmonary infection, guidelines recommended for physical (eg, the use of an insufflation–exsufflation device) and pharmacological measures (eg, the use of bronchodilators). For UTI, guidelines recommended for antibiotics as a treatment measure but recommended against cranberries, methenamine salts, and

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acidification or alkalinization agents as preventive measures. For VTE prophylaxis, five guidelines recommended for low molecular weight heparin (LMWH). Three guidelines recommended against unfractionated heparin, whereas one guideline recommended for it. Most of the supporting evidence was of poor quality (130/139), and the rest was of fair quality (9/139).
CONCLUSIONS: For pressure sores, pulmonary infection, and UTI, evidence of poor to fair quality indicated consistent recommendations for prevention and treatment measures. For VTE, LMWH was consistently recommended, whereas recommendations on the use of unfractionated heparin were controversial.

Keywords: AGREE II; Clinical practice guidelines; Complication management; Pressure sore; Pulmonary infection; Spinal cord injury; Urinary tract infection; Venous thromboembolism

Introduction

Spinal cord injury (SCI) has become an increasingly significant global public health challenge [1]. The Global Burden of Disease 2019 Study showed that the number of patients with SCI worldwide increased from 11.37 million (95% uncertainty interval [UI]: 10.38 to 13.11) in 1990 to 20.64 million (95% UI: 18.93 to 23.61) in 2019 [2]. With high healthcare costs, SCI also represents a heavy burden to healthcare systems and economies [3]. In the United States, the direct costs for the care of patients with SCI are staggering, at a lifetime cost per patient of $1.1−4.8 million [4]. Furthermore, care for SCI patients with complications is more costly than care for those without complications [5].

Pressure sores, pulmonary infection, urinary tract infection (UTI), and venous thromboembolism (VTE) are common complications after SCI and detrimental to patient health [1,6-8]. Pressure sores, defined as localized injuries to the skin and/or underlying tissue, can lead to serious infection and even death without effective management [9]. Pulmonary infection can be caused by impaired cough and secretion clearance due to dysfunction of the expiratory muscles after SCI [10], and it is a leading cause of death in these patients [1]. UTI can greatly affect the daily activities and social functioning of SCI patients without effective management [11,12]. The onset of VTE, consisting of deep vein thrombosis and pulmonary embolism, is insidious and extremely dangerous; this leads to high mortality in patients with SCI [13]. Therefore, the effective and standardized management of these common and detrimental complications is crucial for patients with SCI.

Clinical practice guidelines are developed to promote optimal care for specific health conditions based on available evidence [14]. Though clinical practice guidelines addressing the management of these common complications after SCI have already been published by several authoritative institutions, the quality of these guidelines and the degree of consistency among their recommendations remain unclear, which makes clinicians hard to select high-quality guidelines used to guide practice [15]. Additionally, the evidence that can be used to develop guidelines is constantly emerging, so a critical appraisal of existing relevant guidelines is beneficial to suggest an agenda for future work in complications after SCI [16].

Gerber et al. [17] performed a narrative review of the guidelines for SCI rehabilitation in 2021 without appraising their quality. Liang et al. [18] conducted a critical appraisal of the Paralyzed Veterans of America guidelines for SCI in 2021, but the researchers did not include all available guidelines developed by other authoritative organizations.

Therefore, the study conducting systematic reviews and appraising clinical practice guidelines focuses on the critical appraisal of guidelines on the management of four common complications (pressure sores, pulmonary infection, UTI, and VTE) after SCI. It summarizes relevant recommendations and assesses the quality of their supporting evidence.

Methods

Study design

The systematic review was conducted consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [19] and was registered on PROSPERO (CRD42022331931). The systematic review team consisted of two attendings, one epidemiologist, one guideline methodologist, four interns, and two medical students. All reviewers have experience for assessing and grading at least one guideline using the Appraisal of Guidelines for Research and Evaluation 2nd edition (AGREE II) instrument.

Search strategy

Considering that guidelines published too early may not be applicable to current clinical practice, we limited our retrieval time range to between January 2000 and January 2022 [20]. We searched Medline, Embase, Cochrane, and Web of Science using search strategies (Appendix 1) developed by an academic librarian. We also searched some online guideline databases (ie, National Institute for Health and Care Excellence, Scottish Intercollegiate Guidelines Network, Congress of Neurological Surgeons, National

Health and Medical Research Council Guideline Index, National Guideline Clearinghouse, and Canadian Medical Association Infobase) and Google Scholar (Appendix 2) to supplement our results. Our search results were restricted to English.

Guideline selection

After duplicates were removed, three reviewers independently reviewed the titles and abstracts of the search results to preliminarily exclude the documents that were not relevant to SCI or not guidelines. We then performed a pilot test by randomly selecting 5% of the remaining documents to increase consistency among the three reviewers before the formal review [21]. Discrepancies were resolved through discussion. If necessary, senior scientists were available.

Following a prior study published in the *Annals of Internal Medicine* [20], our inclusion criteria were that guidelines (1) be developed by a nationally recognized committee, a publicly funded institution, or a medical society that provided recommendations on SCI; (2) include a clear methodology section (eg, data source, search strategy, evidence review, and method of formulating recommendation), and (3) be the most updated version.

Quality assessment of guidelines

All included guidelines were independently appraised and scored by three raters using the AGREE II instrument (www.agreetrust.org). This consists of 23 items grouped into six domains: scope and purpose (concerning guidelines' overall aims, health questions, and target population), stakeholder involvement (focusing on the extent of participation by appropriate stakeholders in guideline development), rigor of development (relating to methods of gathering evidence and formulating recommendations), clarity of presentation (concerning guidelines' language, structures, and formats), applicability (pertaining to barriers, facilitative strategies, and resource implications of applying guidelines), and editorial independence (concerning conflicts of interest in guideline development) [22]. All items were scored from 1 (strongly disagree) to 7 (strongly agree) [22]; 1 indicated strong disagreement about the degree to which the item in the guidelines aligned with the criteria in the AGREE II instrument, and 7 indicated for strong agreement.

In accordance with the AGREE II instrument, the score for each domain was calculated as follows: (obtained score − minimum possible score) / (maximum possible score − minimum possible score) [22]. Because the AGREE II instrument does not set a minimum threshold for the score of each domain [22], we set 50% as the minimum threshold referring to a prior study [14]. Guidelines with 5−6 domains scoring greater than 50% were considered "recommended." Guidelines with 1−4 domains scoring greater than 50% were considered "recommended with modifications," and guidelines with no domain scoring greater than 50% were considered "not recommended."

A pilot test in which two included guidelines were randomly selected was performed to improve consistency among ratings in the following formal appraisal. We calculated the intraclass correlation coefficient (ICC) and its 95% confidence interval (CI) to measure agreement among the three raters. Agreement was considered poor when the ICC was 0.01−0.20, fair when it was 0.21−0.40, moderate when it was 0.41−0.60, substantial when it was 0.61−0.80, and good when it was 0.81−1.00 [20]. The median domain score and the interquartile range (IQR) were also calculated. We discussed the discrepancies and consulted senior scientists when necessary. Calculations were conducted using Microsoft Excel 2016 and IBM SPSS Statistics 25.0.

Recommendation extraction

One reviewer extracted recommendations on the management of pressure sores, pulmonary infection, UTI, and VTE along with supporting evidence from the included guidelines. Two reviewers verified the accuracy of their work. Recommendations were categorized as for, against, or neither for nor against (meaning that the guideline stated that there was insufficient evidence to make a clear recommendation) [14]. We considered inconsistencies to exist among recommendations when at least one guideline recommended for a certain measure and another recommended against it.

Quality of supporting evidence for recommendations

Considering that the topic of one prior study [14] was similar to ours, we adopted the evidence assessment system (Appendix 3) used by that study [23] to classify the quality of supporting evidence as poor, fair, or good to enhance uniformity [24,25].

Results

Selection of guidelines

As shown in flow diagram (Appendix 4), 12,017 documents were identified after duplicates were removed. After titles, abstracts, and full-text articles were reviewed, 11 guidelines [26−36] were included. They were developed by the Paralyzed Veterans of America [26−29], Congress of Neurological Surgeons [30], AOSpine [31], Société Internationale d'Urologie and International Consultation for Urologic Disease joint consultation [32], Australian Institute of Sport and Australian Paralympic Committee [33], French Society of Anesthesia and Intensive Care Medicine [34], and Chinese Association of Spine and Spinal Cord Injury [35]. A Japanese guideline [36] jointly developed by the Japanese Society of Spinal Cord Lesion, Japanese Continence Society, and Japanese Urological Association was also included. Four guidelines

[26,27,34,35], three guidelines [26,29,34], four guidelines [32,33,35,36], and five guidelines [26,28,30,31,35] made recommendations on pressure sores, pulmonary infection, UTI, and VTE, respectively. Appendix 5 provides an overview of some features of all included guidelines, which includes the guideline name, published time, development agency, method used in developing process, and the type of complications the recommendations on.

Quality assessment of guidelines

The quality of the included guidelines was appraised across the following domains: scope and purpose (range: 37.0%–93.3%, median: 56.3%, IQR: 52.4%–61.2%), stakeholder involvement (range: 31.1%–85.2%, median: 51.7%, IQR: 33.6%–56.4%), rigor of development (range: 11.9%–73.8%, median: 56.3%, IQR: 39.0%–64.6%), clarity of presentation (range: 73.7%–96.9%, median: 81.5%, IQR: 77.8%–85.5%), applicability (range: 2.2%–39.4%, median: 11.1%, IQR: 7.5%–20.4%), and editorial independence (range: 22.2%–100.0%, median: 55.6%, IQR: 38.9%–83.7%; Table 1). The ICCs ranged from 0.832 (95% CI: 0.697–0.918) to 0.947 (95% CI: 0.898–0.975), which indicated good agreement among the three raters. Though all guidelines met the minimum threshold in the domain of clarity of presentation, none of them reached it in the domain of applicability. Two guidelines [29,33], five guidelines [30,32,33,35,36], five guidelines [30,32,33,35,36], and three guidelines [26,27,29] failed to meet the 50% threshold in the domains of scope and purpose, stakeholder involvement, rigor of development, and editorial independence, respectively. Three guidelines [28,31,34] with 5–6 domains scoring more than 50% were considered "recommended." Eight guidelines [26,27,29,30,32,33,35,36] with 1–4 domains scoring more than 50% were considered "recommended with modifications." Consequently, we extracted relevant recommendations from all 11 guidelines.

Recommendation extraction

Summaries of recommendations are presented in Tables 2–5, and more details and their supporting evidence (randomized controlled trials [RCTs]) are listed in Appendix 6.

Pressure sores

Regarding prevention measures, four guidelines [26,27,34,35] (4/4, 100%) recommended for repositioning patients every 2–4 hours and conducting frequent skin inspections. Four guidelines [26,27,34,35] (4/4, 100%) recommended for the use of pressure reduction equipment such as air, gel, and water mattresses, whereas one guideline [27] (1/4, 25%) recommended against donut-type devices. Regarding treatment measures, two guidelines [27,35] (2/4, 50%) recommended for debridement, dressings, and surgery. Three guidelines [26,27,35] (3/4, 75%) recommended for the assessment and improvement of nutritional

Table 1
Appraisals of guidelines through AGREE II instrument

Guideline	Intraclass correlation coefficient (95% CI)	Scope and purpose (%)	Stakeholder involvement (%)	Rigor of development (%)	Clarity of presentation (%)	Applicability (%)	Editorial independence (%)	Overall rating
AOSpine (2017)	0.832 (0.697 ~ 0.918)	93.3	85.2	69.2	96.9	39.4	100.0	5.5
Congress of Neurological Surgeons (2013)	0.939 (0.882 ~ 0.971)	54.4	33.1	47.5	82.4	7.4	50.0	3.7
Paralyzed Veterans of America (2016)	0.866 (0.754 ~ 0.936)	62.6	58.7	59.7	85.2	21.8	80.6	4.5
Paralyzed Veterans of America (2014)	0.947 (0.898 ~ 0.975)	58.9	53.5	60.2	79.6	7.5	22.2	4.0
AIS and APC (2015)	0.869 (0.760 ~ 0.937)	45.2	33.0	11.9	77.8	2.8	55.6	2.8
JASCoL, JCS, and JUA (2020)	0.880 (0.778 ~ 0.943)	56.3	39.4	36.0	73.7	20.0	86.7	3.7
SIU-ICUD joint consultation (2018)	0.902 (0.815 ~ 0.953)	51.5	31.1	26.6	75.0	10.1	50.0	3.2
Paralyzed Veterans of America (2005)	0.870 (0.760 ~ 0.938)	37.0	61.7	68.9	77.8	2.2	27.8	4.0
Chinese Association of Spine and Spinal Cord Injury (2013)	0.872 (0.765 ~ 0.939)	53.3	34.1	41.9	81.5	11.1	77.8	3.7
Paralyzed Veterans of America (2008)	0.908 (0.826 ~ 0.956)	59.8	54.1	73.8	85.7	15.3	27.8	4.4
French Society of Anesthesia and Intensive Care Medicine (2020)	0.894 (0.802 ~ 0.950)	72.8	51.7	56.3	87.0	20.8	96.7	4.6

AGREE II, appraisal of guidelines for research and evaluation, 2nd edition; 95% CI, 95% confidence interval; AIS, Australian institute of sport; APC, Australian paralympic committee; JASCoL, Japanese society of spinal cord lesion; JCS, Japanese continence society; JUA, Japanese urological association; SIU, International society of urology in France; ICUD, International consultation for urologic disease.

The results of appraisals of all eleven guidelines through the AGREE II instrument are outlined in Table 1. This includes six domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence, and overall rating with intraclass correlation coefficient companied with 95% CI.

Table 2
Recommendations with supporting evidence on management of pressure sores after spinal cord injury from guidelines

Pressure sores				PVA, 2014 [27]	Zhang Z et al., 2013 [35]	PVA, 2008 [26]	Roquilly A et al., 2020 [34]
Prevention							
Skin inspections				+	+	+	+
Frequency	Daily			+			+
Turn or reposition patients				+	+	+	+
Frequency	Every 2 hours			+	+	+	
	Every 2-4 hours						+
Pressure reduction equipment							
Special mattress				+ +	+	+	+
Cushions				+		+	+
Pillows				+			+
Donut-type devices				-			
Mobilisation or exercise				+			+
Keep skin dry				+	+	+	
Avoid temperature increasing				+	+	+	
Education				+	+	+	
Nutrition							
Assess nutritional status				+	+	+	
Provide adequate nutritional intake				+	+		
Treatment							
Cleansing				+ +			
Debridement				+	+		
Dressings				+ +	+		
Electrical stimulation				+ +			
Adjunctive therapies				?	+		
Surgery				+	+		
Situation	Stage III/IV nonhealing			+	+		
Guideline Recommendations	+	+ +	+ + +	?	-	- -	- - -
	Recommended with poor evidence	Recommended with fair evidence	Recommended with good evidence	Recommended neither for nor against	Not Recommended with poor evidence	Not recommended with fair evidence	Not recommended with good evidence

Table 3
Recommendations with supporting evidence on management of pulmonary infection after spinal cord injury from guidelines

Pulmonary infection					PVA, 2005 [29]	PVA, 2008 [26]	Roquilly A et al., 2020 [34]
Prevention and treatment							
Monitor associated indicators					+	+	
Intubate the patients							
Situation	Obvious aspiration or high risk of it				+		
Deep breathing and voluntary coughing					+		
Assisted coughing					+	+	
Insuffilation-exsuffilation treatment					+	+	+
lPPB “stretch”					+		
Glossopharyngeal breathing					+		
Incentive spirometry					+		
Chest physiotherapy					+		+
Intrapulmonary percussive ventilation (IPV)					+		
CPAP and BiPAP					+		
Bronchoscopy					+		
Abdominal binders					+		+
Position	Supine				+		
	Trendelenburg				+		
Medications							
Bronchodilators					+		+
Antibiotics	Prevention				-		
	Treatment				+		
Vaccinations					+		
Mucolytics					?		
Hydrating agents					?		
Guideline Recommendations	+	+ +	+ + +	?	-	- -	- - -
	Recommended with poor evidence	Recommended with fair evidence	Recommended with good evidence	Recommended neither for nor against	Not Recommended with poor evidence	Not recommended with fair evidence	Not recommended with good evidence

IPPB, intermittent positive pressure breathing; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure.

Table 4
Recommendations with supporting evidence on management of Urinary Tract Infection (UTI) after spinal cord injury from guidelines

UTI				Compton S et al., 2015 [33]	Sekido N et al., 2020 [36]	Kreydin E et al., 2018 [32]	Zhang Z et al., 2013 [35]
Population	Athletes			+			
Asymptomatic bacteriuria	Routine dipstick testing			-			
	Treatment			-	-		
Diagnosis							
Urine testing	Microscopy, culture and sensitivity (m/c/s)			+			+
Treatment							
Antibiotics				+		+	+
Duration	7 -14 days					+	
Choice	Prescribed by m/c/s results			+			+
Special consideration							
Alkalizing the urine				+			
Decompression					+		
Drainage					+		
Prevention							
Cranberries				-			
Methenamine salts				-			
Acidification/alkalinisation agent				-			
Antibiotics							
Situation	Routinely			-			
	Athletes with recurrent UTI			+			
	Athletes choosing to dehydrate			+			
Education				+			
Guideline Recommendations	+	+ +	+ + +	?	-	- -	- - -
	Recommended with poor evidence	Recommended with fair evidence	Recommended with good evidence	Recommended neither for nor against	Not Recommended with poor evidence	Not recommended with fair evidence	Not recommended with good evidence

Table 5
Recommendations with supporting evidence on management of Vein Thromboembolism (VTE) after spinal cord Injury from guidelines

VTE			Fehings MG et al., 2017 [31]	Dhall SS et al., 2013 [30]	PVA, 2016 [28]	Zhang Z et al., 2013 [35]	PVA, 2008 [26]
Prophylaxis							
Timing	As soon as possible				+	+	+
	Within 72 h		+	+			
Duration	At least 8 weeks				+		
	3 months			+			
Low molecular weight heparin (LMWH)			+ +	+	+ +	+	+
Unfractionated heparin					①		
Dosage	Fixed, low-dose		+	- -	- -	-	
	Adjusted-dose		-		-		
Oral anticoagulants				-	-②		
Mechanical methods			?	+	+	+	+
Intermittent pneumatic compression					+	+	
Pneumatic compression stockings					+	+	
Plantar venous pumps						+	
Rotating beds				+			
Combined methods			?	+	++		+
Low dose heparin + pneumatic compression stockings				+			
Low dose heparin + electrical stimulation				+			
Unfractionated heparin + intermittent pneumatic compression							+
Vena cava filters							
Situation	Routinely			-	-		
	Special circumstances			+③			+④
Guideline Recommendations	+ Recommended with poor evidence	+ + Recommended with fair evidence	+ + + Recommended with good evidence	? Recommended neither for nor against	- Not Recommended with poor evidence	- - Not recommended with fair evidence	- - - Not recommended with good evidence

①, Recommended against in the prevention of VTE (unless LMWH is not available or contraindicated); ②, Recommended not to be used in the early, acute-care phase but to be considered during the rehabilitation phase following spinal cord injury; ③, Recommended for select patients who fail anticoagulation or who are not candidates for anticoagulation and/or mechanical devices; ④, Recommended in those patients with active bleeding anticipated to persist for more than 72 hours.

status. The quality of evidence ranged from poor (47/51) to fair (4/51).

Pulmonary infection

Regarding physical measures, three guidelines [26,29,34] (3/3, 100%) recommended for the use of mechanically assisted insufflation–exsufflation devices to clear secretions in the airway. Mechanically or manually assisted coughing was recommended for by two guidelines [26,29] (2/3, 66.7%), and the use of chest physiotherapy and abdominal binders were recommended for by another two guidelines [29,34] (2/3, 66.7%). Other physical measures, such as a supine or Trendelenburg position and bronchoscopy, were also recommended for by one guideline [29] (1/3, 33.3%). Regarding pharmacological measures, two guidelines [29,34] (2/3, 66.7%) recommended for medications such as bronchodilators and antibiotics. The quality of evidence for all recommendations was poor (26/26).

Urinary tract infection

Regarding treatment measures, three guidelines [32,33,35] (3/4, 75%) recommended for antibiotics. One guideline [33] (1/4, 25%) recommended for alkalizing the urine during acute UTI, and another guideline [36] (1/4, 25%) recommended for decompressing an obstructed urinary tract and draining infectious urine in certain cases. Regarding prevention measures, one guideline [33] (1/4, 25%) recommended against the use of routine antibiotic prophylaxis, cranberries, methenamine salts, and acidification or alkalinization agents. Two guidelines [33,36] (2/4, 50%) recommended against the treatment of asymptomatic bacteriuria, a special type of UTI. The quality of the relevant evidence was poor (22/22).

Venous thromboembolism

All guidelines recommended for prophylaxis as soon as possible [26,28,30,31,35] (5/5, 100%). This was specifically recommended within the first 72 hours after SCI by two guidelines [30,31] (2/5, 40%). All guidelines [26,28,30,31,35] (5/5, 100%) recommended for LMWH. For unfractionated heparin, two guidelines [28,31] (2/5, 40%) recommended against an adjusted dose, three [28,30,35] (3/5, 60%) recommended against a low dose, and one [31] (1/5, 20%) recommended for a low dose. Regarding mechanical measures, four guidelines [26,28,30,35] (4/5, 80%) recommended for intermittent pneumatic compression, pneumatic compression stockings, and rotating beds. Two guidelines [28,30] (2/5, 40%) recommended against the routine use of vena cava filters, whereas another two [26,30] (2/5, 40%) recommended for their routine use when LMWH or intermittent pneumatic compression were not suitable. The quality of evidence ranged from poor (35/40) to fair (5/40).

Discussion

The systematic review included 11 guidelines, all of which failed to reach the set minimum threshold in the domain of applicability according to the AGREE II instrument. This indicates that barriers, facilitative strategies, and resource implications of applying recommendations were not illustrated clearly in the included guidelines. In involved guidelines, there were 8 [27-33,36] guidelines with recommendations on only one complication and 3 [26,34,35] guidelines with recommendations on more than one complication. Considering that management of patients with complications after SCI is complex and involves care of multiple systems [1], we hope future guidelines can provide a comprehensive management for complications after SCI rather than single complication.

Though lacking high-quality RCTs, preventive measures for pressure sores after SCI such as inspection, repositioning, and the use of pressure reduction equipment were widely recommended for based on nonrandomized trials. This was also why the quality of the supporting evidence of relevant recommendations was considered poor. The nutritional status of patients was also concerned because improved nutrition status is beneficial to the healing of skin wounds [37]. Treatment measures such as cleansing, using dressings, and applying electrical stimulation were recommended for, with several supporting RCTs [38–48]. However, the study population of most RCTs was not limited to patients with SCI, so recommendations based on these should be treated with caution.

Only three guidelines [26,29,34] on pulmonary infection after SCI were included. Physical measures such as the use of mechanically assisted insufflation–exsufflation devices, assisted coughing, and chest physiotherapy as well as pharmacological measures such as bronchodilators were recommended for because they enable the removal of secretions from the airway, which is key to preventing and treating pulmonary infection.

The prevalence of asymptomatic bacteriuria in SCI patients was higher than in general populations [49]. Considering the risk of selecting antimicrobial resistance, two included guidelines [33,36] recommended against treatment for asymptomatic bacteriuria. This is consistent with the European Association of Urology guideline [50], an authoritative guideline in urology. Considering that the target population of the Australian statement [33] was SCI athletes, it recommended for the use of antibiotics for SCI athletes who chose to dehydrate to prevent UTI. Cranberries, methenamine salts, and other acidification or alkalinization agents were recommended against because their use was supported by inconsistent evidence. Appropriate bladder management, such as intermittent catheterization, could reduce the incidence of UTI [51], but this was not within the scope of our study. The main concern related to bladder management was neurogenic bladder, which is not a urinary complication; as such, we believe bladder management should be discussed separately.

For prophylaxis of VTE, there were inconsistencies existing among the recommendations on the direction of low-dose unfractionated heparin. One possible reason for the controversy is that the language restriction of included criteria for evidence varied across guidelines, and they treated evidence differently. One guideline [31] held that the anticipated desirable and undesirable effects for low-dose unfractionated heparin versus LMWH were closely balanced and uncertain according to two low-quality RCTs [52,53], one of which [53] was in German and suggested no statistically significant difference between unfractionated heparin and LMWH. Therefore, this guideline [31] recommended for low-dose unfractionated heparin. However, other guidelines that did not include the RCT in German recommended against it, considering its insignificant curative effect and risk of adverse effects. Supported by several RCTs [52,54-56], the guidelines universally recommended for LMWH. Mechanical methods were widely recommended for due to their high safety, and combined measures were also recommended for based on two small RCTs [54,57]. Guidelines recommended against routinely using vena cava filters due to the lack of high-quality evidence proving their effectiveness and cost-effectiveness.

It is expected that future guidelines will be improved in the applicability by describing facilitators and barriers to guidelines application, providing advice or tools on promoting recommendations to be applied, and considering the potential resource implications of applying the recommendations [58]. Additionally, we found the most common limitation existing in supporting RCTs was that the study population of many RCTs was not limited to SCI patients, which means the RCTs included both SCI patients and patients with other diseases, and because the data of SCI patients could not be extracted and analyzed separately, the results of these RCTs might suffer from bias. It is expected that more RCTs only including SCI patients are generated to perform more accurate assessment in the future. Other complications of SCI, such as, autonomic dysreflexia, cardiovascular complication, neuropathic pain, and depression, also deserve to be concerned, and we hope there are more relevant guidelines published and involved in the critical appraisal in the future.

This study had several strengths. We appraised the included guidelines using the AGREE II instrument, allowing readers to intuitively compare the guidelines' quality. Additionally, we presented recommendations and unified the level of their supporting evidence using an evidence assessment system [14,23]. Moreover, we only included guidelines whose target population is SCI patients instead of the general population, thereby improving the pertinence and accuracy of the study.

Limitations

We only included guidelines written in English, which might have led to the omission of some available guidelines. Another limitation was the fact that we set the minimal threshold at 50% to measure the quality of each domain when assessing the quality of included guidelines with the AGREE II instrument [22]. This may have led to an inaccurate overall quality assessment of included guidelines. Third, due to space restrictions, we only focused on four common complications after SCI: pressure sores, pulmonary infection, UTI, and VTE. Therefore, future studies are needed to focus on other complications.

Conclusion

For pressure sores, pulmonary infection, and UTI, poor- to fair-quality evidence indicated consistent recommendations on prevention and treatment measures. For VTE, LMWH was consistently recommended for, whereas the use of unfractionated heparin was controversial.

Declarations of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.spinee.2022.12.001.

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